ANNEXURE 'A'

Professional Teaching Experience Certificate for Fellowship / Certificate Courses
Director / Mentor

Title of the Course applied for: ONCO PATHOLOGY

This is to certify that Dr. Mrs. Rakhi Jagdale has worked in the Department of Pathology of Shri Siddhivinayak Ganapati Cancer Hospital Miraj Training Centre as per following details:

A) General Experience

Designation	From	To	Total period Year / Months	
Consultant Pathologist	1999	Till date	22	

B) Actual experience in the subject of concerned Fellowship / Certificate Course applied for:

Designation	From	To	Total period Year / Months	
Consultant Pathologist	2020-21	2021-22	2	

(It is mandatory to attach self-attested photocopy of the experience certificate of each Mentor in the Subject of concerned Fellowship / Certificate Course).

Sign & Stamp
Head of the Department

Date 5-7-22

Shri Siddhivinayak Ganpati Cancer Hospital MIRAJ

Sign & Stamp
Dean / Principal /Head of the Institute

Date 5-7-22

To Whomsoever This May Concern:

This is to certify that **Dr. Mrs. Rakhi Vikas Jagdale / Mirje,** MD. (Path) has been working in this hospital from January 2000 till today as a **Consultant & HOD Pathologist** in the Department of Pathology.

She is also a Mentor to the Fellowship Course in Onco Pathology from 2020-21.

Dr. S.D. Gosavi
Dean & Executive Director

Place: Miraj

Date: 16 June 2022

07/07/22

Shri Siddhivinayak Ganpati • Cancer Hospital • MIRAJ

ANNEXURE 'A'

Professional Teaching Experience Certificate for Fellowship / Certificate Courses
Director / Mentor

Title of the Course applied for: HEAD & NECK CANCER SURGERY

This is to certify that Dr. Priyadarshan V Chitale has worked in the Department of Surgical Oncology of Shri Siddhivinayak Ganapati Cancer Hospital Miraj Training Centre as per following details:

A) General Experience

Designation	From	To	Total period Year / Months	
Consultant Surgical Oncologist	December 2006	Till date	20	6

B) Actual experience in the subject of concerned Fellowship / Certificate Course applied for:

Designation	From	To	Total period Year / Months	
Consultant Surgical Oncologist	2016-17	2021-22	9	

(It is mandatory to attach self-attested photocopy of the experience certificate of each Mentor in the Subject of concerned Fellowship / Certificate Course).

Sign & Stamp
Head of the Department

Date 6/7/22

Sign & Stamp
Dean / Principal /Head of the Institute

Shri Siddhivinayak Ganpati Cancer Hospital MIRAJ

Date 6/7/22

To Whomsoever This May Concern:

This is to certify that **Dr. Priyadarshan Vivekanant Chitale,** MS. FMAS., has been working in this hospital from December 2006 till today as a **Consultant Surgical Oncologist** in the Department of Surgical Oncology.

He is also a Mentor to the Fellowship Course in Head & Neck Cancer Surgery from 2016-17.

Dr. S.D. Gosavi
Dean & Executive Director

Shri Siddhivinayak Ganpati Cancer Hospital MIRAJ

Place: Miraj
Date: 25 June 2022

ANNEXURE – "B"

(INSTITUTIONAL INFORMATION)

1. **Particulars of Director / Dean / Principal:** *(Who so ever is Head of Training Centre)*
Name:DR. SHISHIR DATTATRAY GOSAVI Age:63 (*Date of Birth*) 26-11-1959

PG Degree	Subject	Year	Institution	University
Recognized / Not Recognized	Ms (ENT)	1986	G.S. Medical College	Mumbai

Teaching Experience

Designation	Institution	From	To	Total Exp.
Asst. Professor	Sanjeevan Medical Foundation's ENT PGI	1992	1997	5 yrs
Asso. Professor/Reader	- do-	1997	2002	5 yrs
Professor	- do-	2002	2018	16 yrs
Any Other	Dean	2002	2021	Till date
			Gran d Total	29 yrs

2. Management/Society/Inst. Information:

01	i) **Name of the Society/Institution/ Training Centre /University Dept.:**	Sanjeevan Medical Foundation's Dr. D.K.Gosavi Memorial, Shri Siddhivinayak Ganapati Cancer Hospital.
	ii) Postal Address, with PIN:	Sangli – Miraj Road, Miraj 416410.
	iii) Contact Details:	Mob: 9373893801 Tele: 0233-2211601
02	**Society/Institution/ Training Centre Registration Number and date:**	i) Public Trust Act 1950: E 420 Sangli ii) Society's Registration Act.1860:..... .. .. iii) Year of establishment: 1997 iv) Copies of Registration, Constitution and Memorandum of Association attached? *Yes/No– Marked as Appendix 'A'
03	**Hospital Information :** ***(It is mandatory for Training Centre/applying Institute to have their own functional Hospital as per norms)*** i) Name of the Hospital ii) Nursing Home Registration No. iii) Establishment Year	Shri Siddhivinayak Ganapati Cancer Hospital. 178 / 06-04-2017 No.of Beds 100 1997 Mark as Appendix'B'
04	**i) Name of the Training Centre /Institute where course is to be conducted:**	Shri Siddhivinayak Ganapati Cancer Hospital.
	ii) Postal Address, withPIN: iii) Contact Details: iv) E-mail ID:	Sangli – Miraj Road, Miraj 416410. Mob: 7038093095 / 9730026292 Tele:0233-2211601 cancermiraj@gmail.com
	v) List of University approved **Fellowship**/Certificate Course(s) **conducted / already running** at Training Centre with Intake Capacity	**Name of the Course(s) Head & Neck Cancer Surgery and Onco Pathology** Approved Intake Capacity 3 and 1 respectively **Affiliated Since 2017 (if necessary Attach separate List)**
	vi) Training Centre / Institute **willing/desirous to Start/Open** Fellowship/Certificate Course(s) (For New Opening Purpose only)	**Name of the Course(s) ..... Required Required Intake Capacity ..... (if necessary Attach separate List)**
05	Affiliation Fees details: (Bank/DD no./ date/amount/ NEFT/RTGS)	Paid Fees details Attached: * Yes / No. (Pending Fees, if any ;)
06	Financial position of the Society/ Institute in the preceding 03 years:	Audited Statements of Accounts for *Yes / No– Mark as Appendix 'C'
07	Budgetary provision for the FC/CC/DC for the next 03 years	i) 20 . . . - . . Rs .....,
08	Management Resolution seeking Recognition of Institute for FC/CC/DC of MUHS, Nashik:	Resolution No. . . . . Dated . . . . . Copy of Management Resolution attached? *Yes/No– – Mark as Appendix 'D'

09	**Other Information:**	
	a) Land:	*Yes / No. If yes, then Area: 5391 sq.mtr.
	i) Whether the land is owned by the Applicant Institute/Training Centre/ Trust:	Copy of land documents i.e. 7/12 extract. (3076 sq.mtr land is on lease) Property Card, etc. attached? *~~Yes~~/No – Mark as Appendix 'E'
	ii) Whether the land is registered?	*Yes/No. If yes, Registration Number: . . . . . . Dated . . . . . At (Place): . . . . . . Copy of Land Registration Certificate attached? *Yes/No.– Mark as Appendix 'F'
	iii) Any loans, mortgage, etc. shown against the title of the land:	*Yes/No. If yes, amount of loan Rs. /mortgaged for Rs . . . . . . Copy of Loan/Mortgage Deed attached? *~~Yes~~/No. – Mark as Appendix 'G'
	b) Building: i) Total built-up area:	5804.11 sq. mtr. Certified copy of Building Plan attached? *~~Yes~~/No – Mark as Appendix 'H'

3. **Central Library**
   - Total number of Books in library: 361
   - Books pertaining to concerned Fellowship subject: 5
   - Purchase of latest editions of concerned books in last 3 years: - 25

1	Journals	Total	concerned Fellowship subject
2	Indian	2	1
3	Foreign	10	4

- Year / Month up to which latest Indian Journals available : 2016
- Year / Month up to which latest Foreign Journals available : _2016
- Internet / Med pub / Photocopy facility: **available** / not available
- Reading facility out of routine library hours: 10 am to 6 pm.

(Our hospital is recognized under National Cancer Grid Programme and we access the journals online)

(Obtain list of books & journals duly signed by Dean)

4. **Recreational facilities:** **Available / Not available**
   - Play grounds Gymnasium

5. **Hostel Accommodation:**

Particular	UG		PG		Interns	
	Boys	Girls	Boys	Girls	Boys	Girls
No. of Rooms No. of						
Students						
6. Status of Cleanliness						

7. **Ethical Committee (Constitution) :** **YES** / NO

8. **Medical Education Unit (Constitution) :** YES / NO

(Specify number of meetings held annually & minutes thereof)

9. **Any other faculty specific information required :**
(such as Herbal garden / PanchakarmaUnit/Pharmacy / Dental Chairs and Units/as per the requirement of concerned Course) Attach details)

MUHS FELLOWSHIP COURSES - BUDGETED EXPENSES

Year	Seats	Subject	Stipend / PM / Each	Total	
2022-23	2	Head & Neck Cancer Surgery	40,000	960000	
	1	Onco Pathology	40,000	480000	
		Continuation of affiliation		100000	
		Misc expenses (Trav + Late fees)		30000	1570000
2023-24	2	Head & Neck Cancer Surgery	40,000	960000	
	1	Onco Pathology	40,000	480000	
	2	Medical Oncology	40,000	960000	
	1	Onco Anesthesia & Cri Care	40,000	480000	
		Continuation of affiliation		200000	
		Misc expenses (Trav + Late fees)		30000	3110000
2024-25	2	Head & Neck Cancer Surgery	40,000	960000	
	1	Onco Pathology	40,000	480000	
	2	Medical Oncology	40,000	960000	
	1	Onco Anesthesia & Cri Care	40,000	480000	
		Continuation of affiliation		200000	
		Misc expenses (Trav + Late fees)		30000	3110000
					7790000

Shri Siddhivinayak Ganpati • Cancer Hospital • MIRAJ

NAME OF PUBLIC TRUST : SANJEEVAN MEDICAL FOUNDATION, MIRAJ.

BALANCE SHEET AS ON 31ST MARCH 2019

LAST YEAR	FUNDS AND LIABILITIES	AMOUNT RS.	LAST YEAR	PROPERTY AND ASSETS	AMOUNT RS.	AMOUNT RS.
13,75,83,275.81	TRUST FUND:	16,33,50,269.10	12,37,18,346.95	FIXED ASSETS :		20,62,40,357.6
			2,30,42,336.41	LAND AND BUILDING (HOSPITAL)	2,18,73,417.69	
52,41,353.22	LOANS:	6,52,55,142.12	-	CAPITAL WORK IN PROGRESS	8,86,26,178.00	
			9,42,02,646.26	MACHINERY & EQUIPMENTS	8,95,23,337.92	
5,52,49,061.73	CURRENT LIABILITIES AND PROVISIONS:	5,60,60,945.77	40,03,385.75	FURNITURE AND FIXTURE	16,29,742.69	
			18,13,664.10	ELECTRICAL FIXTURES AND FITTINGS	39,96,998.08	
			6,56,314.43	LIBRARY / MEDICAL BOOKS	5,90,683.29	
6,89,31,844.11	INCOME AND EXPENDITURE SURPLUS	5,32,52,970.62				
			5,64,07,112.69	INVESTMENTS AND DEPOSITS		6,14,97,271.1
			1,70,81,802.48	LOANS AND ADVANCES		14,22,077.0
			1,81,43,230.89	SUNDRY DEBTORS		2,40,70,654.2
			1,26,16,792.00	TDS RECEIVABLE PREVIOUS YEAR		1,46,05,246.0
			1,07,26,726.00	TDS RECEIVABLE CURRENT YEAR		47,87,195.0
			66,24,483.91	CLOSING STOCK		52,27,728.7
				CASH AND BANK BALACNES		
			2,10,29,386.82	CASH AT BANK		1,90,05,459.7
			5,61,942.63	CASH IN HAND		10,53,337.7
			75,710.00	INCOME RECEIVABLE		-
26,69,85,534.37		33,79,09,327.61	26,69,85,534.37			33,79,09,327.61

FOR SANJEEVAN MEDICAL FOUNDATION

MANAGING TRUSTEE

TRUSTEE

TRUSTEE

VT & ASSOCIATES
CHARTERED ACCOUNTANTS

AUDITORS

AKSHAY A. ZADBUKE
PARTNER
FRN 110017S M.No.145083

PLACE :SANGLI
DATE: 05.10.2019

THE BOMBAY PUBLIC TRUST ACT 1950

SCHEDULE VIII [Vide Rule 17(1)]

NAME OF PUBLIC TRUST : SANJEEVAN MEDICAL FOUNDATION, MIRAJ.

BALANCE SHEET AS ON 31ST MARCH 2020

LAST YEAR	FUNDS AND LIABILITIES	AMOUNT RS.	LAST YEAR	PROPERTY AND ASSETS	AMOUNT RS.	AMOUNT RS.
16,33,50,269.10	TRUST FUND:	16,70,86,915.48	20,62,40,357.87	FIXED ASSETS :		20,18,64,961.03
			2,18,73,417.09	LAND AND BUILDING (HOSPITAL)	3,36,77,209.90	
			8,86,26,178.00	CAPITAL WORK IN PROGRESS	34,800.00	
			8,95,23,337.92	MACHINERY & EQUIPMENTS	15,77,09,057.45	
6,52,55,142.12	LOANS:	5,52,54,612.68	16,29,742.89	FURNITURE AND FIXTURE	74,41,729.48	
			39,96,998.08	ELECTRICAL FIXTURES AND FITTINGS	25,70,549.54	
5,60,50,945.77	CURRENT LIABILITIES AND PROVISIONS:	4,90,00,369.77	5,90,683.29	LIBRARY / MEDICAL BOOKS	5,31,614.66	
5,32,52,970.62	INCOME AND EXPENDITURE SURPLUS	5,68,84,694.19				
			6,14,97,271.18	INVESTMENTS AND DEPOSITS		5,57,80,161.55
			14,22,077.00	LOANS AND ADVANCES		84,62,593.48
			2,40,70,654.29	SUNDRY DEBTORS		1,70,92,255.27
			1,46,05,246.00	TDS RECEIVABLE PREVIOUS YEAR		1,09,50,031.31
			47,87,195.00	TDS RECEIVABLE 2019-20		48,03,787.00
			-	TDS RECEIVABLE 2020-21		44,07,391.00
			52,27,728.79	CLOSING STOCK		70,98,608.98
				CASH AND BANK BALACNES		
			1,90,05,459.76	CASH AT BANK		1,73,42,186.08
			10,53,337.72	CASH IN HAND		4,34,616.42
33,79,09,327.61		32,82,36,592.12	33,79,09,327.61			32,82,36,592.12

FOR SANJEEVAN MEDICAL FOUNDATION

(DR.SHISHIR D GOSAVI) MANAGING TRUSTEE

(DR AMITA S GOSAVI) TRUSTEE

HRI ARVINDRAO G MARATHE) CHAIRMEN

PLACE :SANGLI

DATE: 26/1/20

V.T. & ASSOCIATES FRN 110017 S CHARTERED ACCOUNTANTS

VT & ASSOCIATES
CHARTERED ACCOUNTANTS
AKSHAY A. ZADBUKE
PARTNER
FRN 110017S M.No.145083

AUDITOR

THE BOMBAY PUBLIC TRUST ACT 1950

SCHEDULE VIII [Vide Rule 17(I)]

NAME OF PUBLIC TRUST : SANJEEVAN MEDICAL FOUNDATION, MIRAJ.

BALANCE SHEET AS ON 31ST MARCH 2021

YEAR	FUNDS AND LIABILITIES	AMOUNT RS.	LAST YEAR	PROPERTY AND ASSETS	AMOUNT RS.	AMOUNT RS.
70,96,915.48	TRUST FUND:	20,43,95,587.53	20,18,64,961.03	FIXED ASSETS :		18,02,00,577.72
			3,35,77,209.90	LAND AND BUILDING (HOSPITAL)	3,09,32,335.03	
			34,800.00	CAPITAL WORK IN PROGRESS	18,10,203.00	
			15,77,09,057.45	MACHINERY & EQUIPMENTS	13,79,56,363.19	
52,54,612.68	LOANS:	4,67,66,254.03	74,41,729.48	FURNITURE AND FIXTURE	23,13,821.61	
			25,70,549.54	ELECTRICAL FIXTURES AND FITTINGS	67,09,401.79	
90,00,369.77	CURRENT LIABILITIES AND PROVISIONS:	7,64,57,301.42	5,31,614.66	LIBRARY / MEDICAL BOOKS	4,78,453.10	
68,84,694.19	INCOME AND EXPENDITURE SURPLUS					
			5,57,80,161.55	INVESTMENTS AND DEPOSITS		9,40,19,614.03
			84,62,593.48	LOANS AND ADVANCES		15,85,595.81
			1,70,92,255.27	SUNDRY DEBTORS		3,67,40,520.52
			1,09,50,031.31	TDS RECEIVABLE PREVIOUS YEAR		-
			48,19,882.00	TDS RECEIVABLE 2019-20		
			43,91,296.00	TDS RECEIVABLE 2020-21		43,91,296.00
				TDS RECEIVABLE 2021-22		29,05,007.79
			70,98,608.98	CLOSING STOCK		49,92,232.28
				CASH AND BANK BALACNES		27,84,298.83
			1,73,42,186.08	CASH AT BANK	23,85,321.11	
			4,34,616.42	CASH IN HAND	3,98,977.72	
36,592.12		32,76,19,142.98	32,82,36,592.12			32,76,19,142.98

FOR SANJEEVAN MEDICAL FOUNDATION

(DR.SHISHIR D GOSAVI)
MANAGING TRUSTEE

(DR AMITA S GOSAVI)
TRUSTEE

(SHRI VIJAY M NAWANDHAR)
TRUSTEE

VT & ASSOCIATES
CHARTERED ACCOUNTANTS

AKSHAY A. ZADBUKE
PARTNER
M.No.145083
AUDITOR

VT & ASSOCIATES * CHARTERED ACCOUNTANTS * FRN 110017 S

PLACE :SANGLI
DATE: 25.11.2021

ANNEXURE – "C"

HOSPITAL INFORMATION

1. Name of the Hospital: SMF's DDKGM Shri Siddhivinayak Ganapati Cancer Hospital Miraj

Total number of OPD, IPD in the Institution and concerned department during the last one year:

In the entire hospital		In the department of concerned Fellowship subject	
OPD	4776	OPD	1000 approx.
IPD (Total No. of Patients admitted)	5846 (multiple admissions)	IPD (Total No. of Patients admitted)	1000 approx.(multiple admissions and cross ref)
		Onco Pathology	Total No. of biopsies and cytology - 4726

2. Hospital Beds Distribution & No of O.T.:

In the entire hospital	
No of Beds	100
No of Beds in ICU	5
No of Beds in IRCU	2
No of Beds in SICU	7
No of Major O.T.	4
No of Minor O.T.	1

3. Available Clinical Material: (Give the data only for the department of concerned Fellowship subject)

- No. of available for clinical service on inspection day:

	On Inspection day	Average of random 3 days
• Daily OPD – 2 PM		
• Daily admissions • Daily admissions in Dept.		22 10
• Through casualty at 10am • Bed occupancy in the Dept.		2 50
• Number of patients in ward (IPD)at 10AM		75
• Percentage bed occupancy at 10Am		68%

- Clinical Procedure(s) & Operative Details related to Fellowship subject/Specialty :

(For further details in this concern, kindly peruse the Guidelines information sheet supplied herewith)

	On Inspection day	Average of random 3 days
•	.....	.....
•	.....	.....2.....
•	.....	.....
•	.....	.....
•	.....	.....

4. Casualty:/ Emergency Department:

Space	
Number of Beds	
No. of cases (Average daily OPD and Admissions):	
Emergency Lab in Casualty (round the clock):	available / not available
Emergency OT and Dressing Room	
Staff (Medical/Paramedical)	
Equipment available	

5. Blood Bank:

(i)	Valid FDA License(copy of certificate be annexed)	Yes / No (in process)	
(ii)	Blood component facility available	Yes / No	
(iii)	All Blood Units tested for Hepatitis C,B, HIV	Yes / No	
(iv)	Nature of Blood Storage facilities (as per specifications)	Yes / No	
(v)	Number of Blood Units available on inspection day		
(vi)	Average blood units consumed daily and on inspection day in the entire Hospital. (give distribution in various specialties)	Average Daily 40	On Inspection day

6. Central Laboratory:

- Controlling Department: PATHOLOGY
- No of Staff : 15
- Equipment Available : Attach separate List
- Working Hours: 24 Hrs.

7. Central supply of Oxygen / Suction: **Available** / Not available

8. Central Sterilization Department **Available** / Not available

9. Ambulance (Functional) **Available** / Not available

10. Laundry: Manual/Mechanical/**Outsourced:**

11. Kitchen **Available** / Outsourced/ Not Available

12. Incinerator: Functional / Non functional **Capacity...../Outsourced**

13. Bio-Medical waste disposal **Outsourced** / any other method

14. Generator facility **Available** / Not available

15. Medical Record Section: **Computerized** / Non computerized

- ICD X classification Used / **Not used**

Sign & Stamp
Head of the Department
Date: Date:

Cancer Hospital • Shri Siddhivinayak Ganpati • MIRAJ

Training Centre Round Seal

Sign & Stamp
Dean/ Principal/ Director of Training Centre

ANNEXURE – "D"

DEPARTMENTAL INFORMATION

(If required Use Separate Sheet for each Department / Fellowship/Certificate Course)

1. **Fellowship Specialty Department to be inspected: 1) Head & Neck Cancer Surgery 2) Onco Pathology**

2. **Date on which independent department of: functioning concerned specialty was created and started**

3. **Mentor's details (From start of department till date) :**

Sr. No.	Name	Full Time/ Part Time	Designation	Qualification	Experience in Yrs. (after acquiring PG Qualification in concerned Subject)
1	Dr. P.V. Chitale	Full time	Consultant Surgical Oncologist	MS. FMAS	15
2	Dr. Rakhi Jagdale	Full time	Consultant Pathologist	MD. (Path)	23

4. **Whether Independent Department of concerned Fellowship subject exists in the Institution :**
   Yes/No: Yes Since when: 2016-17 and 2020-21

5. **Specialty Department Infrastructure Details :**

Facility	Area (sft.)	Available	Not Available
Faculty rooms	1500	√	
Clinics	1000	√	
Laboratory Space	1100	√	
Seminar room	1100	√	
Department Library	300	√	
PG common room	-		
Pre-clinical lab (where ever applicable)	-		
Patient waiting room	2000	√	
Total area	7000 approx.		

6. If course already started, year wise number of students admitted and available Mentors to teach students admitted to Fellowship / Certificate Course during the last 3 years:

Year	Name of the Course	No. of students admitted	No. of Valid Mentors available in the dept. (give names)
2017-18 till date	Head & Neck Cancer Surgery	5	Dr. P.V. Chitale, Dr. Vikas Gosavi, Dr. Vivek Kulkarni and Dr. Shriniketan Kale
2020-21 2021-22	Onco Pathology	2	Dr. Rakhi Jagdale, Dr. Sachin Patil, Dr. Abhijit Petkar

(Local Inquiry Committee shall specifically ensure about availability of eligible/validated Mentor(s) and shall check whether the Training Center met with the Student: Mentor Ratio for the permitted Intake Capacity for each course or else it shall be reported in the Overall Remark Option.)

7. **List of Non-teaching Staff in the department:** **Enclosed list**

Sr. No.	Name	Designation

8. **List of Equipment(s) in the department of concerned Fellowship subject:** Equipment's: List of Important equipment's available and their functional status (List here only- No annexure to be attached)

LIST OF EQUIPMENTS OT		
Sr. No	OT Equipments	QUANTITY
1	Anaethesia Machine G.E	1
2	Anaethesia Machine Drager	1
3	Space lab Anaethesia Machine	1
4	Anaethesia Machine Medisys	1
5	Cautery Machine	1
6	Cautery Machine	1
7	Cautery Machine	1
8	Harmonic Machine	1
9	OT 1 Lamp	2
10	OT 2 Lamp	2
11	OT 4 Lamp	2
12	Bipolar Cautery Machine	2
13	Central Suction Machne	4
14	Sony Moniter	1
15	Sony TV	1
16	Pridex (insufflater 30L)	1
17	Condenser Light Source250W	1
18	Maxer 2000 (Camera Source machine)	1
19	Olympus (Proceser) CVE	1
20	Olympus CLE-E	1
21	Fibrophic Scope	1
22	Colono Scope	1
23	Gastric Scope	1
24	Mirco Motar Machine	1
25	Endosol Light Source	3
26	Autoclave Machine (Modi)	1
27	Autoclave Machine (NAT)	1
28	Water Sterilizar Machine	1
29	Fumigation Machine	2
30	Refrigerator (Godrej)	1
31	AC OT No 1	2
32	AC OT No 2	3
33	AC OT No 3	1
34	AC OT No 4	2
35	Oasis Water Filter	1
36	Hot Line (Fluid Warmer)	1
37	fortable suction machine	2
38	ETCO machine drager G.E OT 1	1
39	ETCO machine Drager OT 2	1
40	ETCO machine Medisys OT 4	1

SIGN DR.VIKAS GOSAVI(MS)

HOD SURGICAL ONCOLOGY

Shri Siddhivinayak Ganpati Cancer Hospital
MIRAJ

INSTRUMENTS IN HISTOPATH DEPT. Updated Date: 07/07/2022

Sr.No	PARTICULARS	Make	M.Sr. No	Status	Q	Received Date
1	Water baths	Labtech Indian	Small	Working	1	2014
2.	Rotatory Microtome (new)	Shandon finesse	A78110100	Working	1	16/07/2013
3.	Olympus Binocular microscope with digital cameraCX41(U1S2)	Japan	CX41RF2	Working	1	07/09/2009
4	Cryotome Thermo 620E (freezing microtome)	Shandon		Working	1	30/12/09
5.	Electronic balance	Essae Indian	BS 852J	Working	1	14/07/2007
6.	Automatic tissue processor- Citadel 2000	Shandon UK	Cb1580 E 0507	Working	1	28/09/2005
7.	Incubator	Bio-tech Indian	04120	Working	1	25/05/2004
8.	Microwave –little chef (LG)	LG Indian	3850 W 3 W012B	Working	1	31/01/2004
9.	Computer with printers	Microtec Indian	JM2k1933	Working	2	02/01/1998 18/03/2005
10	Rotatory Microtome	Shandon UK	325- MT 10109702	Working	1	28/10/1997
11	Cytospin Eziprep Nanocyst mini autoslide processor	LBC	20010076	Working	1	18/05/2022
12	Binocular microscope	Olympus Japan	7H-029361	Working	1	02/10/1997
13	Binocular microscope with Photographic attachment	Olympus Japan	7H-02454,	Working	1	02/10/1997
14	Hot air oven	Modern Indian	2566	Repairing	1	01/09/1997
15	Videocon Refrigerator	Godrej Indian	Ultra	Working	1	24/03/2022
16	Centrifuge (Remi)	Pawar sci Indian	C854/6L FL 6104	Working	1	01/09/1997
17	Paraffin bath with tap	Pawar sci Indian	Sunbim	Working	1	01/09/1997
18	Leica CM1520 Freezing microtome	1	Leica	Working	1	22/03/2018
19	Biogenex i6000 (Automatic IHC stainer)	1	Biogenex	Yet to install	1	
20	Kelvinator Refrigerator	1	Kelvinator	Working	1	2018
21	Ez - Retrival system V3	1	Biogenex	Working	1	06/07/2022

Shri Siddhivinayak Ganpati MIRAJ

List of Non teaching Staff - Surgical Dept.			
1	DR. ARCHANA RAVINDRA DESHMUKH	SURGICAL OPD	DMO
2	DR. TUSHAR APPASAHEB KOTBAGI	SURGICAL OPD	DMO
3	DR. SUSHANT ARUN GAVANDI	SURGICAL OPD	DMO
4	DR.SUPRIYA SATISH SATHE	SURGICAL OPD	DMO
5	DR.AMOL LAXMAN MANDOLKAR	SURGICAL OPD	DMO
6	DR.SHIVANI ANANDA DEVMANE	SURGICAL OPD	DMO
7	DR. NISHITA BHOJARAJ DEVADIGA	SURGICAL OPD	DMO
8	DR. JYOTSNA JAYSING KOKATE	SURGICAL OPD	DMO
9	DR. PRANIT RAJENDRA SUNGARE	SURGICAL ONCO	DMO
10	DR. SAYALI SANJAY DEVKATE	SURGICAL ONCO	DMO

Shri Siddhivinayak Ganpati Cancer Hospital MIRAJ

LIST OF NON-TEACHING STAFF
HISTOPATH DEPARTMENT

Sr. No.	NAME	Designation
1	Mr. Nisar Nadaf	Technician
2	Mr. Uttam Pandhare	Technician
3	Mrs. Vaishnavi Kapduskar	Technician
4	Mr. Salim Nadaf	Technician

6.7.22

Shri Siddhivinayak Ganpati Cancer Hospital MIRAJ

9. **Intensive care Service provided by the Department: (Emergency)**

10. **Specialty clinics being run by the department and number of patients in each :**

Sr. No.	Name of the clinic	Days on which held	Timings	Average No. of cases attended	Name of Clinic In-charge

11. **Services provided by the Department:**

a) Services

i. _____

ii. _____

iii. _____

(b) Ancillary Services

(f) Others: _____

12. **Space:**

Sr. No	Details	In OPD	In IPD
1	Patient Examination/ Checking Arrangement	Available	Available
2	Equipment's	Available	Available
3	Teaching Space	Available	Available
4	Waiting area for patients	Available	Available

13. **Office space:**

Department Office		**Office Space for Teaching Faculty**	
Space (Adequate)	Yes/No	HOD	Available
Staff (Steno /Clerk).	Yes/No	Professors	
Computer/ Typewriter	Yes/No	Associate Professors	
Storage space for files	Yes/No	Assistant Profess or	
		Residents	

14. **Clinical Load of Dept.: No of Surgeries / Procedures Per day Avg 2**

15. **Submission of data to National Authorities if any : ——————**

ANNEXURE – "E"

Information of Director of Training Centre

It shall be verified by the Head of the concerned Training Center,

Sr. No.	Particular		Information to be filled
01.	Name of the Director	:	Dr Vikas Sadashiv Gosavi
02.	Date of Birth	:	14-03-1954
03.	Address	:	c/o Shri Siddhivinayak Ganapati Cancer Hospital, Miraj 416410.
04.	Tel. No./ Mob. No.	:	98231 44302
05.	E-mail id	:	cancermiraj@gmail.com
06.	Nationality	:	Indian
07.	Qualification in details : (attach documentary proof)	:	MS (Gen Surgery)
08.	Teaching Experience / Health Sciences: Profession Experience (Attached document proof with signature of Head of the Institute. Also it is mandatory to attach self-attested Photocopy of the Experience Certificate of each Mentor in the Subject of concerned Fellowship /CertificateCourse)	:	40 yrs
09.	Present Appointment	:	Medical Director
10.	Publications (List & Proof)	:	Encl
11.	Post Graduate Teaching experience (Attach documentary evidence)	:	16
12.	Any other relevant information	:	-

Date: -

Name & Sign. of Director

For the use of affiliated Training Center:

I have verified the eligibility of the above Director as per the criteria of eligibility prescribed by the University vide clause no.7 of the University Direction No. 05/2017(Amended).

Sign & Stamp
Head of the Department
Date: 5-7-22

Sign & Stamp
Dean/ Principal/ Director of Training Centre
Date: 5-7-22

Training Centre Round Seal

Shri Siddhivinayak Ganapati Cancer Hospital MIRAJ

ANNEXURE – "F"

Information of Mentor of Training Centre

It shall be verified by the Head of the concerned Training Center,

Sr. No.	Particular		Information to be filled
01.	Name of the Mentor	:	Dr. Priyadarshan Vivekanand Chitale
02.	Date of Birth	:	27-09-1973
03.	Address	:	c/o Shri Siddhivinayak Ganapati Cancer Hospital Miraj
04.	Tel. No./ Mob. No.	:	98500 57556
05.	e-mail id	:	Chitale007@gmail.com
06.	Nationality	:	Indian
07.	Qualification in details : (attach documentary proof)	:	MS. FMAS.
08.	Teaching Experience / Health Sciences: Profession Experience (Attached document proof with signature of Head of the Institute. Also it is mandatory to attach self-attested Photocopy of the Experience Certificate of each Mentor in the Subject of concerned Fellowship/Certificate Course)	:	20 yrs
09.	Present Appointment	:	Consultant Surgical Oncologist
10.	Publications (List & Proof)	:	Encl
11.	Post Graduate Teaching experience (Attach documentary evidence)	:	20 yrs
12.	Any other relevant information	:	

Date: - 5-7-22

Name & Sign. of Mentor

For the use of affiliated Training Center:

I have verified the eligibility of the above Mentor as per the criteria of eligibility prescribed by the University vide clause no.7 of the University Direction No. 05/2017 (Amended) and University Circular No. MUHS/UDC/FCCC/736/2019 dated 30/09/2019.

Sign & Stamp
Head of the Department
Date: 5-7-22

Sign & Stamp
Dean/ Principal/ Director of Training Centre
Date: 5-7-22

Training Centre Round Seal

Shri Siddhivinayak Ganpati Cancer Hospital MIRAJ

ANNEXURE – "G"

Information of Co-ordinator of Training Centre

It shall be verified by the Head of the concerned Training Center,

Sr. No.	Particular		Information to be filled
01.	Name of the Co-ordinator	:	Dr. Mrs. Ankita Rahul Gosavi
02.	Date of Birth	:	25-12-1988
03.	Address	:	c/o. Shri Siddhivinayak Ganapati Cancer Hospital Miraj
04.	Mob. No.	:	98691 46505
05.	E-mail id	:	cancermiraj@gmail.com
06.	Nationality	:	Indian
07.	Qualification in details : (attach documentary proof)	:	MBBS. MD. DNB. IDCC
08.	Present Appointment	:	Jt. Admn Director & Medical Supdt.
09.	Any other relevant information		-

Date:

Sign. of Co-ordinator

Sign & Stamp
Head of the Department
Date: 5-7-22

Sign & Stamp
Dean/ Principal/ Director of Training Centre
Date: 5-7-22

Training Centre Round Seal

Shri Siddhivinayak Ganpati Cancer Hospital • MIRAJ

ANNEXURE – "H"

DECLARATION

I, the Dean / Director/ Principal of the **SMF's DDKGM Shri Siddhivinayak Ganapati Cancer Hospital Miraj,** Training Centre / Institute solemnly states on affirmation that the information provided by me in Inspection Format as well as uploaded on Training Centre Website along-with all Annexure is true and correct to the best of my knowledge. The said information is provided to me by the concerned teachers and duly verified by me. It is further submitted the teacher's information attached in respective **Annexure-F &** are not working in / at any other Training Centre / Institute or presented themselves at any inspection for the Academic Year **2022-23** as per my knowledge and information provided by the concerned teachers. The teachers in the **Annexure- A &F** are staying in the same city / town / village where the Training Centre/ Institute is situated or adjacent to the city / town / village, where the Training Centre /Institute is situated and having the valid proof of residence of the said city / town / village. The teachers in the **Annexure-A & F** are not practicing in Training Centre working hours or out-side the City where the Training Centre /Institute is situated.

I am further hereby declare that every information or contents in this LIC Format is based on the information provided by the concerned teachers and endorsed by me after due verification and the same is/are absolutely true and correct. If at any stage it is revealed that any information or content given in this declaration is not true and correct, in such event the undersigned / the concerned teacher as the case may be, shall be liable for disciplinary action or penal action or Affiliation of the Training Centre shall be withdrawal, as the case may be.

This declaration is voluntarily signed by me on 4th Day of July 2022 At Miraj

Date: 4-7-2022

Place: Miraj

Shri Siddhivinayak Ganpati Cancer Hospital MIRAJ

Signature of Dean/Principal/Director
Name of the Signatory
(With Seal of the Training Centre)

SANGLI MIRAJ & KUPWAD CITY MUNICIPAL CORPORATION

FORM 'C'

(See Rule 5)

Certificate of Registration under section 5 of the Bombay Nursing Homes Registration Act 1949

No. 178

This is to Certify that Shri / Smt Executive Director Dr. D. K. Gosavi Memorial Shri Siddhivinayak Ganpati Cancer Hospital

has been registered under the Bombay Nursing Homes Registration Act. 1949 in respect of

" Dr. D. K. Gosavi Memorial Shri Siddhivinayak Ganpati Cancer Hospital "

(Here insert the name of the Nursing Home.)

Situated at Miraj and has been authorised to carry on the said nursing home.

No. of Bed's for Other Patient - 100 Bed's

No. of Bed's for Manternity Patient - 00 Bed's

Registration No. 178

Date of Registration 26/07/2007

Place Sangli-Miraj Road, Miraj

Date of issue of certificate 1/04/2021

This certificate of registration shall be valid upto 31st March 2024

MEDICAL OFFICER OF HEALTH, SANGLI MIRAJ & KUPWAD CITY MUNICIPAL CORPORATION (Here insert the name of Local Supervising Authority.)

Signature of the registering authority.

Medical Health Officer
Public Health
Sangli Miraj & Kupwad City
Corporation

सांगली मिरज आणि कुपवाड शहर महानगरपालिका

(सार्वजनिक आरोग्य विभाग)

जा.क्र.मनपा/आरोवि/राआअ/१०८७/२०२१ दिनांक:- १९ /०३/२०२१

परिपत्रक आदेश

प्रति,

डॉ. सिद्धी वीनायक गणपती कॅन्सर हॉस्पिटल.

विषय:- महाराष्ट्र शुश्रूषागृह नोंदणी नियमातील तरतुदीबाबत.

संदर्भ:- सार्वजनिक आरोग्य विभाग, महाराष्ट्र शासन क्र. शु.न.अ.-२०१८ /९७६/प्र.क्र.६०४/कु.क. दि. १४/०१/२०२१ रोजीची अधिसुचना.

सांगली मिरज आणि कुपवाड शहर महानगरपालिकेकडे तुमच्या हॉस्पिटलची बॉम्बे नर्सिंग होम रजिस्ट्रेशन ॲक्ट अंतर्गत नोंदणी आहे. सदर कायदयानूसार नोंदणी व नुतनीकरणासाठी शासन स्तरावर नविन नियमावली संदर्भीय अधिसुचनेद्वारे लागु करणेबाबत कळविले आहे. त्यानूसार महानगरपालिकेकडुन तुमच्या हॉस्पिटलची तपासणी करणेसाठी पथक आलेस वरील संदर्भीय पत्रामध्ये कळविलेनूसार सुविधा असणे आवश्यक आहे. सदर तपासणी दरम्यान त्रुटी आढळल्यास तुमच्या हॉस्पिटलकरीता महानगरपालिकेकडुन बॉम्बे नर्सिंग होम रजिस्ट्रेशन ॲक्ट अंतर्गत देण्यात आलेली नोंदणी रदद करुन पुढील कायदेशीर कारवाई करण्यात येईल याची नोंद घ्यावी.

(डॉ. सुनिल आंबोळे)
वैद्यकीय आरोग्य अधिकारी
सांगली मिरज कुपवाड महानगरपालिका

२० BNA-L

MUHS FELLOWSHIP COURSES - BUDGETED EXPENSES

Year	Seats	Subject	Stipend / PM / Each	Total	
2022-23	2	Head & Neck Cancer Surgery	40,000	960000	
	1	Onco Pathology	40,000	480000	
		Continuation of affiliation		100000	
		Misc expenses (Trav + Late fees)		30000	1570000
2023-24	2	Head & Neck Cancer Surgery	40,000	960000	
	1	Onco Pathology	40,000	480000	
	2	Medical Oncology	40,000	960000	
	1	Onco Anesthesia & Cri Care	40,000	480000	
		Continuation of affiliation		200000	
		Misc expenses (Trav + Late fees)		30000	3110000
2024-25	2	Head & Neck Cancer Surgery	40,000	960000	
	1	Onco Pathology	40,000	480000	
	2	Medical Oncology	40,000	960000	
	1	Onco Anesthesia & Cri Care	40,000	480000	
		Continuation of affiliation		200000	
		Misc expenses (Trav + Late fees)		30000	3110000
					7790000

SBI

Other Bank Transfer

INB Reference Number IRT6199213

Debit Transaction Status Processed

30-May-2022 [02:43 PM IST]

Debit Account Details

SBI Account No	Account Type	SBI Branch	Amount	Commission Amount	Transaction Type	UTR Number
00000010993476304	Savings Account	MIRAJ	INR1,14,000.00	INR0.00	NEFT	SBIN422150553250

Credit Account Details

Account No.	Bank	Branch	Transfer Type	Amount	Purpose
00641450000649	HDFC BANK	NASHIK - MAHARASHTRA	NEFT	1,14,000.00	CONT AFFI LATEFEE 22 23

गा. न. क्र. ७, ७ अ. १२

फॉर्म मिळणेचे ठिकाण - भारत जनरल स्टोअर्स, मिरज.

गांव मिरज तालुका मिरज (जिल्हा - सांगली)

भूमापन क्रमांक गट क्रमांक	हि. क्र.	धारण प्रकार	गा. नं. क्र. ७	खाते नं
८९२	२३५	(खि.ठा.शेती)	मालकांचे नांव 32266 935565 95565	
भूमापन क्रमांकाचे स्थानिक नांव	दे.हि.त.प्रो.३		मॅनेजिंग ट्रस्टी संजिवन मेडीकल फौंडेशन मिरज	
लागवडी योग्य क्षेत्र	एकर / हेक्टर / चौ.	गुंठे / आर / मी.		
जिरायत --	२३९५-००			कुळाचे नाव 96333 35595 खंड
बागायत --				
भातशेती --				
एकूण --	२३९५-००			
पो.				इतर अधिकार
वर्ग (अ) --				
वर्ग (ब) --				
एकूण --				
	रुपये	पैसे		
आकार --				
जुडी अथवा वि.आकार	२-०३			
पाण्याबाबत --				
एकूण --	२-०३			

गा. न. क्र. ७, अ | गा. न. क्र. १२

वर्ष	रीत	हंगाम	पिकांखालील क्षेत्र: मिश्र पिकांचे एकूण क्षेत्र - मिश्रपिकांचा संकेतांक	जलसिंचित	अजल सिंचित	मिश्र पिकांवरील प्रत्येक पिकांचे क्षेत्र - पिकांचे नांव	जलसिंचित	अजल सिंचित	अमिश्र पिकांचे क्षेत्र - पिकांचे नांव	जलसिंचित	अजल सिंचित	पडीक व पिकास निरुपयोगी अशा जमिनीचा तपशील - प्रकार	क्षेत्र	पाणी पुरवठ्याचे साधन	जमीन करणाऱ्याचे नांव	शेरा
2092-93										पड 2395-00					खुद्द	

डी. नॉन्दतर्मैंर होणोवर ... गो. प्रमाणे असे दि. १३।३।९३

तलाठी मिरज

फॉर्म मिळण्याचे ठिकाण - भारत जनरल स्टोअर्स, मिरज.

गा. न. क्र. ७, ७ अ. १२

गांव मिरज तालुका मिरज (जिल्हा - सांगली)

भूमापन क्रमांक गट क्रमांक	हि. क्र.	धारण प्रकार	गा. नं. क्र. ७	खाते नं
६९२	३		मालकांचे नांव (४६५५, १३४२५, ६५८९) (१६६२६, २००४४, २६९३८) ~~स्थानीक मिरज आणि कुपवाड~~ शहर महानगरपालिका	(१६१०९, १६३३३) (१६७०६, १६९०९, १६३४३)
भूमापन क्रमांकाचे स्थानिक नांव	दे. श. वर्ग ३			कुळाचे नाव खंड: ~~भारतीय~~ भा. ग्रामीण काटे. संजीवन मेडिकल फौंडेशन मिरज क्षेत्र ३००६ चौ.मी. ~~जाडेपट्टा काटे.~~ स्वरिव्यंपरा प्रतिष्ठान मिरज क्षेत्र ६२४ चौ.मी.

लागवडी योग्य क्षेत्र	हेक्टर	आर
जिरायत --		
बागायत --	०-४०	
भातशेती --		
एकूण --	०-४०	
पो.		
वर्ग (अ) --		
वर्ग (ब) --		
एकूण --		
	रुपये	पैसे
आकार --		
जुडी अथवा वि.आकार	३-६६	
पाण्याबाबत --		
एकूण --	३-६६	

इतर अधिकार: बिनशेती ३००६ चौ.मी.

गा. न. क्र. ७, अ / गा. न. क्र. १२

वर्ष	रीत	हंगाम	मिश्र पिकांचे एकूण क्षेत्र: मिश्र पिकांचा संकेतांक	जल सिंचित	अजल सिंचित	मिश्र पिकांवरील प्रत्येक पिकांचे क्षेत्र: पिकांचे नांव	जल सिंचित	अजल सिंचित	अमिश्र पिकांचे क्षेत्र: पिकांचे नांव	जल सिंचित	अजल सिंचित	पडीक व पिकास निरुपयोगी अशा जमिनीचा तपशील: प्रकार	क्षेत्र	जमिनीच्या कसवणुकीचे साधन	जमीन करणाराचे नांव	शेरा
२०१२/१३											पड				स्वतः	

पीक पाहणी केली दि. १३/३/१३

कॉम्प्लेक्स होस्पिटल

तलाठी मिरज

Gram : SWASTHYA
Telex : 011 85025 BH IN

Phone : 2206 76 76
Fax : 022-2208 08 71

BOMBAY HOSPITAL

12, New Marine Lines,
MUMBAI - 400 020.

Ref. _____

EXP:BH:MS:317:2004

12/08/2004

This is to certify that Dr. Priyadarshan V Chitale, MS (General Surgery) has worked in the following capacities in this institution:

Designation	Department	Unit	From	To
SR RESIDENT OFFICER	CANCER SURGERY	DR J J VYAS M.S. DR G T HEDGE MBBS,M.S,(BOM)	01/08/2002	31/07/2003

During the above period his/her work and conduct were satisfactory and attendance regular.

Bombay Hospital is a recognised Postgraduate teaching Hospital by Bombay University and M.C.I.

There are together 830 beds in Bombay Hospital & Medical Research Centre of Bombay Hospital.

There are 22 Operation Theatres. Facilities exist for treating patients in various Departments viz General Surgery, Thoracic Surgery, Obstetric & Gynaecology, Cardiovascular Surgery, Neuro Surgery, Orthopaedics, Plastic Surgery, General Medicine, Cardiology, Neurology, Psychiatry, Artificial Kidney(Dialysis), Intensive Coronary Care Unit, Intensive Care Unit, (Adults) Endocrinology, Skin, E.N.T., Ophthalmology, Dental, Oncology, Urology, Nuclear Medicine & Ultrasonic Department & Nerve Muscle Research Wing, C.T. Scan, Therapeutic Drug Monitoring Department, Urodynamic Laboratory & Neonatology including Intensive Care Unit (Newly Born).

The Bombay Hospital has a well-equipped Central Laboratory, Blood Bank & X-ray Department (Diagnostic & Therapeutic including Cobalt therapy), Physiotherapy Department, Emergency Department & an Out-patient Department, Retina Clinic & Dental Speciality Section & Endoscopic Department.

MEDICAL SUPERINTENDENT
BOMBAY HOSPITAL
Dr. Rajkumar V. Patil
Medical Superintendent,
Bombay Hospital & Medical Research Centre
12, Marine Lines, Mumbai - 20

Official Publication of the Indian Association for the Study of Sexually Transmitted
Indian Journal of Sexually Transmitted Diseases and AIDS
Home
Current issue
Instructions
Submit article

Indian J Sex Transm Dis. 2015 Jul-Dec; 36(2): 195–197.
doi: 10.4103/0253-7184.167175
PMCID: PMC4660565

Thyroid cancer in a long-term nonprogressor HIV-1 infection

Uday A. Phatak, P. V. Chitale,[1] and Rakhi V. Jagdale[2]

Department of Medical Oncology, Medical Oncology Unit II, Shri Siddhivinayak Ganapati Cancer Hospital, Miraj, Sangli, Maharashtra, India
[1]Department of Surgical Oncology, Shri Siddhivinayak Ganapati Cancer Hospital, Miraj, Sangli, Maharashtra, India
[2]Department of Oncopathology, Shri Siddhivinayak Ganapati Cancer Hospital, Miraj, Sangli, Maharashtra, India
Address for correspondence: Dr. Uday A. Phatak, Consultant Physician, Medical Oncology Unit II, Shri Siddhivinayak Ganapati Cancer Hospital, Miraj - 416 410, Sangli, MH, India. E-mail: uday.phatak@gmail.com

Abstract

Go to:

Long-term non-progressor HIV infection (LTNP-HIV) is seen in <1 percent of HIV-afflicted population. There are definite criteria for the diagnosis of LTNP-HIV. Malignancies either solid tumors or haematological cancers have not been reported in such population. We report here a rare case of follicular thyroid carcinoma in LTNP-HIV infection. She never had any opportunistic infections. She did not receive anti-retroviral therapy in the entire course of illness and continued to have good quality of life. Treatment of follicular thyroid cancer was similar to other patients without HIV infection. This could be the first case study from India.

Keywords: Follicular thyroid cancer, HIV-1, long-term nonprogressor HIV infection

INTRODUCTION

Go to:

Long-term nonprogressor HIV infection (LTNP-HIV) is seen in <1% HIV positive population. Natural history of this subset of patients is entirely different.[1] So far, there are no studies on cancers in LTNP-HIV patients in the literature. We report here a very rare case of follicular thyroid carcinoma in LTNP-HIV infection. This could be the first case report from India.

CASE REPORT

Go to:

A 30-year-old female, doctor by profession, presented with midline painless swelling in the neck for 3 months. It was slowly progressive but did not cause any pressure effects on nearby structures. She was having HIV-1 infection for last 10 years. She never had fever, weight loss, or any opportunistic infections due to HIV-1 infection. Details of investigations done 10 years ago such as HIV-1 viral load and CD4 and CD8 counts are not available at present. She was never treated with prophylactic drug treatment for opportunistic infections or with antiretroviral therapy during this period. She never suffered from thyroid illness before. None of her family members had history of thyroid dysfunction.

Clinical examination revealed a solitary nodule of 4 cm in the left lobe of thyroid. Cervical lymphadenopathy was not found. Ultrasonic study of thyroid gland showed an isoechoic solid nodule. Fine-needle aspiration cytology reported as a cellular follicular lesion. Thyroid function tests were normal. She underwent left hemithyroidectomy. Histopathological gross evaluation of left hemithyroidectomy specimen measuring 6.3 × 6.3 × 3.0 cm showed a well-circumscribed homogenous, nodular brownish mass measuring 4.5 × 3.5 × 2.8 cm. Adjacent nonneoplastic thyroid was nodular grey-white. Microscopy revealed a widely invasive, follicular carcinoma demonstrating prominent capsular and vascular invasion with tumor plug completely transregressing the fibrous capsule and present within a blood vessel covered by endothelium. No extra-thyroid extension was seen. Adjacent thyroid parenchyma shows lymphocytic thyroiditis [Figure 1]. There was no spread to other

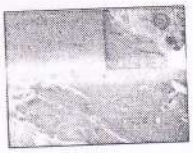

Figure 1
Widely invasive follicular carcinoma of thyroid. Arrow shows capsular invasion. Inset shows adjacent Hashimoto's thyroiditis

Completion thyroidectomy was performed. Histopathological evaluation of completion thyroidectomy specimen showed Hashimoto's thyroiditis. Eleven adjacent lymph nodes were free of tumor. After 4 weeks, she underwent radioactive-Iodine whole body scan that demonstrated residual disease in the neck. Radioiodine ablation of the disease was done. She was treated with levothyroxine 100 μg daily for hypothyroidism after radioiodine treatment and calcium carbonate 1 Gm 3 times a day along with weekly cholecalciferol 60,000 IU for immediately for postoperative hypoparathyroidism. Her CD4 and CD8 counts were 756 cells/mm ^{3} and 819 cells/mm ^{3} , respectively and the viral load was 136 copies/ml. Diagnosis of LTNP-HIV infection was considered as per the current criteria of LTNP-HIV.

Go to:

DISCUSSION

HIV-1 infection is common viral infection in India. There are subsets of HIV-1 infection in which the viral load is not very high, T cell subpopulations (helper/suppressor) cells are slightly reduced and patients can survive more than 8 years in the absence of antiretroviral therapy for HIV-1 infection. This subset is seen in only <1% of HIV-positive population. We considered LTNP-HIV infection rather than élite controller as the viral load was more than 100 HIV-RNA copies/ml and helper T cell count was stable over the past 10 years, in the absence of antiretroviral therapy in this case study. The diagnostic criteria of LTNP-HIV include: (i) Helper cell population (CD4 cells) more than 500 cells/mm ^{3} (ii) viral load <1000 copies/ml (iii) stable disease over a period of 8 years without antiretroviral therapy for HIV infection. Prevalence of LTNP is <1% of HIV-positive patients in clinical practice.[1] Most of the patients are asymptomatic.

Incidence of cancers either AIDS-defining cancers (ADCs) or non-AIDS-defining cancers (NADCs) in LTNP-HIV infection has not been reported earlier. Prevalence of cervical lesions in LTNP-HIV patients was studied in Africa.[2] Thyroid involvement in HIV-positive patients may have variety of causes. It may be involved due to infections or there could be drug-related thyroid dysfunction in HIV infection,[3] but primary malignancy of thyroid in LTNP-HIV-1 patients is not known. Etiology of the NADCs and ADCs is not well understood. Most of the patients with AIDS-associated cancers have viral etiology. Human papillomavirus is responsible for oral and cervical cancers, Epstein-Barr virus is related to non-Hodgkin's lymphoma (NHL) and human herpes virus 8 for Kaposi's sarcoma (KS). No such viral etiology is attributed in the pathogenesis of thyroid malignancy.[4]

HIV/AIDS-related cancers, either AIDS-defining malignancies (ADMs) or non-ADMs (NADMs) are often seen in HIV infection with advanced stage. With highly active antiretroviral therapy, the prevalence of KS and NHL has declined significantly. Thyroid cancers in HIV/AIDS are an uncommon and unusual type of NADM. [5] Mbulaiteye *et al* reported rising incidence of cancers of thyroid, kidney, and uterus and of conjunctiva in HIV/AIDS in Africa.[6] Whether genetic factor(s) play any role in the pathogenesis of thyroid cancers in HIV-positive patients is not clear.[4] Papillary thyroid carcinoma[7] and medullary thyroid carcinoma[8] were reported in advanced HIV positive patients. They were receiving antiretroviral therapy for HIV infection unlike our patient.

Pathogenesis of LTNP-HIV infection is a mystery. Viral, genetic and host-related factors have been postulated in the development of LTNP-HIV infection. Patients with HIV-1 infection progress if they have abnormalities of nef gene or have high level of beta-2-microglobulin. While some genes protect against the progression.[1] CCR5 is a co-receptor for transmission of HIV-1 infection. Mutation of CCR5 gene is the most common abnormality in LTNP-HIV. Such mutation can be seen in Indian families as well.[9] Usually, individuals with homozygous delta 32 allele are resistant to HIV infection in spite of multiple exposures to HIV-infected persons while those with heterozygous delta 32 mutation have lesser viral replication and slower progression of HIV infection.[10] We have not evaluated our patient for molecular markers. Until date, patient has got good quality life following total thyroidectomy. How long will she remain LTNP-HIV or will she progress in future is not known.

Nil.

Conflicts of interest

There are no conflicts of interest.

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Laparoscropic Surgery

Laparoscopic Surgery for Malignancy

PJ Shukla*, PV Chitale*, CS Ravichand*

Introduction and Background

Since the first report of laparoscopic cholecystectomy by Mouret in 1987 there is an upsurge of laparoscopic procedures for benign diseases such as laparoscopic cholecystectomy, Nissen's fundoplication, inguinal hernia repair and appendicectomy.1 The initial successful and wide spread application of laparoscopic technique in benign diseases resulted in maturity of surgical skill and confidence in laparoscopy among the surgeons. This subsequently made surgeons apply laparoscopic technique for resection of malignant diseases.

Technological advances took rapid strides in last 20 years. With refinement in instrumentation and availability of newer energy sources laparoscopic resections in malignancy have become more successful and with fewer complications.

The main advantage of laparoscopic surgery over an open procedure is that it requires smaller incision, which translates into less pain, less pain medication, better cosmesis, earlier ambulation and quicker recovery.

Role of Laparoscopy in Malignancy

Laparoscopy is used in cases of malignancy as - diagnostic and staging procedure, therapeutic procedure, palliative procedure.

Laparoscopy is used either as
1) complete laparoscopy or as
2) hand assisted laparoscopy

Laparoscopy in Diagnosis and Staging of Malignancy

Despite the advances in imaging technology, conventional imaging techniques have been found to be inadequate in diagnosing and staging the disease in oncology.

Most important benefit of laparoscopy is to diagnose advanced disease without subjecting the patient to major exploration, associated pain and longer hospitalization. A non-therapeutic laparotomy adds cost, creates patient discomfort and delays alternative therapy till healing occurs. This is especially true in cases of peritoneal carcinomatosis which is easily missed on imaging. Ability of laparoscope of viewing deep and intricate structures, facility of laparoscopic biopsy and laparoscopic aided imaging (as laparoscopic ultrasound, doppler) is helpful in diagnosis and staging of retroperitoneal adenopathy, pancreatic tumours, adnexal masses, mesenteric tumours and the occult diseases in abdomen.

Ca Esophagus

Presence of distant nodal metastases and carcinomatosis contradicates the oesophageal resection. Non invasive imaging is found to overstage the disease in considerable proportion of patients, bereaving them of the curative resection. Thoraco-laparoscopy offers facility of accurate staging of lymph nodal disease by lymph node biopsy.

Gastric Cancer

The dismal prognosis associated with gastric cancer makes it essential to select the early cases in which a curative resection can be offered. Laparoscopy aids in the staging of gastric cancer by detecting peritoneal

nodules, gastric serosal infiltration, adherence to adjacent structures, presence of lymph node metastases, presence of liver metastases, ascites and cytological evaluation of peritoneal washings.2 The laparoscopic staging accuracy in gastric cancer is about 90% and laparoscopy has been found to predict resectability in 87% of cases.

Hepato-Biliary and Pancreatic Tumours

Laparoscopic staging of liver tumours (primary and secondary) has low yield as compared to imaging. But Laparoscopic ultrasound (LUS) may prove to be helpful in deciding resectability of hepatic tumours.3 Laparoscopy is most accurate for identifying peritoneal disease and additional hepatic disease thereby preventing non therapeutic laparotomies. However, metastatic lesions below the capsule of liver and tumour invasion of the retroperitoneum and portal vein are the main considerations when determining local resectability. Laparoscopy combined with LUS is more specific in defining local resectability of pancreatic tumour.4

Laparoscopy in Treatment of Malignancy

Cancer surgery poses some unique challenges for the application of laparoscopy in oncology – a) relationship of a tumour to the tissues that surround it is critically important in cancer staging, specimens or whole organs should be removed intact (en bloc) so that the pathologists can properly examine them and measure and document the depths and margins of tumour invasion and resection, b) lack of evidence of improving outcomes of resections such as decreased hospital stay, decreased pain, early recovery, decreased costs, and earlier returns to work and c) any negative impact on survival e.g. induction of carcinomatosis, port site recurrences.

Oesophageal Cancer

During standard oesophageal resections, mobilization of oesophagus with mediastinal dissection is done thoracoscopically and gastric mobilization and resection is done laparoscopically. Avoidance of thoracotomy is thought to result in less pain and reduced respiratory complications

Gastric Cancer

Minimally invasive procedures include gastrectomy via laparoscopy and hand-assisted resections. Laparoscopic D1 gastrectomy seems ideal for early gastric cancer. A total D2 gastrectomy is advisable for middle- third and upper third lesions, but distal gastrectomy is sufficient for antral lesions.

Laparoscopic gastric resections are – a) Laparoscopic partial or total gastrectomy with internal reconstruction of upper GI tract b) Assisted laparoscopic partial or total gastrectomy – reconstruction is through minilaparotomy.

Pancreatic and Hepatobiliary Cancer

Pancreaticoduodenectomy, distal pancreate-ctomies, and liver resections are reported to be done laparoscopically. For liver malignancies, laparoscopic radiofrequency ablation and cryoablation under laparoscopic ultrasound guidance allow detection and treatment of small metastases.

Colorectal Cancer

All types of colonic and colorectal resection as anterior resection, abdominoperineal resection and total mesorectal excision are done laparoscopically. The laparoscopic procedure does not deviate from the steps of the traditional radical excision as it also includes high ligation of the vessels, adequate length of the distal margin from tumour, adequate lymphadenectomy and mesorectal excision. The resection margins and lymph node yield is not lower in laparoscopic procedure.5 The results of clinical outcome of surgical therapy (COST) trial suggest that laparoscopically assisted colectomies are equivalent to open colectomies in terms of recurrence and overall survival and have advantage of faster perioperative recovery.6

Laparoscopy in Palliation of Malignancy

Palliative procedures which are done laparoscopically are Gastro-Jejunostomy, Intestinal Bypass, Colostomy, Ileostomy, Feeding Jejunostomy / Gastrostomy.

Complications

Case selection is most important to reduce number of complications and conversion rate.

Injury to Adjacent Structures

In cancer patient infiltration of important structures by tumours makes such structures more susceptible for injury.

Port Site Herniation
Despite poor nutritional status and hypoalbuminaemia, the postoperative herniation through trocar site is not frequent in cancer patients. Closure of fascia at port site when it is of size more than 0.5 cm ensures this.

Complications related to the Learning curve
Laparoscopy is more than a new technique; it is a completely different way of operating. The visualization is different, the instruments are different, and the tactile aspects are very different. Intracorporeal suturing, for example, is a skill that requires a great deal of practice.

Port Site Recurrence
Port site metastasis (PSM) is recurrence of tumour at small wounds created for placement of ports during laparoscopy. The initial reported incidence of such recurrence ranged from 0 to 21%. Improved understanding of the mechanism of port site recurrences has prompted the surgeons to take appropriate precautions as e.g. use of plastic retrieval bag and use of non-touch technique during delivery of the specimen. This has reduced the incidence of port site recurrences to as low as less than 1%.

Conclusion
Over the past two decades laparoscopy has emerged as a valuable tool in the diagnosis and management of malignancy. The evolution of technology at hectic pace continues to confound the surgeon as we peruse the literature. There is no doubt that technological feasibility of executing major oncological procedures by laparoscopy has been established. Although long term oncologic safety is yet to be established in all laparoscopic procedures, short term outcomes are favourable and the issue of 'port site' recurrence seems to be waning.

Possible causes of tumour cell dissemination in laparoscopic surgery for cancer

Possible Cause	Intervention to Potentially Minimize This Cause
Aerosolization of cancer cells by sudden loss of pneumoperitoneum "Chimney Effect"	Controlled release of pneumoperitoneum
Tumour spillage from manipulation and instrumentation	Avoid excessive manipulation of tumour; limiting the instruments inserted
Tumour spillage at extraction site	Use protected tumour extraction (plastic bag) No touch technique
Immunosuppressive effect of pneumoperitoneum	Irrigate the abdomen with tumoricidal solution

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*GI Surgical Services, Department of Surgical Oncology, Tata Memorial Hospital, Mumbai.

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JEHANGIR HOSPITAL & MEDICAL CENTRE

32, SASSOON ROAD, PUNE - 411 001
TEL : 6122551, 6050550. FAX : 6050866
E-mail : jehangirhospital@vsnl.com

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We wish him all the best in his future endeavors.

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JEHANGIR HOSPITAL & MEDICAL CENTRE
32 SASSOON ROAD PUNE - 411 001
TEL [illegible] FAX : 6050866
E mail jehangirhospital@vsnl.com

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This is to certify that

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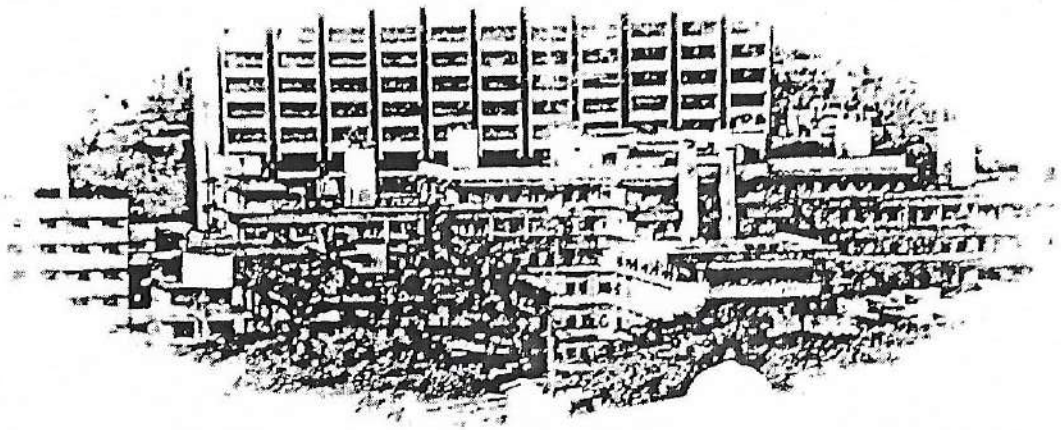

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(K. DINSHAW)
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Dr. Priyadarshan V. Chitale
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E-mail : medimail@tmc.ernet.in
Website : www.tatamemorialcentre.com

Dr. Ernest Borges Mar
Mumbai - 400 01
Phone : 022-24
Fax : 022-24

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टाटा स्मारक अस्पताल
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(K. SUBRAMANIAN)
H.R.D. OFFICER

Dr. Priyadarshan V. Chitale,
C/o Dr. S.M. Paranjape,
2 Jagannath M.V. Pandaloskar Marg,
Off Subhash Road,
Vile Parle (East), Mumbai

डॉ. ई. बोर्जेस मार्ग, परेल,
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E-mail : medimail@tmc.emet.in
Website : www.tatamemorialcentre.com

Dr. Ernest Borges Marg, Parel,
Mumbai - 400 012, India.
Phone : 022-2417 7000
Fax : 022-2414 6937

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certify [ ] that the withinsigned

Rakhee Ramesh Mirje

of the Govt. Medical College

having been examined for the Degree of Bachelor of Medicine and Bachelor of Surgery, and on being found qualified for the same, in October 1993

the Degree of

Bachelor of Medicine & Bachelor of Surgery

has been conferred on her at Kolhapur, on the twentyfirst day of the month of January in the year two thousand.

In Testimony whereof are set the Seal of the University and the Signatures of the Registrar and the Vice-Chancellor.

Ag Registrar

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Vice-Chancellor.

WE the **Chancellor, Vice-Chancellor** and **Members** *of the* **Management Council,** *on the recommendation of the* **Academic Council** *of the* **Shivaji University,**

certify that the withinsigned

Rakhee Ramesh Mirje

having been examined for the Degree of Doctor of Medicine (Pathology Branch), and on being found qualified for the same, in October 1997,

the Degree of

Doctor of Medicine

has been conferred on her at **Kolhapur,** *on the twentyfirst day of the month of January in the year two thousand.*

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शासकीय वैद्यकीय महाविद्यालय, मिरज.
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(Residence) : 2231799 Extn. 300

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MHC Class I Related Antigen A and B and NKG2D Receptor Expression in PAP smear: A Newer Paradigm of Diagnoses in Cervical Cancer

Jivita R Kshirsagar[1], Poonam A Bedge[1], Shashikant R Desai[2], Rakhi Mirje[3], Raghvendra A Bohara[1] and Meghnad G Joshi[1]*

[1]*Department of Stem Cells & Regenerative Medicine, D. Y. Patil University, D. Y. Patil Vidyanagar, Kasba Bawda, Kolhapur 416006, MS, India.*

[2]*Stem Plus Biotech, C/S No. 1317/2, near Shivaji Maharaj Putala, Gaonbhag, Sangli-416416, MS, India.*

[3]*Department of Pathology, Shri Siddhiviyak Ganpati cancer Hospital, Miraj, Sangli, MS, India*

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***Correspondence Address:** Meghnad G Joshi, Associate Professor and Head of the Department, Department of Stem Cells and Regenerative Medicine, DY Patil University, DY Patil Vidyanagar, Kasaba Bawda, Kolhapur -416006, Maharashtra, India, Tel: +919767677772; Email: drmeghnadjoshi@gmail.com

Abstract

Cervical cancer (CC) is the leading second most common cancer in India in the past two decades. It has been seen that early detection of CC can lead to curing of diseases successfully. There is a pressing need to establish an effective biomarker that would precisely detect early CC. Recently lots of attention has been passed on Major histocompatibility complex class I related chain A and B (MICA/B) antigens. This molecule is stress-inducible ligand that is over expressed in several cancers. However presence of this antigen is not yet been studied in cervical cancer (CC) patients. The present research studies for the first time expression of MICA/B antigen on PAP smear samples of CC patients. The PAP smear samples of control and CC patients were analyzed by Haematoxylin and eosin staining (H&E), MICA/B Immunoflurocence staining and double-immunofluorescence staining with anti-MICA/B and NKG2D antibody. Our results are highly motivating and clearly suggest the increased presence of MICA/B and decreased NKG2D receptor expression molecules. This decreased NKG2D expression might result in immune escape and disease progression. So far there is no data is available of any such studies on relationship between expression : of MICA/B in PAP smear of cervical cancer patients.

Introduction

Cervical cancer (CC) is the leading second most common cancer in India in the past two decades. Its multiple causes, prevention potential make cervical cancer an important disease for in-depth studies [1,2]. High risk women such as multiple sexual partners, multiple pregnancies, poor genital hygiene, malnutrition, use of oral contraceptives, and lack of awareness, commercial sex workers, Specific types of oncogenic HPV-16, 18 and HIV (human immunodeficiency virus) positive women are more prone [3]. Incidence of cervical cancer is more in 55-59 years and a considerable population report in the late stages of disease. Hence, there is a pressing need to establish an effective biomarker that would precisely detect early CC. Cervical intraepithelial neoplasia (CIN) is a precancerous lesion if diagnosed, can be treated effectively to prevent progression to cervical cancer. It well understood that the cells under stress will over express Major histocompatibility complex class I related chain A and B (MICA/B) antigens [4,5]. MICA is a stress-inducible ligands that bind to the immunoreceptor NKG2D and play an important role in mediating cytotoxicity of NK and T cells [6,7]. These are the molecules up regulated in response to various stimuli of cellular stress including heat shock, infection with viruses, malignant transformation and inflammation.

Expression of MICA/B is increased in several malignancies such as Oral, Cervix, and Breast Cancer [8]. There is no data available on expression of MICA/B in Pap smear. In this study, we propose to study immunohistochemical expression of MICA/B as potential biomarkers for the detection of early stage of CC in Pap smear to indicate CC progression. MICA/B will be a biomarker for early detection or monitoring. Improvements in CC diagnosis, monitoring and response are immense need of CC research. New approach of diagnosing CC by Pap smear will be a non invasive technique that will help to decide the treatment outcome future direction. So far there is no data is available of any such studies on relationship between expression of MICA/B in pap smears of CC. This screening test will be a cheap, effective

that can help to detect disease early and may reduce the burden of skyrocketing costs.

Materials and Methods

The use of specimens from human subjects is approved by the Institutional Review Board of DY Patil University. Provided informed consent of patients was taken. Patients (n= 10) having age group 25 to 50 years of age and an expected survival of at least 1 year are involved in this study. Patients having any serious illness, infection, psychiatric illness, pregnant, nursing woman were excluded from the study. Pap smears from healthy females (n=5) were used as contols. Pap smears of proven CC patients were collected from D Y Patil hospital, Kolhapur and Shri Siddhiviyak Ganpati cancer Hospital, Miraj. The cells were collected from the outer opening of the cervix at the transformation zone where the outer squamous cervical cells meet the inner glandular endocervical cells. Smears were taken on the positively charged slides (pathnsitu biotech). Pap smears of both control and Cancer cervix were fixed with chilled acetone-methanol (1:1), air dried and kept at -40ºC. Before processing, slides were washed with D/W containing 0.05% tween 20. Serum blocking was done by goat serum and slides were incubated with PE conjugate MICA/B (Molecular Probes, USA) for one hour at room temperature followed by wash with D/W containing 0.05% tween 20. Double staining was done using MICA/B (Alexa 488) and NKG2D (Alexa 594). Slides were mounted with DAKO mounting media.

Results and Discussion

Cervical cancer is the most common malignancy particularly in India. Nowadays, cervical screening is necessary in every woman above 40 yrs because cervical precancers do not show any signs and symptoms at its early stage. In India, even though a major effort is taken to expand cytology services, then also it is not be possible to screen even one-fourth of the population in the near future. Due to lack of awareness regarding cervical cancer in women and failure to regular screening, the carcinoma cells undergo invasive phase and develops CIN progression. These women are more prone to invasive cancer in the future. The focus must be emphasized on detection, prevention and cure of cervical cancer in a highly populated country like India to prevent its extensive spread. The early detection will definitely help to reduce the morbidity and mortality of CC. Most of the time disease gets diagnosed in late stage and patient have to undergo radiation and brachy therapy. Because of the side effects of the therapy, it is important to detect the CC in its early stage and to reduce the side effects and high risk of patients

HE staining of control slide showed many sheets of glandular cells. The sheets were tightly crowded but lacked feathering at the edges (Figure 1A). Slides of CC showed a disrupted, irregular and honeycomb like pattern of thickened cell borders and overlapping nuclei (Figure 1B). MICA/B that binds to the immunoreceptor NKG2D mediates cytotoxicity of NK and T cells. When MIC molecules release from the cell surface, they escape from immune recognition and responsible to form tumor cells and thus an aggressive tumor growth. Expression of MICA/B is increased in several types of malignancies. NK cells defense against viral pathogens via cytokines and chemokines secretion and kill infected cells. NK cells plays crucial role in tumor immunosurveillance. Low levels of expression of MICA/B in the pap smears of control (Figure 2A) was observed. Expression in CC patient was strong in glandular cells (Figure 2B).

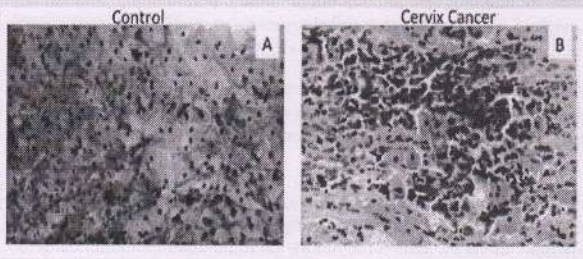

Figure 1: Haematoxylin and eosin staining of PAP smear.

A.Control showed sheets of glandular cells,

B.Cervical cancer patient showed disrupted, irregular and honeycomb like pattern.

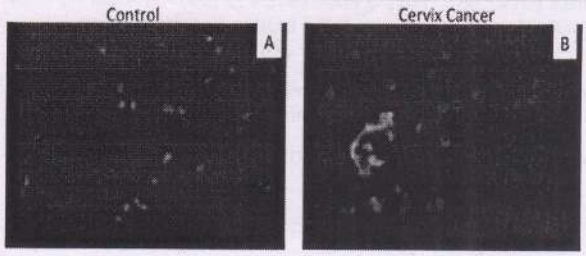

Figure 2: MICA/B Immunoflurocence staining of PAP smear.

A.Low levels of expression of MICA/B in cells.

B.Cervical cancer patient showed intense expression of MICA/B (Red) in glandular cells.

(Microscope field at a magnification of X40).

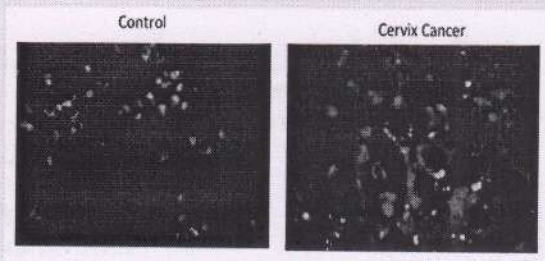

Figure 3:

A.Merged images revealed that control patient showed NKG2D+ cells (Red).

B.Cervical patient showed Strong MICA/B expression (Green) while NKG2D (Red) was very less.

(Microscope field at a magnification of X40).

Recently, it has been stated that activating NK cell receptor ligands MICA (NKG2D ligand) are differentially expressed during the progression to CC [9,10]. The aim of the present

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work was to study MICA/B and NKG2D expression in patients with CC. Expression of NKG2D in control sides was moderate (Figure 3A) However, decreased expression was observed in CC slides (Figure 3B). NKG2D is constitutively expressed on NK and T cells to mediate recognition and destruction of MIC A/B-expressing cells. Decreased NKG2D expression might result in immune ecape. The role of MICA/B and NKG2D is well studied in tumors and its possible role in tumor immune recognition or suppression but data regarding its study in Oral, Cervix, and Breast cancer are very few. In this study, immunohistochemical expression of MICA/B + NKG2D receptor on Pap smear were studied as potential biomarkers to indicate cervical cancer disease progression. However, the expression of triggering receptors MICA/B + NKG2D from patients with cervical cancer remains unknown.

Conclusion

In summary, the present research clearly suggests that the increased presence of MICA/B and decreased NKG2D receptor expression molecules in Cervical cancer (CC) patients for the first time. This decreased NKG2D expression might result in immune escape and diseases development. The results are highly encouragering and have immense potential to use in clinical setting. These results can be clinically correlated and can be used to predict the diseases progression and helps clinician to start appropriate therapy. Tough the sample size used in the research is comparatively small but the available results are giant leap in cervical cancer research. Our lab in D.Y. Patil University is continually working on the expression of this molecule in oral and breast and critically correlating the clinical correlation and near future we may come out with some more existing research.

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Dental Research Journal

Case Report

Gingival plasma cell granuloma

Amitkumar B Pandav[1], Alka V Gosavi[1], Dhaneshwar N Lanjewar[1], Rakhi V Jagadale[2]

[1]Department of Pathology, Government Medical College, [2]Department of Surgical Pathology, S.S.V.G. Cancer Hospital, Miraj, Maharashtra, India

ABSTRACT

Plasma cell granuloma, also known as inflammatory pseudotumor is a tumor-like lesion that manifests primarily in the lungs. But it may occur in various other anatomic locations like orbit, head and neck, liver and rarely in the oral cavity. We here report an exceedingly rare case of gingival plasma cell granuloma in a 58 year old woman who presented with upper gingival polypoidal growth. The histopathological examination revealed a mass composed of proliferation of benign spindle mesenchymal cells in a loose myxoid and fibrocollagenous stroma along with dense infiltrate of chronic inflammatory cells predominantly containing plasma cells. Immunohistochemistry for kappa and lambda light chains showed a polyclonal staining pattern confirming a diagnosis of plasma cell granuloma.

Key Words: Inflammatory pseudotumor, plasma cell granuloma, plasma cells, polyclonal plasma cells

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Address for correspondence:
Dr. Amitkumar Bapuso Pandav,
Department of Pathology,
Government Medical
College, Miraj, Maharashtra,
India.
E-mail: dramitpandav@
gmail.com

INTRODUCTION

Gingival Plasma cell granulomas are extremely rare. These are non-neoplastic, tumor-like lesions of unknown etiology and are composed predominantly of polyclonal plasma cells. In 1968, Bhaskar, Levin and Firch first reported the cases of gingival plasma cell granuloma.[1] Although Plasma cell granuloma (PCG) occurs most commonly in lungs, other organs may be involved. In head and neck, the areas most commonly involved are the orbit and paranasal sinuses, but they have been also described in the larynx, pterygomaxillary space, tonsils, ears, tongue, lip, oral mucosa, periodontal tissues and rarely gingiva.[2] Literature reviewed shows that gingival plasma cell granuloma is exceedingly rare and very few case reports of gingival plasma cell granuloma have been observed. Intraoral PCG occurs in a wide age range of 19 months to 63 years, but most of the cases of gingival PCG are observed in 4th and 5th decades of life and there is a slight female predominance.[3,4] Clinically gingival PCG presents as a nodular, polypoidal mass with smooth surface. It does not produce significant systemic symptoms. Routine laboratory examination is normal and microbiological culture results are negative. Radiologically some oral lesions have shown infiltrative margins giving an appearance of a malignant tumor.[5] Hence such lesions should be histologically examined to decide the exact nature of these lesions.

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CASE REPORT

A 58-year-old woman was admitted in November 2010 who presented with an enlarging, painless mass in the oral cavity. The mass was present since five years and was slowly increasing in size. There was no history of trauma or surgery to the oral cavity. She had no systemic symptoms. On oral examination, the mass was polypoidal, nontender, firm measuring 3 × 2 cms and was located on the inner aspect of upper gingiva extending from right middle incisor to the left canine region. The mass did not involve the palate. Radiological examination and serum

electrophoresis were normal. Routine laboratory examination was normal. The mass was excised and sent for histopathological examination.

Pathologic findings

Grossly, the lesion was polypoidal and solid measuring 3 × 2 × 1.5 cms with smooth white cut surface [Figure 1]. Microscopically, the mass was lined by stratified squamous epithelium with focal ulceration. The mass was composed of nodular infiltrates of mature plasma cells admixed with lymphocytes and histiocytes on the background of loose myxoid and collagenized stroma showing scattered fibroblasts and myofibroblasts [Figures 2 and 3]. In areas, the lymphoplasmacytic infiltrate was prominent around the blood vessels. Russell bodies were also seen [Figure 4]. Mitotic figures or nuclear atypia were not seen. Immunostaining for kappa and lambda light chains revealed a polyclonal plasma cell population [Figures 5 and 6].

DISCUSSION

Plasma cell granuloma is a rare tumor like lesion characterised histologically by fascicles of spindle mesenchymal cells admixed with chronic inflammatory cells predominantly plasma cells. It has various components like fibroblasts, myofibroblasts, inflammatory cells (plasma cells, lymphocytes, histiocytes, mast cells and eosinophils). The stroma is collagenous and/or myxoid. All these components are arranged in varying proportions and thus create a marked histological diversity. Depending upon the predominant components, it has various nomenclatures like plasma cell granuloma, plasma cell pseudotumor, inflammatory pseudotumor, inflammatory myofibroblastic tumor, and myofibrohistiocytic proliferation.[6]

The aetiology of PCG/inflammatory pseudotumor (IPT) is unknown. The histologic diversity has led to conflicting opinions regarding the inflammatory or neoplastic nature of this lesion. The finding of human herpesvirus-8 DNA sequences and over expression of human interleukin 6 and cyclin D1 has been recently reported in seven cases.[7] Kim *et al.* suggested that interleukin-6 (IL-6) and phospholipase C-γ1 may induce heavy plasma cell infiltration in cyclosporine-induced gingival overgrowth.[8] Debate exists about the inflammatory or neoplastic nature of this lesion, with majority of reports siding with the post inflammatory reactive process. Some cases show a predominance of mature plasma cells and lymphocytes that are mixed with histiocytes and only a minor mesenchymal component. The plasma cells are polyclonal[6,7] favouring inflammatory nature. Other cases are composed predominantly of bland fibroblasts and myofibroblast spindle cells arranged in interlacing fascicles or storiform pattern with only a minor component of inflammatory cells. The spindle cells stain positive with antibodies to vimentin and actin, and rarely, occasional cells stain with desmin, which is consistent with fibroblasts and myofibroblasts. However spindle cells of some lesions have been shown to possess a persistent abnormality involving chromosome 2p23 a ALK gene locus, which is consistent with a neoplastic nature of this lesion.[9]

PCG/IPT may be misinterpreted by the pathologists as nodular fasciitis, fibromatosis, fibrosarcoma or plasmacytoma. Nodular fasciitis rarely occurs in the oral cavity and it is characterised histologically by the presence of loose myxoid matrix containing short linear curved fascicles of spindle cells. Fibromatosis of the oral cavity usually occurs in young adults and it is characterised histologically by broad interlacing fascicles of mature fibroblasts with a variable degree of collagenisation. An inflammatory component is absent. Oral PCG needs to be distinguished from the recently described follicular dendritic cell tumor of the oral cavity, which runs an indolent course with a tendency of local recurrence. It can closely mimic inflammatory pseudotumor with whorls or fascicles of plump spindle cells in an inflammatory background of lymphocytes and histiocytes. In contrast, plasma cells constitute a significant proportion of the chronic inflammatory cells in inflammatory pseudotumor. The distinction can be established by the positive staining for CD21, Ber-MAC-DRC, and Ki-M4 in follicular dendritic cell tumor.[3]

In view of predominance of plasma cells in our case the differential diagnosis considered was plasmacytoma. In plasmacytoma, there are diffuse sheets of neoplastic, variably differentiated, monoclonal plasma cells. Mitotic activity and amyloid deposition may be present and the inflammatory cells are very sparse.[10] The present case showed admixture of lymphocytes and plasma cells along with Russell bodies. Immunohistochemistry showed polyclonal plasma cells. The other polyclonal lesions of gingiva include plasma cell gingivitis, which is usually not a

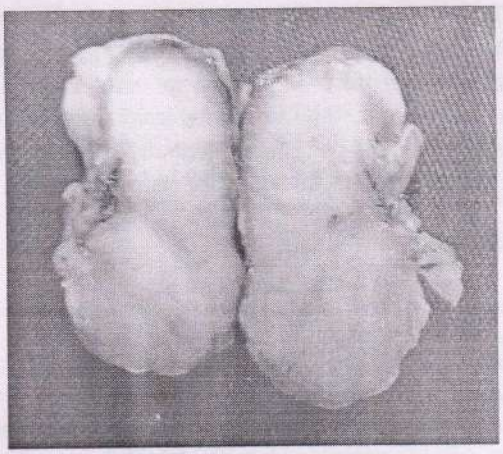

Figure 1: Gross photograph showing polypoidal mass with smooth white cut surface

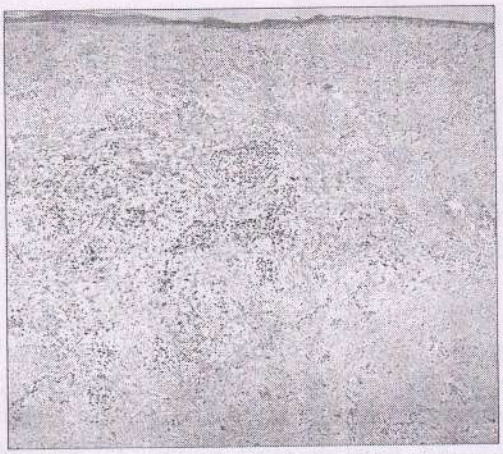

Figure 2: Histological picture showing spindle cell proliferation admixed with dense Lymphoplasmacytic infiltrate (H and E ×100)

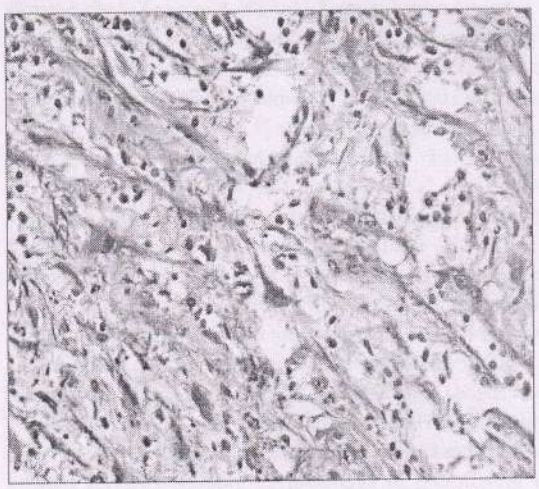

Figure 3: Histological picture showing fibroblasts and myofibroblasts (H and E ×400)

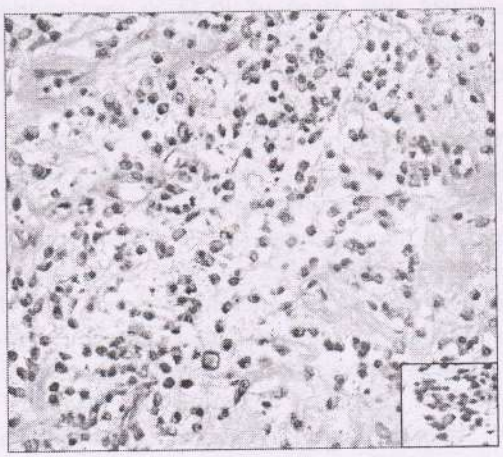

Figure 4: Histological picture showing predominance of plasma cell along with Russell bodies.Inset shows Russell body (H and E ×400)

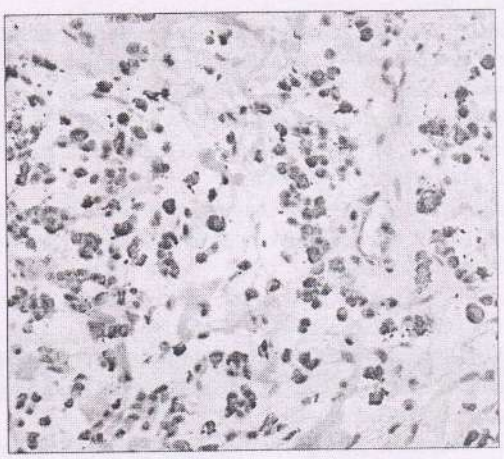

Figure 5: Immunohistochemistry for kappa chains

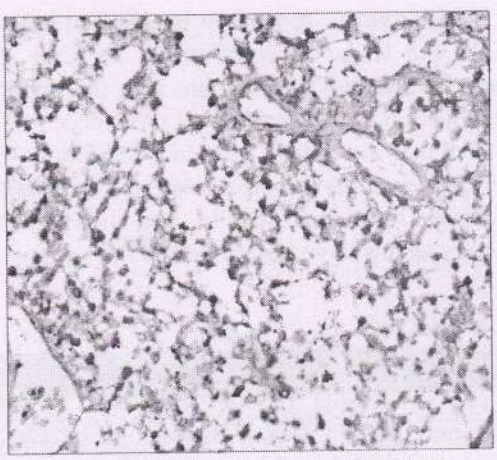

Figure 6: Immunohistochemistry for lambda chains

localised nodular lesion but presents as generalised oedematous and erythematous elevations.[10]

Naderi *et al.* in their study of 2068 cases of reactive lesions of oral cavity found that peripheral giant cell

granuloma was the most prevalent lesion of gingiva.[11] However plasma cell granuloma of gingiva is a very rare lesion. In 1968 Bhaskar, Levin and Firch[1] reported 45 cases of PCG of periodontal tissue and this appears to be the first report on this pathologic entity on the gingival tissue. Thereafter very few case reports have been documented in the literature. Most of these are in the form of single case reports. Acevedo and Buhler,[12] Earl and lowry,[4] Ide and Shimoyama,[4] Peacock ME,[13] Shin JM,[14] Karthikeyan and Pradeep,[10] Baltaciaglu,[1] Namboodiripad,[15] Phadnaik,[1] Balaji Manohar and S Bhuvaneshwari,[16] have described single case reports of PCG of the gingiva. Their clinical presentation and histopathological findings are similar to those observed in the present case. KIM SS and Eom D have described two cases of PCG in cyclosporine induced gingival overgrowth.[8] In January 2011 Kim YS, Lee SK described 14 cases of PCG out of 59 chronic inflammatory gingival lesions examined. They divided the gingival plasma cell granuloma into three histological types viz. plasma cell predominant type (PPT), mixed inflammatory cell type (MICT), and sclerosed fibrosis type (SFT). The results of immunohistochemical studies on these cases suggest that a gingival plasma cell granuloma shows variable gene expression for cell-mediated immunity and stromal tissue degeneration, undergoing sclerotic fibrosis with a persistent inflammatory reaction.[17] Idle *et al*. States that pure PCG should not be called as inflammatory pseudotumor and the term IMT should be applied only for genuine lesions of myofibroblasts.[4]

PCG in the oral cavity is usually benign and simple excision of the lesion is curative. In our case the patient was followed up for 6 months after the surgery. During this period the patient had no recurrence of the lesion. After that the patient was lost for follow up. Although surgery is the principal treatment, regression and response to corticosteroids and nonsteroidal inflammatory agents have been noted in rare cases.[7]

CONCLUSION

Plasma cell granuloma of the gingiva is a rare entity that may be confused with a malignant tumor on clinical and radiographic grounds.[5] The gross and microscopic similarities to other oral spindle cell tumors can also be misinterpreted as those of a more aggressive lesion. So awareness of oral PCG/inflammatory pseudotumor and its distinctive morphologic features is important in avoiding the misdiagnosis. It is also important to recognize this entity as a benign inflammatory lesion to avoid unnecessarily extensive and potentially destructive surgery. We report here this case for its rarity.

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Original Article

AIDS-associated Cancers : An Emerging Challenge

Uday A Phatak*, Ravindra Joshi**, Dinesh K Badakh***, Vikas S Gosavi#, Jayanti U Phatak†, Rakhi V Jagdale‡

Abstract

Objectives: To study the incidence and effects of anti-retroviral therapy along with cancer chemotherapy on outcome of AIDS associated Cancers in Indian patients.

Method: 3832 cancers patients were investigated over a period of 5 years. 46 AIDS-associated cancers were identified. HIV status was evaluated by ELISA, Western Blot, viral load and CD4/CD8 counts. Patients were treated with different modalities of cancer management and anti-retroviral therapy was discussed with the patient and relatives. Patients were followed up 6 monthly.

Results: Incidence of AIDS-associated cancers was 1.2 percent. AIDS-Defining Cancers (ADC) were seen in 26 (54.35%) while non-AIDS-Defining Cancers (NADC) were observed in 21 (45.65%). Non Hodgkin Lymphoma was the commonest form of AIDS-defining cancers in 21 (84%) patients, cervical cancers in 4 (16%) women while there was not a single case of Kaposi's Sarcoma. AIDS associated cancers were common in males. Mean age was 38.5 years. Only 33.5% patients received treatment for HIV and cancers. Development of immune reconstitution syndrome was observed in 9.09% patients. Hepatitis B infection was seen in only one patient (2.17%).

Conclusions: AIDS-associated cancers are seen in advanced stage of HIV infection. Concurrent chemotherapy and anti-retroviral therapy for ARL is significantly effective. Cervical cancers and non-AIDS-defining cancers do not show predictable response to anti-retroviral therapy. Mortality in non-AIDS related cancers was significantly higher than AIDS related cancers.

Introduction

There are about 2.5 million HIV patients in India and the calculated prevalence in Maharashtra is around 0.62 per cent.[1] Survival of HIV patients improved significantly with better control of opportunistic infections and administration of Highly Active Anti-Retroviral Therapy (HAART). [2]

Real incidence of AIDS-associated cancers in Indians is not known. There are only few reports in Indian literature.[3-5] It may be roughly 3-4 per cent in Indians while in developed countries; it may be 10-34 per cent.[2,3] HIV associated cancers are mainly divided into two groups. AIDS-defining Cancers (ADCs) include Non-Hodgkin's Lymphoma, invasive cervical cancer and Kaposi's sarcoma. Other types of cancers in HIV patients are included in non-AIDS-defining Cancers (NADCs).[2]

We studied 3832 different types of cancers in Shri Siddhivinayak Ganapati Cancer Hospital, Miraj (Maharashtra) over a period of five years (January 2003-November 2008). Of them, 46 AIDS associated cancers were diagnosed. The present study focuses on these patients, their treatment effects of combination chemotherapy and antiretroviral therapy and overall outcome.

Patients and Method

Shri Siddivinayak Ganapati Cancer Hospital is a dedicated cancer hospital in Miraj, District Sangli (Maharashtra), India. Number of cancer patients from Western Maharashtra, Konkan, Northern Karnataka seek advice and treatment for oncological problems. During 2003-2008, 3832 cancer patients were enrolled in this study. All the cases were thoroughly investigated and hematological, biochemical and radiological investigations were performed. Histopathological study was performed by a team of pathologists and patients were classified according to ICD 10 code system. Treatment options like chemotherapy, surgery, or multimodality treatment were discussed with patients by respective specialists. Table 1 shows distribution of different cancers studied during last 5 years.

HIV infection is diagnosed by ELISA test and confirmed by Western blot test. Staging of HIV infection was done with CD4+/CD8+ counts. Viral load was estimated in these patients before administration of antiretroviral therapy and then 6 monthly to evaluate the response to HAART. Serum LDH was estimated for evaluation of disease activity. Patient and relatives were given complete information about the nature of both the diseases, further plan of management and expenses involved in this. Detail study of opportunistic infection was done and accordingly these conditions were managed. Different treatment options of highly active anti-retroviral therapy (HAART) were discussed with patients. Reverse transcriptase inhibitor (RTI) - or protease inhibitor (PI) based antiretroviral therapy, its monthly expenses, interaction between chemotherapeutic agents, their toxicities were discussed in detail with the patient and relatives.

All AIDS-associated cancer patients were evaluated monthly before next chemotherapy cycle and then every 3 or 6 monthly. Follow-up was continued after completion of chemotherapy or radiotherapy for status of HIV infection and evaluation for recurrence / relapses of cancers.

Results

3832 cancer patients were enrolled for this study. There

*General Medicine, Department of General Medicine, **Medical Oncology, Department of Medical Oncology, ***Radiation Oncology, Department of Radiation Oncology, #General Surgery, Department of General Surgery, †Microbiology, Department of Medical Microbiology, ‡General Pathology, Department of Pathology, Shri Siddhi Vinayak Ganapati Cancer Hospital, Miraj

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Table 1 : Distribution of different cancers according to ICD10 coding system during 2003-08.

Type of Cancer	ICD10 Code	Male	Females	Total	HIV associated Cancers	Percent
Head and Neck	C00-14	836	319	1155	4	0.35
Gut	C16-18,C21	243	148	391	3	0.77
Uterus, tubes, adnexa	C51-52,C54-55	0	357	357	2	0.56
Metastases	C 97	224	117	341	3	0.88
Breast Cancer	C50	0	269	269	1	0.37
Other Blood Cancers	C90-95	157	96	253	0	0.00
Genitourinary Cancers	C64-68	198	42	240	1	0.42
Cervical Cancer	C53	0	173	173	4	2.31
NHL	C82-85,C96	108	60	168	21	12.50
Lung and Mediastenum	C34	60	27	87	1	1.15
Brain Tumors	C70-72	66	16	82	2	2.44
Prostate	C61	72	0	72	0	0.0
Ovary	C56	0	52	52	2	3.85
Soft Tissue Sarcoma	C49	31	18	49	1	0.09
Bone Tumors	C40-41	20	16	36	0	0.00
Liver, GB, Pancreas	C22-25	24	10	34	1	2.95
Thyroid and Endocrine	C73-74	12	13	25	0	0.00
Hodgkin's Lymphoma	C81	13	10	23	0	0.00
Skin Cancers	C43-44	5	8	13	0	0.00
Eye & Orbit	C69	8	4	12	0	0.00
Total		2077	1755	3832	46	1.20

Table 2 : Clinicopathological details of 46 HIV associated cancers

Number of cancer patients in this study	Number	Percentage
Male	2077	54.20
Females	1755	45.80
HIV Associated Cancers	46	1.20
HIV Associated Cancers in males	32	1.61
HIV Associated Cancers in females	14	0.76
Mean age of AIDS related Lymphoma (ARL)	40.8 years	
Mean age of non AIDS-related cancers	41.2 years	
Pediatric AIDS-associated cancers	03	6.52
Adult AIDS-associated cancers	43	93.48
HBV positive AIDS related Cancers	01	2.17
Median CD4+ count	162.8 /mm^3	
HAART started for AIDS related cancers	11	23.91
HAART not started for patients AIDS related cancers	35	76.09
Reconstitution syndrome following HAART	01	9.09
Types of Non-Hodgkin's Lymphoma	21	
Diffuse large B cell Lymphoma	18	85.71
Primary Central Nervous system Lymphoma	1	4.76
T cell Non-Hodgkin's Lymphoma	1	4.76
Lymphoblastic Lymphoma	1	4.76

were 2077 were males and 1755 females. Male-to-female ratio was 1.18:1. Head and neck cancer was the most common type followed by cancers in females (breast cancers and gynecological cancers), gastrointestinal cancers and other types. There were 46 (1.20%) AIDS-associated cancers. Of these 21 had non-AIDS related cancers and 25 AIDS related cancers. The latter comprised of, Non-Hodgkin's Lymphoma in 21 patients (84%) and 4 (16%) of invasive cervical cancers. There was no case of Kaposi's sarcoma in our study.

In this study, AIDS-related cancers (ARL) were more common in males than females, with a ratio of 2.29:1. Pediatric AIDS-associated cancers were seen in only 6.52 per cent of patients. Median CD4 count was 162.8/mm^3 indicating advanced stage of HIV infection while viral load hanged between 50,000 to 393,000/ml. Of 46 cases of AIDS-related cancers, only 11 (23.91%) received antiretroviral therapy. One patient (9.09%) developed reconstitution syndrome characterized by sudden aggravation of tubercular lymphadenopathy and hyperlipidemia due to protease inhibitor based HAART. In NHL group, diffuse large B cell lymphoma was found in 85.71% patients while 14.61% had other forms of NHL. At the end of 2008, 11 (23.91%) patients are alive, 31 (67.39%) dead and remaining 4 (8.7%) lost to follow up.

Discussion

Pattern of AIDS-associated cancers in Indian patients differed significantly from developed countries where there were cases of Kaposi's sarcoma. In developed countries, Kaposi's sarcoma was the commonest cancer followed by non-Hodgkin's lymphoma.[2] We and Dhir et al did not find a single case of Kaposi's sarcoma in our studies.[4] Only one case of Kaposi's sarcoma was found in an autopsy study of 162 AIDS patients in another Indian study.[5]

AIDS related lymphoma (ARL) was the commonest cancer in our study. All these patients had advanced stage, B symptoms, extranodal involvement such as bone marrow, central nervous system etc at the time of presentation. Mortality in AIDS-associated cancers was higher when these patients had low CD4 count and Karnofsky performance score, presence of extranodal disease, an advanced clinical stage, presence of bone marrow involvement, an age more than 35 years and a high serum lactate dehydrogenase concentration.[7] Risk of development of NHL in HIV patients is almost 100-300 times higher than general population when they have low CD4 count, high viral load and not receiving anti-retroviral therapy.[8]

There are no specific guidelines for the treatment of ARL. Patients with ARL do not tolerate conventional chemotherapy. They develop severe myelosuppression and opportunistic infections. When low-dose chemotherapy was administered, results were suboptimal.[9] Addition of HAART to standard chemotherapy with support of different growth factors, improved the outcome of AIDS related Non-Hodgkin lymphoma

patients. Different chemotherapy regimes such as infusional CDE, m-BACOD with G-CSF, EPOCH, CHOP and chemotherapy with Rituximab were tried for the management of these patients.[7,9] German ARL study group investigated concurrent administration of HAART and CHOP regime in 72 patients with ARL. They reported 79 per cent complete remission and longevity up to 47 months. Toxicities were not very severe. Now combined modality is considered standard-of-care ARL.[10] In HAART era, goal of treatment of ARL is complete remission, not palliation.[11]

We managed ARL with standard CHOP regime along with Reverse Transcriptase inhibitor (RTI) based antiretroviral therapy (HAART). Patients tolerated chemotherapy and HAART well and could complete chemotherapy without any interruption. Patients were treated with different anti-retroviral regimes such as Emtricitabine, Lamivudine, Efavirenz or Zidovudine, Lamivudine, Efavirenz or Loponavir/Ritonavir-based anti-retroviral therapy. Zidovudine was omitted if patients developed myelosuppression. Similarly, Didanosine was not used as it causes peripheral neuropathy or exacerbates chemotherapy induced peripheral neuropathy. PI-based antiretroviral therapy is very expensive, can cause or worsen chemotherapy induced neutropenia by inhibiting cytochrome P450/CYP3A enzyme system.[12] Some protease inhibitors may reduce the hepatic metabolism of cyclophosphamide or anthracycline.[13] There has been some concern about tumorigenesis with Protease inhibitors like Nelfinavir. Nelfinavir was tumorigenic in animal studies but not in clinical studies in humans so far.[19] Ritonavir caused significant regression of cancers like head and neck cancers. Its Inhibitory effect was boosted by ionizing radiation in animal studies with minimal toxicity.[15]

Ebstein-Barr virus, human papilloma virus or Human Herpes Sarcoma virus induced AIDS-defining cancers, while "non-viral" theory is proposed in the pathogenesis of non-AIDS-defining cancers.[7, 15, 20]

Immune reconstitution inflammatory syndrome (IRIS) following HAART was seen in ARL after receiving chemotherapy and antiretroviral therapy. Few AIDS-associated cancer patients on HAART develop exacerbation of inflammatory condition. This could be due to persistence of immunodeficiency in spite of chemotherapy and HAART. Development of IRIS indicated improvement in immunity and over all prognosis of such patients may be better.[14]

In this study, all cervical cancers had advanced stage at the time of presentation with significant complications. Though, cervical cancer is an AIDS-defining Cancer, there could be variable response to anti-retroviral therapy. If HIV-infected women receive HAART in early stage, there could be regression of malignant lesions. Surprisingly, there was no correlation with CD4 count and clinical response to HAART in different clinical studies.[16, 17]

Patients with non-AIDS related cancer had aggressive malignancies and poor performance status. Mortality was significantly higher in this group. Response to HAART and cancer management was not uniform and predictable when treated with antiretroviral therapy.[18] Recent study showed that with the use of antiretroviral therapy for HIV infection, there was a decline in AIDS-defining Cancers and an increase in non-AIDS-defining Cancers. It was attributed to development of skin cancers in white population.[2]

CD4 count was considered as a surrogate marker and correlated with the disease activity and prognosis in some types of malignancies. Thus median survival was only 4 months when CD4 count was less than 100/mm^3, but 11 months if more than 100/mm^3 in the absence of HAART. CD4 count correlates well with progress of Kaposi's Sarcoma and Non-Hodgkin's Lymphoma but not with cervical cancers.[17]

Although AIDS-related cancers improved significantly with HAART, and mortality reduced by 70 per cent, the same results were not seen in non-AIDS-related cancers.[7]

Conclusion

Number of HIV associated cancers is increasing due to increased survival rates and the age of HIV positive patients. Pattern of AIDS related cancers in Indian patients differs significantly from developed countries. Non-Hodgkin's lymphoma is the commonest type of AIDS related cancer, followed by non-AIDS-related cancers. Kaposi's sarcoma is not found in our study. AIDS-defining cancers respond to combined treatment with chemotherapy and antiretroviral therapy but in non-AIDS-related cancers, outcome is poor. Concomitant chemotherapy and HAART is considered as the standard-of-care for ARLs.

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Case Report

Thyroid cancer in a long-term nonprogressor HIV-1 infection

Uday A. Phatak, P. V. Chitale[1], Rakhi V. Jagdale[2]

Department of Medical Oncology, Medical Oncology Unit II, Shri Siddhivinayak Ganapati Cancer Hospital, [1]Departments of Surgical Oncology and [2]Oncopathology, Shri Siddhivinayak Ganapati Cancer Hospital, Miraj, Sangli, Maharashtra, India

Address for correspondence:

Dr. Uday A. Phatak, Consultant Physician, Medical Oncology Unit II, Shri Siddhivinayak Ganapati Cancer Hospital, Miraj - 416 410, Sangli, MH, India. E-mail: uday.phatak@gmail.com

Abstract

Long-term non-progressor HIV infection (LTNP-HIV) is seen in <1 percent of HIV-afflicted population. There are definite criteria for the diagnosis of LTNP-HIV. Malignancies either solid tumors or haematological cancers have not been reported in such population. We report here a rare case of follicular thyroid carcinoma in LTNP-HIV infection. She never had any opportunistic infections. She did not receive anti-retroviral therapy in the entire course of illness and continued to have good quality of life. Treatment of follicular thyroid cancer was similar to other patients without HIV infection. This could be the first case study from India.

Key words: Follicular thyroid cancer, HIV-1, long-term nonprogressor HIV infection

INTRODUCTION

Long-term nonprogressor HIV infection (LTNP-HIV) is seen in <1% HIV positive population. Natural history of this subset of patients is entirely different.[1] So far, there are no studies on cancers in LTNP-HIV patients in the literature. We report here a very rare case of follicular thyroid carcinoma in LTNP-HIV infection. This could be the first case report from India.

CASE REPORT

A 30-year-old female, doctor by profession, presented with midline painless swelling in the neck for 3 months. It was slowly progressive but did not cause any pressure effects on nearby structures. She was having HIV-1 infection for last 10 years. She never had fever, weight loss, or any opportunistic infections due to HIV-1 infection. Details of investigations done 10 years ago such as HIV-1 viral load and CD4 and CD8 counts are not available at present. She was never treated with prophylactic drug treatment for opportunistic infections or with antiretroviral therapy during this period. She never suffered from thyroid illness before. None of her family members had history of thyroid dysfunction.

Clinical examination revealed a solitary nodule of 4 cm in the left lobe of thyroid. Cervical lymphadenopathy was not found. Ultrasonic study of thyroid gland showed an isoechoic solid nodule. Fine-needle aspiration cytology reported as a cellular follicular lesion. Thyroid function tests were normal. She underwent left hemithyroidectomy. Histopathological gross evaluation of left hemithyroidectomy specimen measuring 6.3 × 6.3 × 3.0 cm showed a well-circumscribed homogenous, nodular brownish mass measuring 4.5 × 3.5 × 2.8 cm. Adjacent nonneoplastic thyroid was nodular grey-white. Microscopy revealed a widely invasive, follicular carcinoma demonstrating

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prominent capsular and vascular invasion with tumor plug completely transregressing the fibrous capsule and present within a blood vessel covered by endothelium. No extra-thyroid extension was seen. Adjacent thyroid parenchyma shows lymphocytic thyroiditis [Figure 1]. There was no spread to other organs. Stage I follicular carcinoma was diagnosed.

Completion thyroidectomy was performed. Histopathological evaluation of completion thyroidectomy specimen showed Hashimoto's thyroiditis. Eleven adjacent lymph nodes were free of tumor. After 4 weeks, she underwent radioactive-Iodine whole body scan that demonstrated residual disease in the neck. Radioiodine ablation of the disease was done. She was treated with levothyroxine 100 μg daily for hypothyroidism after radioiodine treatment and calcium carbonate 1 Gm 3 times a day along with weekly cholecalciferol 60,000 IU for immediately for postoperative hypoparathyroidism. Her CD4 and CD8 counts were 756 cells/mm^3 and 819 cells/mm^3, respectively and the viral load was 136 copies/ml. Diagnosis of LTNP-HIV infection was considered as per the current criteria of LTNP-HIV.

DISCUSSION

HIV-1 infection is common viral infection in India. There are subsets of HIV-1 infection in which the viral load is not very high, T cell subpopulations (helper/suppressor) cells are slightly reduced and patients can survive more than 8 years in the absence of antiretroviral therapy for HIV-1 infection. This subset is seen in only <1% of HIV-positive population. We considered LTNP-HIV infection rather than élite controller as the viral load was more than 100 HIV-RNA copies/ml and helper T cell count was stable over the past 10 years, in the absence of antiretroviral therapy in this case study. The diagnostic criteria of LTNP-HIV include: (i) Helper cell population (CD4 cells) more than 500 cells/mm^3 (ii) viral load <1000 copies/ml (iii) stable disease over a period of 8 years without antiretroviral therapy for HIV infection. Prevalence of LTNP is <1% of HIV-positive patients in clinical practice.[1] Most of the patients are asymptomatic.

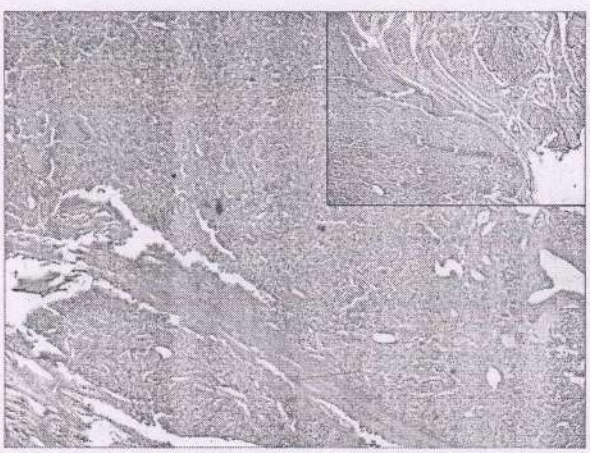

Figure 1: Widely invasive follicular carcinoma of thyroid. Arrow shows capsular invasion. Inset shows adjacent Hashimoto's thyroiditis

Incidence of cancers either AIDS-defining cancers (ADCs) or non-AIDS-defining cancers (NADCs) in LTNP-HIV infection has not been reported earlier. Prevalence of cervical lesions in LTNP-HIV patients was studied in Africa.[2] Thyroid involvement in HIV-positive patients may have variety of causes. It may be involved due to infections or there could be drug-related thyroid dysfunction in HIV infection,[3] but primary malignancy of thyroid in LTNP-HIV-1 patients is not known. Etiology of the NADCs and ADCs is not well understood. Most of the patients with AIDS-associated cancers have viral etiology. Human papillomavirus is responsible for oral and cervical cancers, Epstein-Barr virus is related to non-Hodgkin's lymphoma (NHL) and human herpes virus 8 for Kaposi's sarcoma (KS). No such viral etiology is attributed in the pathogenesis of thyroid malignancy.[4]

HIV/AIDS-related cancers, either AIDS-defining malignancies (ADMs) or non-ADMs (NADMs) are often seen in HIV infection with advanced stage. With highly active antiretroviral therapy, the prevalence of KS and NHL has declined significantly. Thyroid cancers in HIV/AIDS are an uncommon and unusual type of NADM.[5] Mbulaiteye *et al.* reported rising incidence of cancers of thyroid, kidney, and uterus and of conjunctiva in HIV/AIDS in Africa.[6] Whether genetic factor(s) play any role in the pathogenesis of thyroid cancers in HIV-positive patients is not clear.[4] Papillary thyroid carcinoma[7] and medullary thyroid carcinoma[8] were reported in advanced HIV positive patients. They were receiving antiretroviral therapy for HIV infection unlike our patient.

Pathogenesis of LTNP-HIV infection is a mystery. Viral, genetic and host-related factors have been postulated in the development of LTNP-HIV infection. Patients with HIV-1 infection progress if they have abnormalities of nef gene or have high level of beta-2-microglobulin. While some genes protect against the progression.[1] CCR5 is a co-receptor for transmission of HIV-1 infection. Mutation of CCR5 gene is the most common

abnormality in LTNP-HIV. Such mutation can be seen in Indian families as well.[9] Usually, individuals with homozygous delta 32 allele are resistant to HIV infection in spite of multiple exposures to HIV-infected persons while those with heterozygous delta 32 mutation have lesser viral replication and slower progression of HIV infection.[10] We have not evaluated our patient for molecular markers. Until date, patient has got good quality life following total thyroidectomy. How long will she remain LTNP-HIV or will she progress in future is not known.

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Conflicts of interest
There are no conflicts of interest.

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Melanotic neuroectodermal tumour of infancy: A clinicopathological study with emphasis on histopathology and IHC

Madhura D. Phadke[1], Jaydeep N. Pol[2], Rakhi V. Jagdale[3], Nitin N. Hombalkar[4], Zeba Nisar[5,*], Girish A. Kadkol[6]

[1-3,5,6]Consultant Pathologist, [4]Paediatric Surgeon, [1,2,5,6]Onco Pathology Center Mahatma Gandhi Cancer Hospital Miraj, [3]Shree Siddhivinayak Ganapati Cancer Hospital Miraj, [4]Hombalkar paediatrics Surgery Hospital, Miraj, Maharashtra, India

***Corresponding Author: Zeba Nisar**
Email: dr.zeba.ahmed@gmail.com

Abstract

Aims: To explore clinical, Histopathological and IHC features of MNTI with systematic literature review.
Settings and Design: Hospital based retrospective study.
Methods and Materials: Data of all cases of MNTI diagnosed over a period of seven years i.e. from 2008 to 2015 was retrieved. H&E sections and IHC sections were studied. Strict histological and recently updated criteria were applied and patients with a confirmed diagnosis of MNTI were included in the study. A systematic literature review was conducted by searching the PubMed and National Centre for Biotechnology Information database.
Statistical analysis used: Microsoft Excel 2010
Results: Present case series is 19th in the English literature and 2nd in the Indian literature. Mean age of presentation is 5 months. Average duration of symptoms is 2.1 months. Male preponderance was found i.e. M:F ratio of 2:1. Histopathology and if necessary, followed by IHC is required for the confirmation of diagnosis. No histological marker can predict its behaviour.
Conclusions: A number of known pathologic entities can present at infancy but confirmation of the diagnosis requires histopathological examination and IHC, if necessary. Any unusual growth in infants that appear inconsistent with normal variation and reported history should be referred in time to a pathologist for assessment and diagnosis. A diagnosis of MNTI should be suspected in any tumour in an infant with round cell morphology and a careful search for large melanin containing epithelial cells will help in accurate diagnosis.

Keywords: Melanotic neuroectodermal tumour of infancy, Round cell tumour, Melanin pigment, Melanoticprogonoma, Retinal anlage tumour

Key Messages: A diagnosis of MNTI should be suspected in any tumour in an infant with round cell morphology and a careful search for large melanin containing epithelial cells will help in accurate diagnosis.

Introduction

Melanoticneuroectodermal tumour of infancy (MNTI), described first in 1918 by Krompecher, is a rare, benign pigmented neoplasm of neural crest origin occurring in infants.[1] The majority of these tumours (90%) arise in the head and neck region, mostly affecting anterior maxilla.[2] MNTI is a locally aggressive, rapidly growing tumour.[3] Rate of recurrence is 20% within six months.[3]Beacause of its rapid growth potential there can be a misdiagnosis of malignancy, though the incidence of malignancy development is rare.[4] Clinical and radiological findings may suggest a diagnosis of MNTI, but histopathological examination and if necessary, followed by IHC is required for the accurate diagnosis.

We hereby report three cases of MNTI and discuss the clinical, histomorphological and IHC features of this rare tumour with systematic review of literature. As per author's knowledge this is the 19th case series in the English literature and second in the Indian literature.

Materials and Methods

This retrospective study comprises three cases of MNTI diagnosed over a period of seven years (from 2008 to 2015). All cases were documented; detailed clinical information was recorded from the case sheets. This included age and sex of the patients, duration of illness and site of biopsy. All three tumours were resected or biopsied, and pathological examination was performed on representative fixed-tissue samples embedded in paraffin and stained with H&E.

Haematoxylin& eosin stained sections were studied and the following histological features were evaluated:

1. Pattern of growth
2. Morphology of cells and their relative preponderance
3. Presence of melanin pigment

Subsequently, IHC was done. The following antibodies were used according to histomorphological features: Synaptophysin, GFAP, CK, EMA, HMB45, Vimentin, NSE, Desmin, Chromogranin& S100.
Strict histological and recently updated criteria were applied and patients with a confirmed diagnosis of MNTI were included in the study.

Systematic Review

A systematic literature review was conducted by searching the PubMed and National Centre for Biotechnology Information database using the keyword search term melanotic neuroectodermal tumour of infancy case series and the Medical Subject Heading term neuroectodermal tumour, melanotic. All case series of MNTI cases published hitherto were included. Excluded were reports published in a language other than English and without an English-language abstract. This yielded a total of

18 publications, which included 97 cases. (Table 1) This analysis included gender, age at diagnosis and tumour site.

Ethics: Procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 2000

Results

Between 2008 to 2017, three cases of MNTI were diagnosed. The clinical characteristics of the three cases are summarized in Table 2. On systematic review, it was found that the present case series is nineteenth in the English literature and second in the Indian literature. Also, in "case two" the lesion was present at femur which happens to be the seventh case to be reported in the world literature. The mean age of presentation was five months. There was a male preponderance. Average duration of symptoms was 2.1 months. Most predominant symptom was gradually increasing swelling.

FNAC could be done only in the last case. Cellular cytosmears showed disperse pattern, predominantly composed of round cells which outnumbered large epithelial cells. Among the dual population of cells, the round cells showed occasional rosettes.(Fig. 2b) While, the large epithelial cells formed small cohesive clusters with brown pigment.(Fig. 2a) A cytomorphological diagnosis of Round cell tumour was made & possibilities of Rhabdomyosarcoma, Neuroblastoma, MNTI and NHL were considered. The presence of melanin containing large cells which were found on a careful search is the key diagnostic feature of MNTI. Hence a final FNAC diagnosis of Round cell tumour suggestive of MNTI was given.

Histopathological features of all the three cases are summarized in the table below. (Table 3)

IHC features of all the cases are summarised in the table below. (Table 4)

Table 1: Previously reported case series of MNTI

S. No.	Study	Number of cases	Mean age (months)	M:F ratio	Site
1	Allen M.S. et al [7] 1968	3	4.6	02:01	Maxilla-1, Mandible-1, Skull-1
2	Cutler L.S. et al[2] 1981	2	4	01:01	Maxilla-2
3	Johnson R.E. et al[8] 1983	7	6	1.3:1	Maxilla-4, epididymis-1, Temporal bone-1 & femur-1
4	Mirich et al.[9] 1990	5	9	04:01	Maxilla-4, Calvaria-1
5	Pettinato G. et al[10] 1991	10	12.35	09:01	Maxilla-5, epididymis-1, mandible-1, skull-1 & soft tissue cheek-1
6	Pierre- Kahn[11] 1992	3	16.6	02:01	Skull- 2, brain-1
7	Yu et al[12] 1992	2	20	all males	Skull- 2, brain-1
8	Slootweg et al[13] 1992	2	9	all males	Maxilla-2
9	Demas et al[14] 1992	2	3.5	all females	Maxilla-2
10	Kapadia et al.[15] 1993	20	4.8	0.17:1	Maxilla-13, Mandible-3, Brain-1, Dura-2 & skull-1
11	Nelson et al[16] 1995	2	6.5	all males	Maxilla-1, Mandible-1
12	El Saggan et a[17]l 1998	2	5.5	all males	Maxilla-2
13	Khoddami et al [18]1998	3	5.3	02:01	Maxilla-3
14	de Souza et al[19] 1999	3	7.5	all females	Maxilla-3
15	Kaya S. et al[20] 2000	2	2.25	01:01	Maxilla-2
16	Barett A.W.[21] 2002	8	5.92	07:01	Maxilla-7, mandible-1
17	Chaudhary A.[22] 2009	18	4.2	02:01	Maxilla-18
18	Butt F.M.A.[23] 2009	3	10.5	02:01	Maxilla-3

Table 2: clinical features of three cases of MNTI

Case No.	Age (year of diagnosis)	Sex	Duration	Site	Symptoms
1.	7 months (2008)	Female	2 months	Left upper gingival (Fig. 1a)	Mass extruding from the mouth, No airway or pharyngeal compression
2.	4 months (2012)	Male	15 days	Left lower femur	Swelling left lower thigh
3.	4 months (2015)	Male	Since birth	Right upper gingiva & maxillary region (Fig. 1b)	Gradually increasing maxillary swelling & difficulty in taking feeds due to obstruction

Table 3: Histomorphological features of the cases

Case No.	Procedure done	Gross features	Microscopy
1.	Excisional biopsy	• Dark brown, firm mass. • Measured 5.5 X 4.9 X 4.7 cm • Overlying mucosa was ulcerated and showed brownish discoloration.	• Polypoidal mass showing predominantly large cuboidal • To polygonal cells, some containing melanin pigment • Arranged in pseudoalveolar pattern. (Fig.3b) • Admixed round cells in the fibrocollagenous stroma. • Large polygonal epithelial cells outnumbered round cells. (Fig.3a)
2.	Needle biopsy	Multiple light brown bits, largest measured 2x0.2x0.2 cm	• Round cell tumour. • Foci of polygonal cells with intracytoplasmic brownish pigment. (Fig.3c) • Large polygonal epithelial cells were equal in number as the round cells.(Fig. 3d)
3.	Wide local excision of mass with partial maxillectomy	• Polypoidal mass with normal overlying mucosa • Measured 4.5X4X3.7 cm • C/S: solid, encapsulated, grey white mass beneath the mucosa with brownish black discoloration.(Fig.4a)	• Biphasic pattern: Small and large cells • Small cells – small, round, hyperchromatic nuclei with • scanty eosinophilic cytoplasm, mimicking neuroblast • Large cells- cuboidal epithelial cells with large round to • oval vesicular nuclei with abundant eosinophilic cytoplasm arranged in pseudoalveolar or tubular patterns • Few cells show brown intracellular melanin granules • Round cells outnumbered large polyhedral epithelial cells. (Fig. 4 b-f)

Table 4: IHC profile of the three cases of MNTI (*Large polygonal epithelial cells)

Case No.	Type of cells	Synaptophysin	GFAP	CK	EMA	HMB45	Vimentin	NSE	Desmin	Chromogranin	S100	Mic-2	LCA
(Fig. 5 & 6)	LPEC*	-	-	+	+	+	+	-	-	-	-	ND	ND
	Round cells	+	+	-	-	-	-	+	-	+	-	ND	ND
(Fig. 5 & 6)	LPEC*	-	ND	+	+	+	ND	-	-	-	-	+	-
	Round cells	+	ND	-	-	-	ND	+	-	+	-	-	-
(Fig. 5 & 6)	LPEC*	-	-	+	+	+	+	-	-	-	-	ND	ND
	Round cells	+	+	-	-	-	-	+	-	+	-	ND	ND

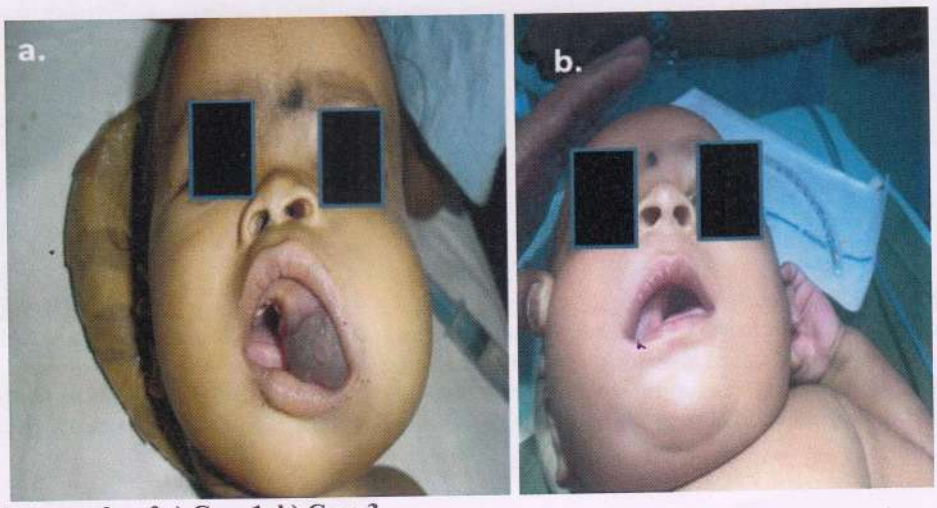

Fig. 1: Clinical photographs of a) Case 1, b) Case 3

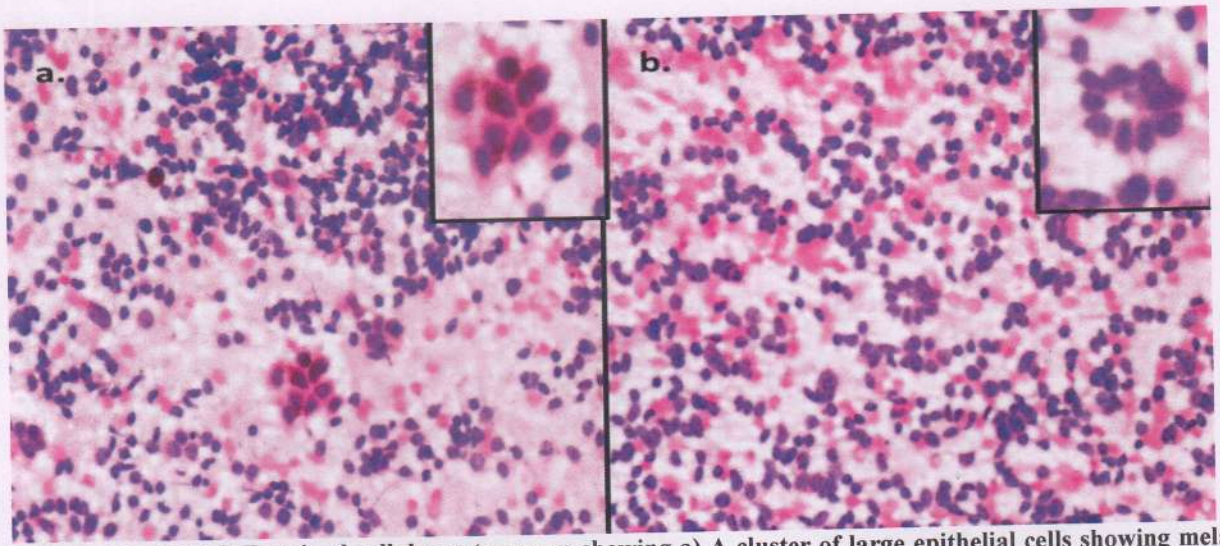

Fig. 2:From case 3, H & E stained cellular cytosmears showing a) A cluster of large epithelial cells showing melanin pigment (inset showing higher magnification for the same) with many round cells in the background, b) Round cells arranged in rosette (inset showing higher magnification for the same) Magnification: 10X

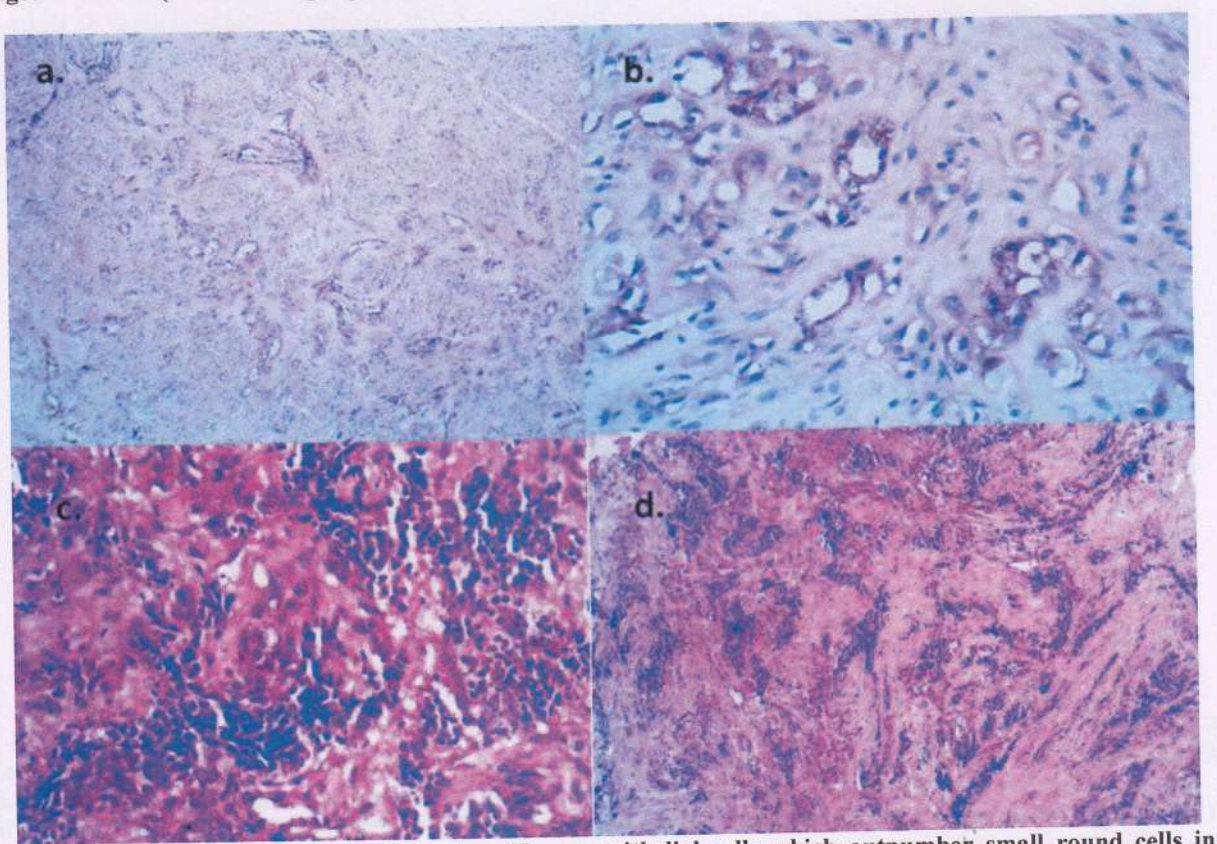

Fig. 3: Case 1, H&E stained sections showing:a)Large epithelial cells which outnumber small round cells in the background, b) Large epithelial cells with melanin pigment with few round cells in the background.
Case 2, H&E stained sections showing: c) Large cells with focal melanin pigment admixed with equal proportion of small round cells, d) Round cells and Large epithelial cells almost in equal proportion. Magnification: a) & d) – 10X, b) & c) – 40X

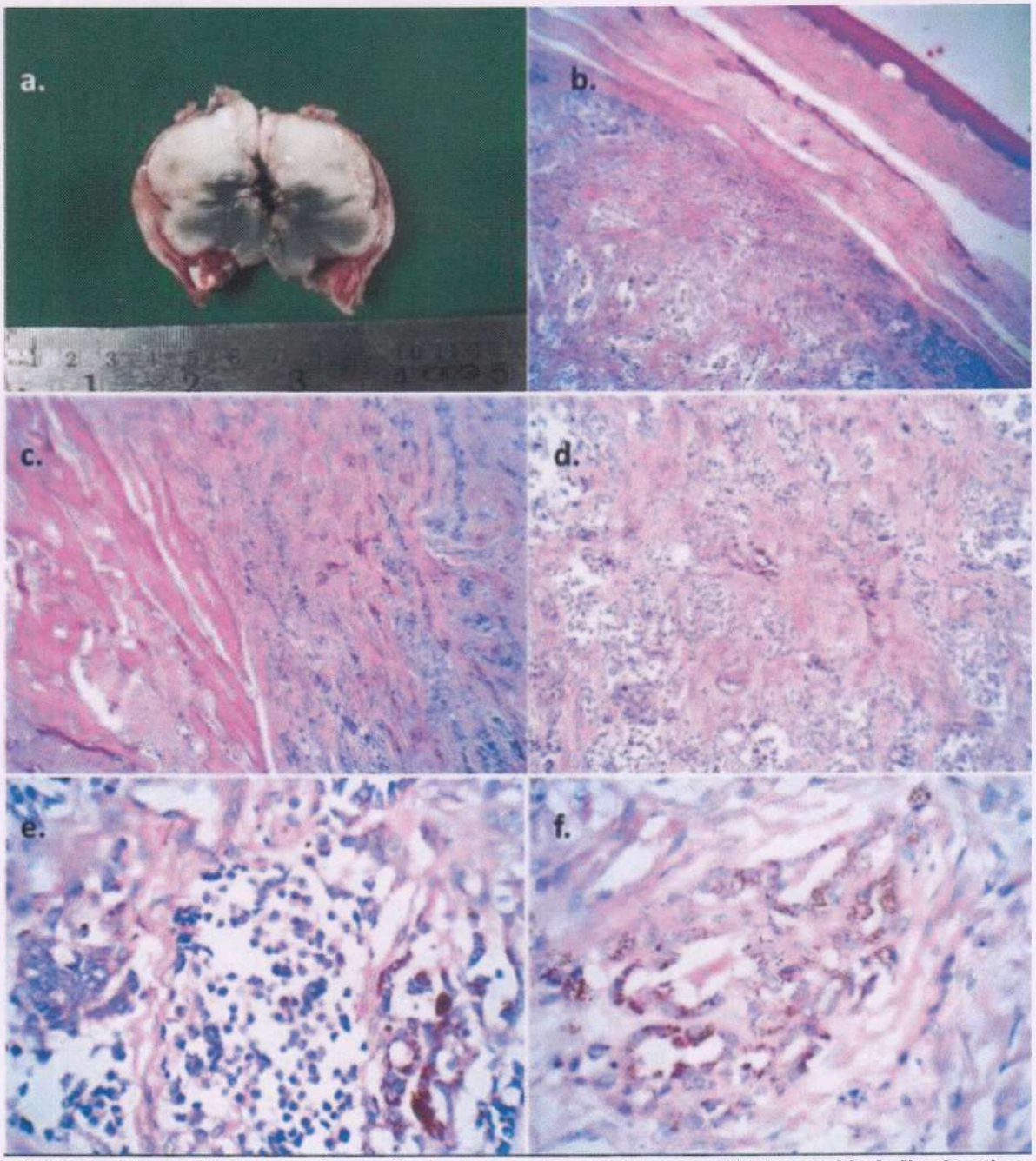

Fig. 4: a) Gross picture of the tumour in case 3, showing a submucosal tumour with brown-black discoloration on cut surface. H&E stained sections showing b) Well circumscribed submucosal tumour with dual population of cells, c) Tumour cells infiltrating bony trabeculae d) Round cells outnumbering large epithelial cells, e) Round cells with admixed large cells, f) Clusters of large epithelial cells containing pigment. Magnification: b) to d) – 10 X, e) to f) - 40 X"

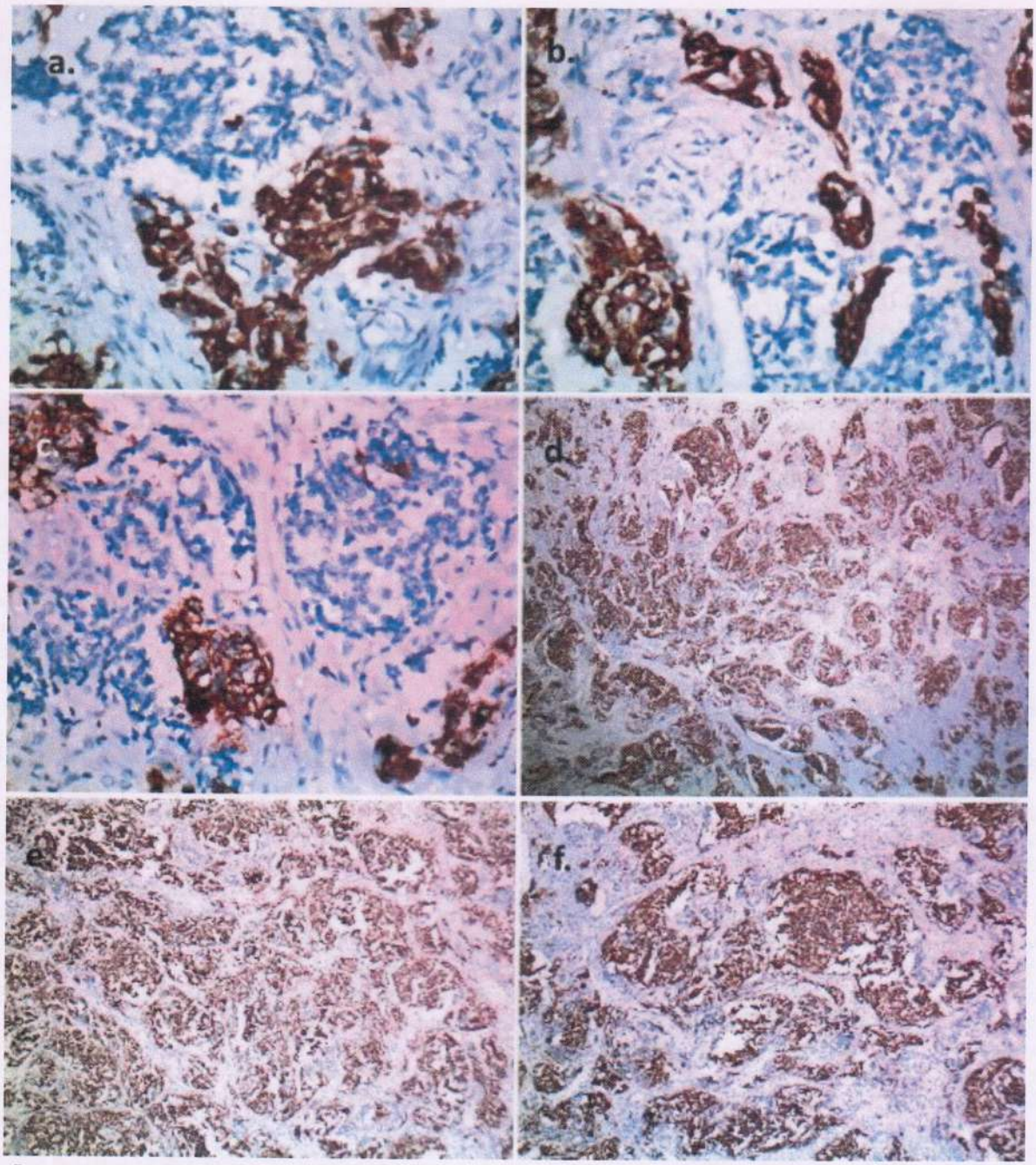

Fig. 5: Large polygonal epithelial cells were positive while small round cells were negative for IHC markers- a) CK, b) EMA, c) HMB45. Small round cells were positive while large polygonal epithelial cells were negative for IHC markers- d) NSE, e) Synaptophysin & d) Chromogranin. Magnification: a) to c) - 40X, d) to f) -10X"

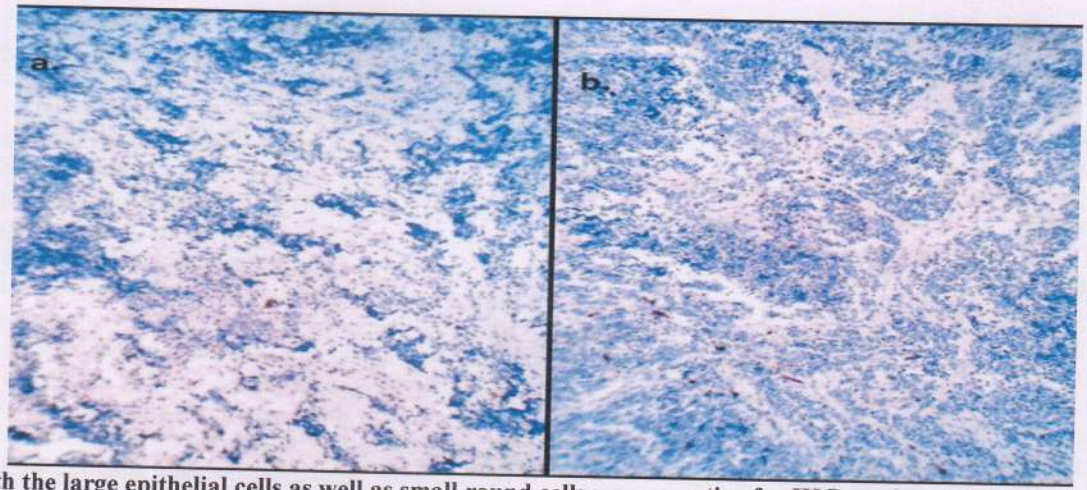

Fig. 6: Both the large epithelial cells as well as small round cells were negative for IHC markers a) S-100, b) Desmin

Discussion

MNTI is defined as a locally aggressive, rapidly growing tumour consisting of biphasic population of small neuroblast-like and larger melanin-producing epithelial cells.[3] The tumour has various synonyms in the English literature, such as Melanotic Progonoma and Retinal anlage tumour, both these synonyms are obsolete and not recommended according to WHO 2017 Classification of Head & Neck Tumours.[3] This variable nomenclature reflects the uncertainty about the tumour's origin, which prevailed for half a century, until Borello and Gorlin[5] proposed the neural crest origin of this tumour in 1966. This was based on the fact that a subset of these patients excreted large amounts of vanillyl mandelic acid (VMA) which is associated with other neuroendocrine tumours.[6]

Neural crest cells are multipotent embryonic cells that ultimately differentiate into various structures, including the odontogenic ectomesenchyme, melanocytes, and neural ganglia. These cells display mesodermal and ectodermal morphologic features at different stages of their ontogeny, explaining the difficulty in deciphering the embryologic origin of these tumours and possibly explaining the biphasic cellular phenotype such tumours display.[6]

More than 90% cases are infants, with a median age of five months.[3] Though rare, some cases are reported in adults also.[3]There are 18 case-series of MNTI in the English literature.[2, 7-23] Since the first description in 1918, 472 cases were reported until last extensive review in 2015 by Rachidi S. et al.[6]

These studies are summarised in the table below.(Table 1)The mean age of presentation in the previous case series ranged from 2.25 to 16.6 months. The mean age in our case series is 5 months. Currently, age at manifestation is considered to be a strong prognostic indicator of MNTI. Infants who manifested within the first 2 months of birth were associated with a high risk of recurrence which generally occurred within 6 months from treatment. In contrast, manifestation from 2.5 to 4 months was associated with an intermediate risk and manifestation after 4.5 months of age had a minimal risk of recurrence.[6]Also, Rachidi et al[6] found that an older age correlated statistically with disease-free survival.

Though no gender predilection was reported by Stowens and Lim (1974),[24] but a male to female ratio of 1.48 was given by Kruse-Losler[25] in 2006 after a review of 140 cases. Also in a review by Rachidi et al[6] which considered all the reported cases of MNTI from year 1918 to 2013, a male to female ration of 1.43 was given. In majority of the previous case series there is male preponderance. According to WHO 2017 Classification of Tumours of Head and Neck,[3] there is a slight male predilection. In our case series too there isamale preponderance (Male: Female ratio of 2:1).

More than 90% of the cases occur in the craniofacial regions, most commonly in the maxilla (>60%), followed by skull, mandible (6%) and brain. Outside Head and neck, the most common sites are the testis and epididymis. Rare cases occur in the ovary, uterus, mediastinum, scapula, and bones and soft tissue of the extremities.[3] In the previously reported case series as well as reviews the most common site is maxilla. In our study the most common site is Maxilla. Johnson R.E.[8] first reported MNTI at femur. As per authors' knowledge there are only six cases of MNTI of femur in the English literature.[8, 26-30] One of the cases of this case series has presentation at femur which is the seventh case to be reported in the English literature.

The MNTI clinically presents as a rapidly growing, painless, expansile, unencapsulated partly pigmented mass, typically in the maxillary region.[31] The pigmentation cannot be always observed through the overlying tissue.It tends to occur as a single lesion. However, multiple lesions have also been reported.[31] Lesion was solitary in all the cases of the present case series. Also, the non-ulcerative bluish-black gingival mass is often confused with an eruption cyst. It might appear malignant due to its rapid growth.[33] MNTI usually carries one of the primary central incisors outward with it, if in the maxilla. It does not carry both central incisors because the tumour arises from one side of midline. The lesion is destructive and radiographs show local irregular resorption of bone and displacement of tooth buds.

The only radiopaque components present are those of the developing teeth buds.[33] In most of the studies including the present one the clinical histories are very similar and consisted of rapidly enlarging mass, most occurring in the first six months of life and discovered by parents.

In addition to the typical clinical presentation, the cytomorphology is also distinctive showing round cells with large polygonal cells in varying proportion. Usually a diagnosis of malignant round cell tumour is made with a differential diagnosis of Rhabdomyosarcoma, Neuroblastoma and NHL. However presence of large polygonal cells containing melanin pigment is clue to the diagnosis of MNTI. Typical cytomorphological diagnosis was done in only one of the three cases of this case series.

Microscopically, the two principle components of this tumour are the cuboidal pigment containing cells and the neuroglia like cells, both the type of cells are known derivatives of neuroectoderm. The cell population consisting of cuboidal epithelial cells have open vesicular nuclei clustered in alveolar or tubular patterns. These cells typically have abundant brown intracellular melanin granules. The second type of cells is small, round and dark with hyperchromatic nuclei and minimal cytoplasm. These cells vanillyl mandelic acid (VMA). These cells aggregate in loose nests or islands againstthe back ground of fibrovascular tissue.[34] The tumour may show infiltration into adjacent bone as seen in the second case of our case series.(Fig. 4c) Fontana stain can be used to highlight the melanin. IHC help in confirmation of the diagnosis in doubtful cases lacking typical histologic features.[35]

On IHC, the large epithelial cells are positive for cytokeratin, EMA, HMB 45, synaptophysin, vimentin and neuron specific enolase. The smaller cells are positive for neuron specific enolase, glial fibrillary acidic protein and synaptophysin.[10] S-100 protein is usually non-reactive.[10] In our case series too there was similar polyphenotypic expression of neural, epithelial and melanotic markers.

The incidence of malignancy is rare and accounts for 2% of all cases. Few reported malignant cases had more mitoses, increased vascularity and focal necrosis. Diagnosis of malignancy is based on increased growth rate, infiltration and metastasis.[4]

The preoperative distinction of this tumour from other round cell tumours of infancy is essential in order to plan complete resection and therefore reducing the possibilities of tumour recurrence.[36] Though high level of urinary excretion of VMA and serum AFP is characteristic of MNTI but it's not always present.[37] Because of the urgent need for surgery, laboratory testing for urinary excretion of VMA was not done in all these three cases.

The differential diagnoses for a rapidly growing mass in the maxillary area or femur for this age group includes Abscess, Haemangioma, Arterio-venous malformations, Epulis, Neuroblastoma, Rhabdomyosarcoma, Melanoma, Ewing's sarcoma, Metastatic retinoblastoma, Lymphoma and Teratoma.

Clinical context can narrow down the differential. Non-neoplastic haemangioma and lymphangiomas have bluish discolorations and a predilection for the head and neck region in children and tend to develop rapidly within a few months after birth.[33] Congenital Epulis is always present at birth, and can be alarmingly large and may interfere with the infant's ability to take feed, as did the lesion reported in our case series.[32] Congenital Epulis is almost always reported to be pedunculated whereas MNTI is usually sessile.[32] Teratomas can be differentiated from MNTI only by histopathology by demonstrating tissues from different germ layers.[38] Neuroblastoma is a malignant tumour occurring in infants and young children, and may arise at any site in the sympathetic nervous system, most commonly in the abdomen. Metastatic neuroblastoma occurs most commonly in the mandible, presenting clinically by the deviation of the mandible on mouth opening, periorbital ecchymosis and Horner's syndrome, which are not seen in MNTI.[39] Ewing's sarcoma is a rare malignant tumour of neuroectodermal origin affecting the skeletal system, with long bones being the commonest location. It is rarely seen before the age of five years. Its occurrence in head and neck is rare and even if it occurs it is more common at mandible than maxilla. Clinically, this tumour is aggressive, characterised by rapid growth and high probability of micro-metastasis at the diagnosis. Whereas MNTI is painless, occurs in infants and most commonly located at maxilla.[40] In the second case of our case series the lesion was present at femur for which we did an IHC marker CD99 to rule out Ewing's sarcoma. Embryonal rhabdomyosarcoma occurs in children less than 15 years of age, clinically these tumours exhibit a fast growth reaching large dimensions and generally painless. Mostly the cases are present in the oral cavity: palate or the tongue. The patient may present with pain, paresthesia, and loss of teeth or trismus as a result of advanced tumour stage, infiltration and location. MNTI can be differentiated by its painless nature, and the most common site of occurrence is the maxilla.[41] Oral mucosa melanomas can be differentiated from MNTI in terms of age of occurrence (fourth to seventh decades) and site i.e. palate. Endemic type of Burkitt's lymphoma occurs in the jaws and facial bones, whereas the non-endemic type occurs at other sites.[42] The mean age of presentation is between 7 and 14 years, whereas MMTI occurs in infants, and both the lesions can be differentiated only by histopathology.[43]

The treatment of choice consists of complete surgical excision with lymph node dissection.[8] The overall incidence of local recurrence is 20% within six months.[3] Even large lesions,[44] or those incompletely excised,[45] can have a good prognosis, but the resection should be thorough because even 5 mm of clearance may be inadequate to prevent recurrence.[46] Recurrence may be the consequence of incomplete removal of the primary tumour, seeding during surgery, or tumour multicentricity.[47]

Rachidi et al[6] stated that the age at diagnosis is an important prognostic marker, where younger patients are more likely to develop recurrence. Based on these findings, he recommended closer monitoring of patients diagnosed within the first 2 months of life, especially all recurrences occur within 6 months from intervention.

MNTI is a benign tumour of neuroectodermal origin with rapid growth potential which makes its early diagnosis crucial to limit its expansion. However, the rarity of this tumour leads to diagnostic delay. As pointed out in this case series, a number of known pathologic entities can present at this age but confirmation of the diagnosis requires histopathological examination and IHC if necessary. No histological feature or biological marker is known to predict behaviour.[3] Any unusual growth in infants that appear inconsistent with normal variation and reported history should be referred in time to a pathologist for assessment and diagnosis. A diagnosis of MNTI should be suspected in any tumour in an infant with round cell morphology and a careful search for large melanin containing epithelial cells will help in the accurate diagnosis. Delay in diagnoses lead to more tissue resection which in turn makes rehabilitation difficult and a costly affair.

Conflict of Interest: None.

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QUALITY ASSESSMENT PROGRAM IN HISTOPATHOLOGY: A PILOT STUDY FROM MAHARSHTRA

SHOBHA AGASHE, ALKA GOSAVI, RAKHEE JAGDALE*, JAYDEEP POL*,
Department of Pathology, Lecturer in Pathology, Govt. Medical College, Miraj, Maharashtra, India*

ABSTRACT

Histopathology reports are important quality assurance tools and evaluation of pathological diagnoses described in them is an integral part of total quality control and quality improvement program. We describe a program based on slide circulation which was aimed at both continuing education to upgrade knowledge and proficiency testing of histopathologists. The performance of the participating pathologists was analyzed and the degree of agreement was also studied. The results showed improvement indicated by rising level of performance in 35.3% of consistent participants and increasing trend in the average score. The degree of agreement was comparatively low (65.29%). The practicability of this program and its acceptability as an EQAS was also investigated.

Key Words: Quality Assurance (QA) in histopathology, proficiency testing, External Quality Assessment Scheme (EQAS).

INTRODUCTION

Quality may be defined as a measure of excellence and is an important aspect of any laboratory. A laboratory must give consistently correct results as the patient is benefited by this. It is also expected that similar results are obtained on the same material at different centers. Various quality control and quality improvement programs have been advocated to measure the efficiency of techniques and proficiency of pathologists[1-14]. In the literature, the quality control programs in clinical pathology and hematology are now widely accepted throughout the world; but histopathologists have been slow to adopt this concept. The reluctance is usually ascribed more to the belief that evaluation of histopathological diagnosis is impracticable as it deals with opinions and is largely subjective. The diagnostic opinions which are often predictions of behavior of a morbid process and verified only by future events, may seem objectively untestable. Nevertheless, the likelihood of correct diagnosis generally reflects the professional training, experience, good judgement and competence of interpreter and hence evaluation in histopathology should be possible if meaningful and reliable methods are developed.

Quality assurance in histopathology is desirable and includes the evaluation of both processes and outcomes[7]. The processes are concerned with the receipt, description and processing of specimens while outcomes include pathological diagnoses and the reports that describe them. It also consists of timely clear communication and schemes for quality assessment in histopathology which have bee tried in the past. For any quality assurance program it is desirable to maintain a document that describe it and should include the jouunalistic elements c "Who, what, when and how"[7]. In this article, w report the result of a study consists of circulation c slides at state level and evaluation of performanc of the participating pathologists. The study i similar to Australian study[1] and West of Scotlan study and fulfills the design consideration recommended by National EQA forum U.K[6].

MATERIAL AND METHODS

Maharashtra state chapter of Indian Associatio of Pathologists and Microbiologists was conductin slide circulation project for last several years. It wa an important avenue of continuing educationa program. But in spite of good histopathologi material, the participation was not active and th approach was quite casual. To make this projec more attractive scoring system was added anc some of the circulated slides having diagnosti controversies were identified and these wer discussed in a histopathlogy slide seminar at th Annual Conference. The results of this exercis were declared and the awards were given to the to scorers during this annual meet. This ventur aroused great interest in the participatin pathologists and more efforts were taken to reac the top. The team lead by one of the authors (S Agashe) participated in these programs and receivec first rank with an award of 'Excellence i Histopathology' twice. Later on in 1997, she wa entrusted by the state chapter authorities to conduc

this program for next 3 years. This challenging work was accepted willingly and enthusiastically by her.

We conducted this program for 3 years. It consisted of circulation of histopathology slides along with evaluation of the diagnoses offered by participating pathologists. Each year, all the academic centers and private pathologists, keeping academic interest from Maharashtra state were requested to contribute 3 to 4 interesting histopathologic lesions from their routine work. This was the first communication in which detail instructions were given for selecting the lesion and sending the slides. They were requested to prepare and send 25-30 slides from the same tissue block-each slide showing the representative lesion. The diagnosis must be possible by studying one or two provided sections. Lesions requiring many sections to make a diagnosis or which need further studies like immunohistochemistry were included for the circulation, but they were not considered for evaluation. The diagnosis of these cases was not revealed until such cases were presented and discussed by the contributors, in the slide seminar during the Annual Conference. The contributors were also asked to send the slides along with brief clinical details, relevant investigations, gross findings but no diagnosis. all the slides were collected by the convenor. The slides were coded. Names of the contributors were not disclosed. This was to have complete unbiased opinion on the slides which may be associated with the name of the specialized center or developing institute. The slide sets along with clinical information were distributed to all the contributors. This was the second communication which invited list of diagnoses on these slides in a span of 2 months. Along with this, contributors were requested to send the drafted report (microscopic findings) with the diagnosis of the cases, which they had contributed.

Most of the contributing centers participated in the evaluation program but there were few dropouts. There were 30-33 contributors and 23-24 participants every year. Only 17 centers were consistent in sending the list of diagnosis for 3 consecutive years. After receiving list of diagnosis from all the participants for assessment, a list of contributors' diagnosis was sent to all.

The assessment was done by the convenor using contributors' diagnosis as the reference diagnosis. the answer sheets submitted by the participants were also coded. During assessment, the degree of agreement on all the slides was studied which was denoted by Facility Index (F. I.). Facility Index points out the easiness of the slide and is a good indicator of agreement. e.g. a slide with 100% F.I. indicates disagreement. Slides with low F.I. i.e. <30% were reopened and the contributors were requested to present and discuss these cases in a slide seminar during the Annual Conference.

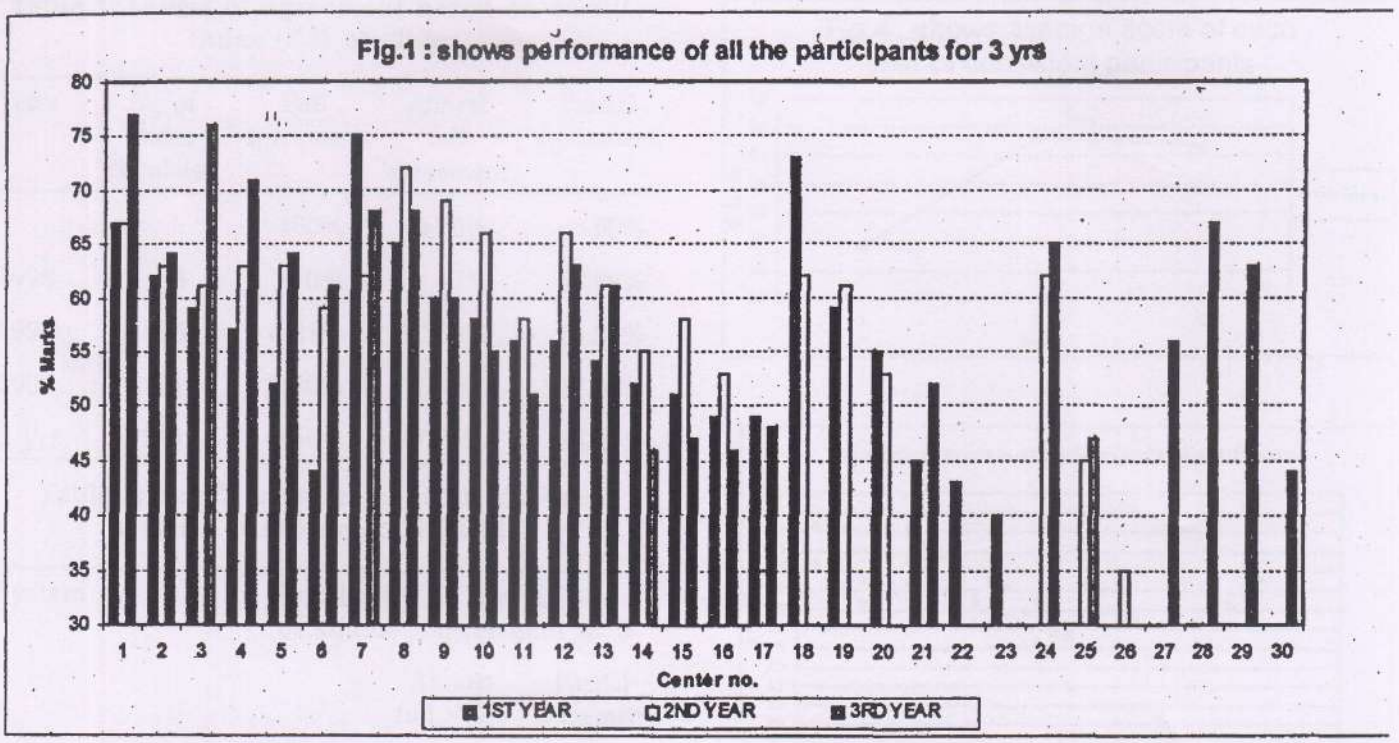
It was very interesting to note an almost unanimous opinion by majority of the participants on certain slides, which was different from that of the contributor. Obviously such slides had low F.I these slides were studied and an Agreement Index (A.I.) was calculated. A. I. means the percentage of participants agreeing upon one diagnosis which is different from that given by the contributor. In other words A. I. indicates consensus opinion.

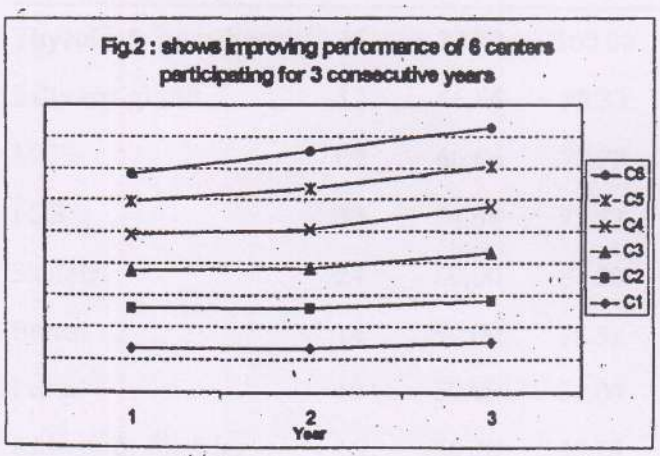
While calculating the marks of a particular center the slides contributed by the center and the slides for discussion were deleted and then mark sheet of each participant was prepared. In this way, the performance of the participants was judged and the degree of agreement on all slides was analyzed. The results were declared during the Annual Conference and certificates and awards were given to the top scorers. At the end of each year, a file was sent to all the contributors, which contained drafted report of each case along with the diagnosis, facility index of each case with graphical presentation, A.I when it was > 70% suggesting consensus diagnosis score of the said center and graphical presentation of the performance of all the participants. This was to make them able to assess their own performance in relation to average but keeping the secrecy of the marks obtained by other participants.

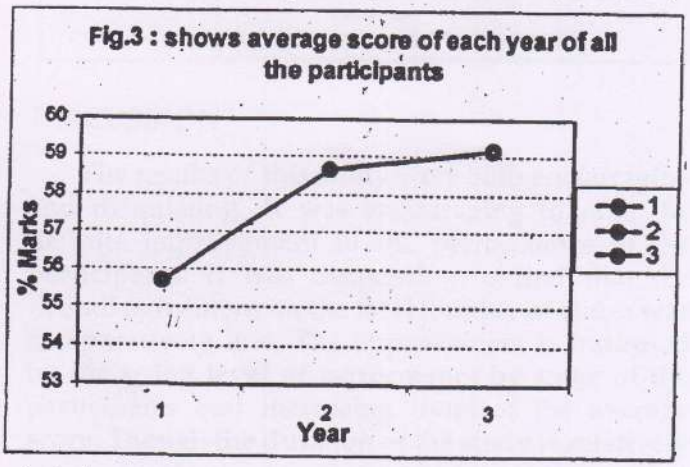
OBSERVATIONS AND RESULTS

The results of this pilot study consist of analysis of performance of the participants and the degree of agreement on the slides.

Performance of participants: The number of centers participating for assessment varied each years which was 23 for the first and second year and 24 for the third year. As the centers participated variably, the total number of centers participating for three years were 30. Only 17 centers were consistent in participating for all the three years (Fig 1). This also shows that there were few dropouts who showed either poor performance (center no 21,22and 23) or deterioration in performance (center no 18,20). There were 4 new participants in the third year indicating the







increasing acceptability and popularity of the program. It was interesting to note that out of the consistent 17 centers, 6 (35.3%) showed improvement in their performance in successive years (Fig 2). The average score of each year was calculated considering all the participants in that year, which showed an increasing trend (Fig 3). The average score of each year of the consistent participants was also calculated which showed a notable increase in the second year and a negligible decline in the third year (Fig 4). A scattergram of performance (Fig.5) of the participants was plotted. The centers with poor performance can be easily identified as they fall outside the main cluster.

Agreement on slides: The degree of agreement based on facility index (F.I.) of slides was also analyzed. A high value of F.I. indicates good agreement. The slides were studied to look for the level of agreement (Table 1). Though, there were very few slides with full agreement (i.e. 100% F.I.), the number of such cases increased each year. The other levels of agreement i.e. almost full and partial agreement also increased in the second year and remained almost same in the third year. The overall agreement achieved on 291 slides was 65.29%, which means >50% of participants agreed on 65.29% slides. Similar levels were calculated for benign and malignant tumors which revealed almost equal agreement viz. 63.63% and 64.22% respectively. Table no 2 shows the extent of agreement reached on the slides from different tissues. The greatest

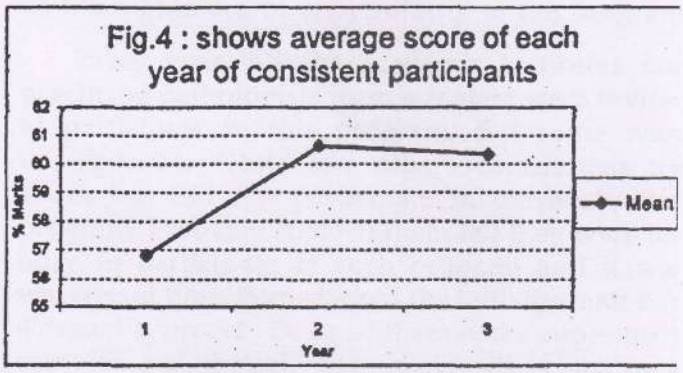
Table 1: Levels of agreement based on Facility Index (F.I) of slides.

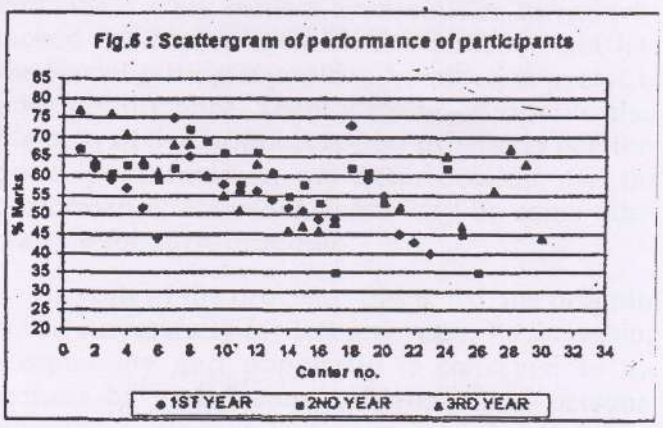
Years	No of slides circulated	Full agreement	Almost full agreement	Partial agreement
		100%	>70%	>50%
1998	95	0%	40%	57.89%
1999	95	6.31%	51.50%	70.53%
2000	101	9.90%	51.50%	67.33%
3 yrs	291	5.50%	47.76%	65.29%

Table 2: Levels of agreement for different systems based on F.I. of slides

System	Total no of slides	Levels of agreement in %	
		Almost full >70%	Partial agreement >50%
Thyroid & parathyroid	11	72.72	100.00
Salivary gland	12	66.66	83.33
MGS	09	66.66	77.77
FGS	33	54.54	72.72
Skeletal	24	50.00	87.50
Breast	14	50.00	78.57
Lung	10	50.00	60.00
Kidney & Bladder	16	50.00	68.75
Skin	31	48.38	61.29
Nervous system	17	47.05	76.47
GIT & Liver	46	45.65	60.86
Infective etiology	23	47.45	65.21
Lymph node	22	45.45	68.18
Soft tissue	22	22.72	36.36

degree of agreement was achieved on lesions of thyroid, salivary gland and male genital system while least on lymph node, GIT and soft tissue tumors. This study is an ongoing process and we expect database for analysis in future.





DISCUSSION

The results of this study were both encouraging and disquieting. It was encouraging to note the definite improvement in the performance of the participants. It was disquieting to find that the overall agreement on the total number of slides was comparatively low. The improvement is indicated by the rising level of performance by some of the participants and increasing trend of the average score. Though the duration of the study is relatively short to draw any inference, we hope that continuation of such a program will increase awareness about the proficiency and will definitely improve the quality of histopathologists in future.

In histopathology when a group of pathologists agree on a diagnosis, it is likely to be the correct one. Determination of accuracy is practically a matter of consensus. Substantial agreement among pathologists though not an absolute measure of accuracy is effectively the best available measure of accuracy. Various statistical methods have been used for measuring levels of agreement[15,16]. We have used a simple method for calculating levels of agreement and have emphasized on analyzing various reasons for disagreement. We agree with Sherwood and Hunt who in their concluding

remarks have said that studies based on statistical analysis amply show that pathologists differ but such study would no longer be an EQAS. Our study reveals low level of agreement as compared to others (Owen -77%, Penner-78%, Sherwood_77%, Husain-87%). The reason for this may be that we have assessed the slides assuming contributor's diagnosis as the correct diagnosis. while others have considered consensus opinion or the expert panel opinion as the final diagnosis. another reason for the discrepancy may be that the slides were not identified as those of the general pathologists' interest and those of the specialist pathologists' interest. The concept of specialist pathologist is new to Indian scenario, except for few centers.

Most of the pathologist are general pathologists dealing with al the branches of histopathology. e.g. a general pathologist is unlikely to be conversant with skin adnexal tumors which on the other hand is a day to day affair for a dermatopathologist. The pathologists participating in this programs were from metros as well as from general hospitals in small towns. This might have affected the agreement level.

While analyzing the causes of low agreement level it was also pointed out that at times the diagnosis offered by the contributor was wrong or the terminology used was improper or vague. This was indicted by disagreement on such slides by all the participants. This may be a fallacy of this study but we though it was necessary to increase the palatability of the program, especially during preliminary stages of introduction of any EQAS in histopathology in this region.

It was also observed that in spite of proper instructions to the contributing pathologists, some of the slides included for assessment were very rare or difficult lesions and needed further studies to arrive at a diagnosis. Naturally the agreement level for these slides was low. Some of such controversial slides were reopened and were reviewed and discussed at the annual meet. The low agreement level also reflects on the performance of the participants. We therefore like to suggest that a panel of experts should screen the slides before they are accepted for circulation. Contributor's diagnosis should not be taken as a reference diagnosis for the assessment of the participants. Instead, participants should be evaluated against expert panel opinion or consensus opinion meaning thereby the diagnosis offered by more than 50% of the participants. Though all this may be the wishful thinking, it gives us the nightmare of unpopularity of the program

Every year, all the academic institutes anc practicing pathologists from our state were invitec to participate in this program. But some wer unresponsive while few others contributed th slides but did not participate in the evaluatio program. Probably some of them felt they were to busy to participate in such program and it wa wastage of time. Some lacked the initiative and hac a casual approach. Some of them had a superiorit complex and thought their diagnosis is final anc cannot be evaluated by anyone else. At the othe end, there were centers from smaller towns wh lacked confidence more than experience and hac the fear of getting exposed or humiliation in case o poor performance. There were few dropouts also Majority of the dropouts appear to because of eithe poor performance or deterioration in th performance. However, there may be some othe reasons for such dropouts.

In spite of the problems discussed, the progran is run successfully for last few years. Its increasin acceptability and popularity is conveyed to th authors by verbal communications and persona letters by various pathologists. It is also indicatec by newer entries.

The project outlined in this paper involves a slide club run at a state level along with evaluatior of participants. Our scheme does not directl evaluate the quality of performance as it is actuall practiced and as it directly affects patients care, as advocated by Penner. The use of randomly selected material from patient file is advised by him so tha routine diagnostic material is tested. However, this does not arouse interest in the participants and may not be of any educational value. The organizers of West of Scotland scheme are of the opinion that the response is better to material that the participants consider both of interest and having educational content. We are of the same opinion and feel that the results of our study will indirectly reflect on day to day practice.

CONCLUSIONS

Our scheme fulfils most of the design considerations recommended by the National EQA Forum, U.K, regarding the selection of material, qualification of organizer, number of participants and reporting of results. The project is a good educational exercise for consultants and trainee pathologists fulfilling the aim of continuing medical education. It allows the histopathologist to monitor

his/her performance in relation to the average. It is possible to identify the bad performer so that some remedial action can be taken. It also allows the participant pathologist to compare his reporting style and diagnosis with his colleagues. The discussions on controversial slides also help in continuing education.

In conclusion, we feel that this type of project will be a dual track educational and quality assurance program and with few modifications can be adopted as a statewide EQAS in histopathology, also supplementing the internal audit.

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Reprint Address : Dr. Alka Gosavi. M.D (Pathology)
798, Behind Dr. Limaye's Eye Hospital,
Vishrambag, Sangli. 416415

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ORIGINAL ARTICLE

Secondaries of Synovial Sarcoma in Vagina: A Diagnostic Dilemma

Rakhi V. Jagdale[1] · Jaydeep N. Pol[2] · Zeba Nisar[2] · Sachin J. Patil[1] · Abhijit S. Pethkar[1]

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Abstract

Objective/Background Synovial sarcoma (SS) is a clinically, morphologically, and genotypically distinctive neoplasm, accounting for approximately 10% of soft tissue sarcomas, which usually afflicts young-to-middle-aged adults and typically occurs in the deep soft tissues of the extremities, particularly the thigh and knee regions. The aim of this study is to describe a case of metastatic synovial sarcoma of vaginal wall with primary in the thigh. This is the first report documenting its occurrence in the vagina as a metastatic tumour. This is the first case of vaginal synovial sarcoma in the Indian literature.

Method A 57-year-old female presented with vaginal bleed. A thorough workup was done including clinical examination, histopathological examination of the biopsy from vaginal mass, IHC, and review of slides from the thigh swelling. A systematic literature review was conducted by searching the PubMed and National Centre for Biotechnology Information database.

Result Physical examination revealed fleshy mass at the anterior vaginal wall and a thigh swelling. On histopathological examination of the vaginal mass followed by IHC, a diagnosis of synovial sarcoma was made and the slides of the thigh mass were reviewed which revealed similar morphology and IHC profile. Hence, a final diagnosis of synovial sarcoma of thigh with metastasis to vaginal wall was made. Four case reports of primary SS of the vagina were found on reviewing the literature.

Conclusion To the best of our knowledge, this is the first report documenting the occurrence of synovial sarcoma in the vagina as a metastatic tumour and overall fifth report to document its occurrence in the vagina. All other four previously reported cases were primary SS of the vagina.

Keywords Synovial sarcoma · Vagina · Metastatic · TLE-1

Introduction

Synovial sarcoma (SS) is a clinically, morphologically, and genotypically distinctive neoplasm, accounting for approximately 10% of soft tissue sarcomas, which usually afflicts young-to-middle-aged adults and typically occurs in the deep soft tissues of the extremities, particularly the thigh and knee regions [1].

Synovial sarcoma may sometimes arise at unexpected sites, including the vulva in the female genital tract [2]. This is, to the best of our knowledge, the first report documenting its occurrence in the vagina as a metastatic tumour and overall fifth report to document its occurrence in the vagina, all other four being primary tumours.

Materials and Methods

A 57-year-old female referred from a gynaecologist presented with per vaginal bleed for 15 days.

As per the patient and medical records shown by her, she developed a swelling at the upper part of the right thigh with features of deep vein thrombosis 14 months back. The swelling rapidly increased in size within 15 days, and the patient had limping gait for the same. She visited a clinician 3 months after the development of swelling, and CT scan of the thigh, trucut biopsy of thigh swelling, and CT scan and chest X-ray were performed. Chest CT and X-ray revealed lung nodules. The trucut biopsy was then reported as spindle cell sarcoma, for

✉ Zeba Nisar
dr.zeba.ahmed@gmail.com

[1] Shri Siddhivinayak Ganapati Cancer Hospital, Miraj, India

[2] The Oncopathology Centre, Mahatma Gandhi Cancer Hospital, Miraj, India

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which she was given palliative chemotherapy and radiotherapy. Chemotherapy included injection Adriamycin 75 mg for 21 days, injection IFOS 1.2 gm/m^2–1.8 gm, and injection Mesma 3 ampoules at 0, 4, and 8 h for 21 days × 3 cycles. Following this treatment, the right thigh swelling reduced in size but bilateral lung nodules persisted on CT. Hence, 12 cycles of radiotherapy were given. Five months after radiotherapy, she developed vaginal bleed.

Clinical examination, pelvic USG, and histopathological examination of the biopsy from the vaginal mass were done. Pathological examination was performed on representative fixed tissue samples embedded in paraffin and stained with H and E. The following histopathological features were evaluated:

- Biphasic pattern with spindle and glandular elements
- Haemangiopericytomatous pattern
- Mitotic activity

Histopathological examination was followed by immunohistochemistry evaluation. IHC markers used were CK, EMA, SMA, CD99, Bcl-2, CD56, TLE-1, desmin, S-100, and CD34. For immunohistochemical analysis, paraffin-embedded sections cut at 5 mm were deparaffinized and rehydrated and peroxidase blocking was done with 3% H_2O_2 freshly prepared. Antigen retrieval was performed for 10 min at 90 degrees treatment in EZ-Retriever System v.3 manufactured by BioGenex. The sections were then stained with automated stainer i6000 manufactured by BioGenex. All antibodies were ready to use; hence, dilution was not mentioned. Intensity, distribution, and source of all the antibodies used are summarized in Table 1. Slides from thigh swelling were also reviewed.

Systematic Review

A systematic literature review was conducted by searching the PubMed and National Centre for Biotechnology Information database using the keyword search term Synovial sarcoma of the vagina and the Medical Subject Heading term synovial sarcoma of the vagina. All cases published hitherto were included. Excluded were reports published in a language other than English and without an English-language abstract. This yielded a total of four publications (Table 2). This analysis included gender, age at diagnosis, size, occurrence (whether primary or metastatic), clinical history, treatment, and follow-up.

Ethics: Procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 2000.

Results

On gynaecological examination, there was a fleshy mass measuring 4.5 × 4 cm at the anterior vaginal wall and urethral region which bled on touch. The swelling did not extend till cervix though it involved the urethral region. Pelvic USG revealed a fleshy mass at the anterior wall of the vagina with endometrial fluid collection. On general examination, there was a deeply situated swelling at the upper part of the right thigh measuring ١٥ × ٨ cm. According to the patient, this swelling was present for 14 months. Clinical photograph could not be produced as the patient denied giving consent for the same.

CT abdomen pelvis contrast study revealed multiple metastases in the basal lung, large soft tissue mass of size 10.8 × 10.5 cm in the right groin and the upper thigh with areas of calcification and minimal sclerosis, and erosion of pubic bone and ramus.

Biopsy of the vaginal mass done outside reported it as Poorly differentiated malignant tumour? Squamous cell carcinoma.

On resectioning of the received blocks, microscopic examination of the haematoxylin-and-eosin-stained sections from the vagina showed an ulcerated tumour composed predominantly of spindle cells with oval to elongated hyperchromatic nuclei and scanty cytoplasm (Fig. 2c) arranged in fascicles and bundles. In areas, the tumour

Table 1 Distribution, intensity, and source of antibodies used

Sr.	Antibody	Distribution	Intensity	Source
1	CK	Cytoplasmic	Moderate	BioGenex
2	EMA	Membranous and cytoplasmic	Moderate	BioGenex
3	SMA	Cytoplasmic	Moderate	BioGenex
4	CD 99	Membranous	Strong	Dako
5	bcl-2	Cytoplasmic	Strong	BioGenex
6	TLE-1	Nuclear	Strong	Cell Marque
7	Desmin	Cytoplasmic	Negative	BioGenex
8	S-100	Cytoplasmic and nuclear	Negative	BioGenex
9	CD34	Membranous	Negative	BioGenex

Table 2 Previous case reports of synovial sarcoma of the vagina

Sr.	References	Age (years)	Size	Diagnosis	Occurrence	History	IHC	Treatment	Follow-up
1	Okagaki et al. [8]	24	3 × 2.5 × 2 cm	Synovial tumour	Primary	Mass for 2 years	ND	Radical hysterectomy, with bilateral salpingectomy, partial vaginectomy and left pelvic lymph node dissection	ND
2	Pelosi et al. [9]	40	5 × 4 cm	PDSS	Primary	Abnormal vaginal bleed and anaemia	Vimentin, EMA, CD99, CK7 and 19, bcl2, and calretinin +	Wide local resection of anterior vaginal wall	Lung metastasis after 11 months
3	Minig et al. [10]	40	5.5 cm	PDSS	Primary	Necrotic polypoidal lesion at vagina	c/w PDSS	Neoadjuvant followed by radical surgery with post-op brachytherapy and radiation	Lung metastasis at 11 and 16 months. Successfully removed both the times and disease free after 24 months
4	Sumathi et al. [5]	43	8 cm	PDSS	Primary	Long history of mass	Focal CK, EMA+; CD99, bcl-2, and focally+	Resection with hysterectomy. Local recurrence after 2,4,6, and 8 years, resected and given palliation	DOD after 8 years
5	Present case	57	10 × 8 cm	Biphasic SS	Secondary	Vaginal mass with bleeding for 15 days. Thigh swelling for 2–3 years	CK+ EMA+ SMA+ CD99+ Bcl2- desmin-S100-CD34- CD56+ TLE1+	Resection of vaginal mass followed by palliative chemotherapy for thigh mass	DOD after 2 years

showed haemangiopericytomatous pattern (Fig. 1b). Increased mitotic activity was noted (> 15/10 hpf) (Fig. 2b). In focal areas, the tumour also exhibited round cell morphology. The tumour also revealed clusters of cells with epithelial morphology arranged focally in glandular pattern. Areas of haemorrhage and tumour necrosis were also noted. With this biphasic morphologic pattern, a differential diagnosis of carcinosarcoma (malignant mixed Mullerian tumour), SS, malignant mixed tumour, and sarcomatoid carcinoma was made.

On immunohistochemistry evaluation, the tumour cells expressed CK, EMA, SMA, CD99, Bcl-2, and CD56 and showed bright nuclear expression for TLE1 (Fig. 3). The tumour cells were negative for desmin, S-100, and CD34 (Fig. 4). With this morphology and IHC profile, a diagnosis of synovial sarcoma was made on review. The slides of the

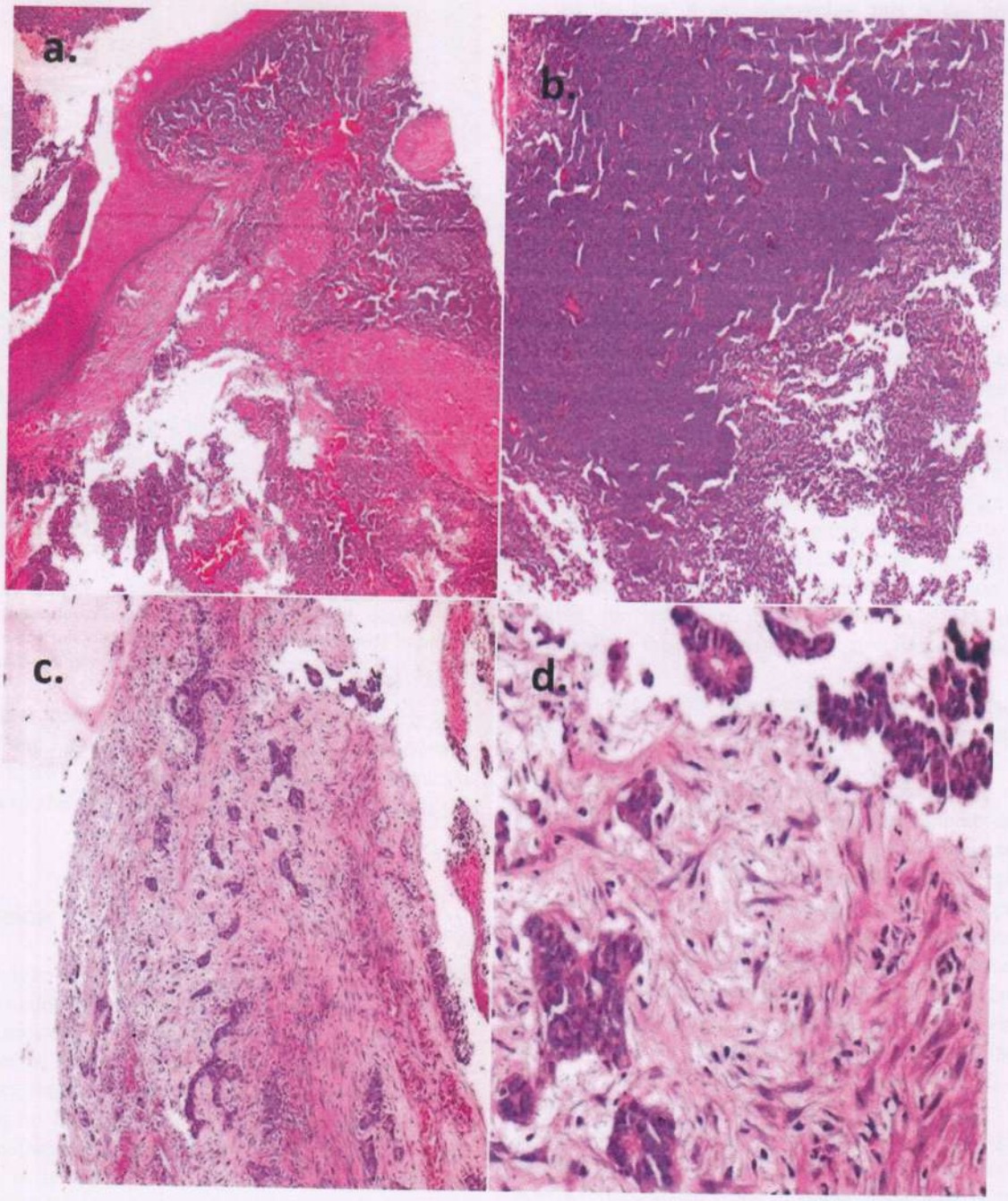

Fig. 1 H&E-stained sections from the vagina showing a tumour: a submucosally located, b spindle cell element with haemangiopericytomatous pattern, c, d showing glandular differentiation. Magnification: a ×4, b, c ×10, d ×40

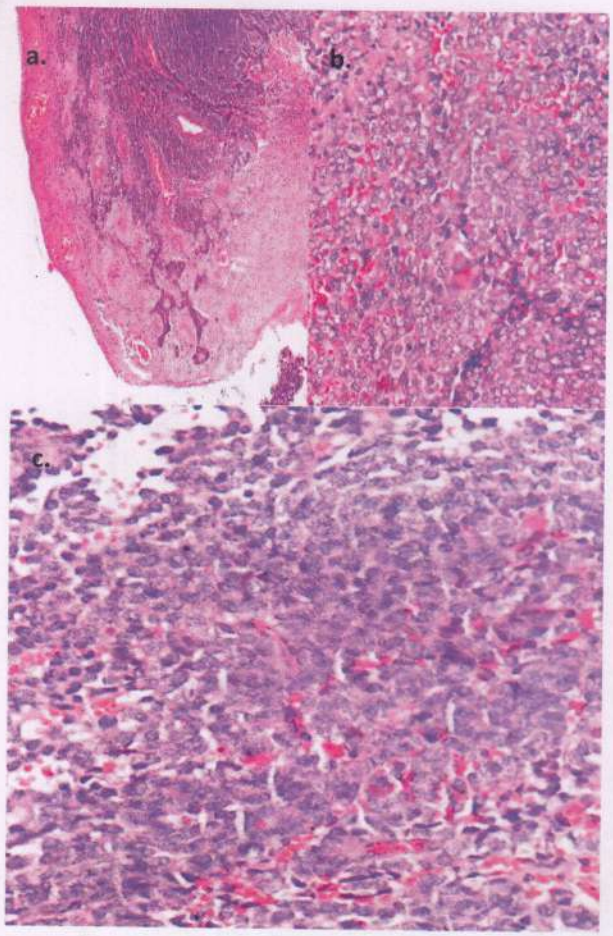

Fig. 2 H&E-stained sections from the vaginal tumour revealed: **a** biphasic pattern with spindle and glandular elements, **b** tumour cells with increased mitotic activity, **c** oval spindle cells with hyperchromatic nuclei and scanty cytoplasm. Magnification: **a** ×4, **b**, c ×40

thigh mass were reviewed which revealed similar morphology and immunoprofile (Fig. 5). Hence, on reviewing clinical history and slides, a final diagnosis of synovial sarcoma of the thigh with metastasis to vaginal wall was made.

Discussion

Primary synovial sarcomas of the vagina are very rare, grouped under "other rare tumours" category of "Miscellaneous tumours of vagina" according to the WHO 2014 classification of tumours of female reproductive organs. Secondary tumours of the vagina are defined as tumours spreading to the vagina from other anatomical sites by direct extension, implantation from primary pelvic tumours, or lymphovascular dissemination. Among these secondary tumours, synovial sarcomas have not been mentioned in the WHO 2014 classification of tumours of female reproductive organs [3]. Synovial sarcoma is defined as a mesenchymal tumour, which displays a variable degree of epithelial differentiation, including gland formation, and has a specific chromosomal translocation t(X; 18) (p11; q11) that leads to formation of a SS18-SSX fusion gene [4].

There are 16 cases of synovial sarcomas reported in the English literature, occurring in the female genital tract including vulva, vagina, and fallopian tubes [5–7, 10].

To the best of our knowledge, this is the first report documenting its occurrence in the vagina as a metastatic tumour and overall fifth report to document its occurrence in the vagina. All other four previously reported cases were primary SS of the vagina. This is the first case of vaginal synovial sarcoma in the Indian literature. Previously reported cases of synovial sarcoma in the vagina are summarized in Table 1.

Schiffman et al. [11] reported a case of biphasic synovial sarcoma in the vaginal wall in a 49-year-old female which on further investigations was found to be extending from a thigh tumour. The author labelled it as vaginal extension of SS from the thigh; hence, we have excluded it from the literature of secondary SS of the vagina. The patient was given orthovoltage irradiation of the left hip, and she died within 5 months of appearance of symptoms. Also, the author mentioned that in the case of malignant vaginal tumours, the possibility of spread from an extravaginal site should always be considered.

Synovial sarcomas can develop at any age [4]. In the previously reported cases of synovial sarcomas of the vagina, the mean age of occurrence is 36.75 years. In contrast to this, the patient in the present case aged 57 years.

Mean size of the tumour among the previously reported cases is 5.37 cm, while that in our case report is 4.5 × 4 cm.

Morphologically, most synovial sarcomas are characterized by a highly cellular, monotonous spindle cell proliferation, at times deceptively bland, either throughout the lesion (monophasic type) or admixed with an epithelial component (biphasic type). A dual mesenchymal–epithelial differentiation is also evident immunohistochemically in most monophasic variants; they typically show coexpression of vimentin, cytokeratins, and epithelial membrane antigen (EMA) [12]. Other markers which have emerged are CD99, bcl2, calponin, and TLE1 [13]. In the case reported herein, the tumour cells expressed CK, EMA, SMA, CD99, Bcl-2, CD56, and TLE1.

Most synovial sarcomas fall into the morphologic categories of biphasic, monophasic (the most common), and poorly differentiated types, the latter characterized by areas of high cellularity, nuclear pleomorphism, numerous mitoses, necrosis, and round cell morphology (seen in 75%

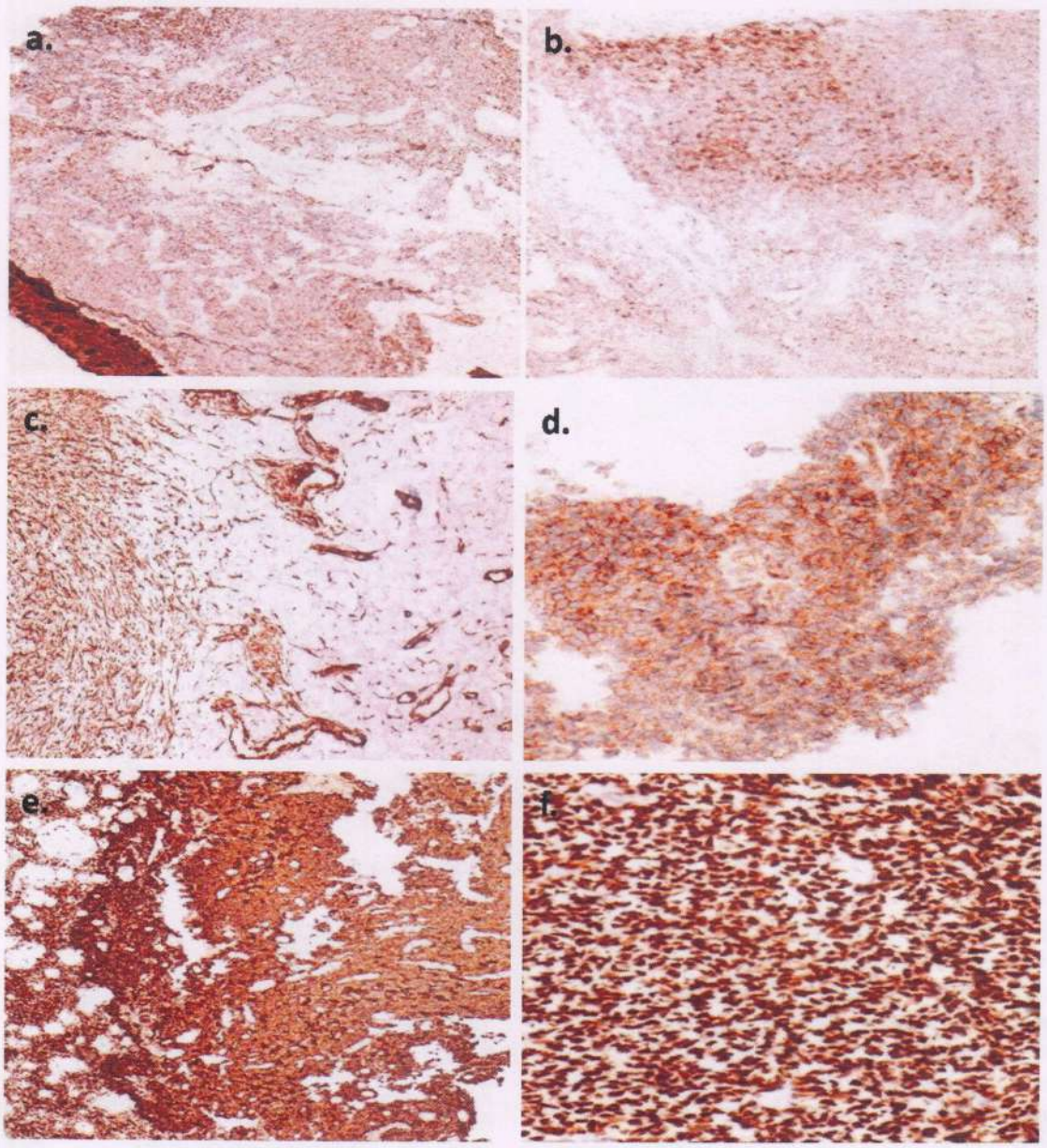

Fig. 3 Tumour cells expressed the following IHC markers: **a** CK, **b** EMA, **c** SMA, **d** CD99 [membranous positivity], **e** Bcl-2, and **f** TLE-1 [nuclear expression]. Magnification: **a**–**c**, **e** ×10, **d**, **f** ×40

of the previously reported cases of vaginal synovial sarcomas), and areas of typical biphasic or monophasic synovial sarcoma. Purely epithelial variants are extremely rare [12]. Those synovial sarcomas reported in the female genital tract have been a mixture of biphasic, monophasic, and poorly differentiated (Table 1). The case reported herein is of biphasic type.

The differential diagnosis of synovial sarcoma in the vagina includes several spindle to small round cell tumours, but leiomyosarcoma (accounting for the most common histology in single tumour series in the vagina [14]), the spindle cell variant of squamous cell carcinoma, and the rare mixed tumour of the vagina, either benign or malignant [8], represent the most important and difficult differential diagnoses. The chief differential diagnoses of synovial sarcoma in the vulvovaginal region are somewhat different from those in other locations and depend largely on whether the tumour is monophasic or biphasic [5]. The biphasic pattern with a high-grade spindle cell mesenchymal component admixed with epithelial elements raises the possibility of a carcinosarcoma (malignant mixed Mullerian tumour). Most carcinosarcomas in the female genital

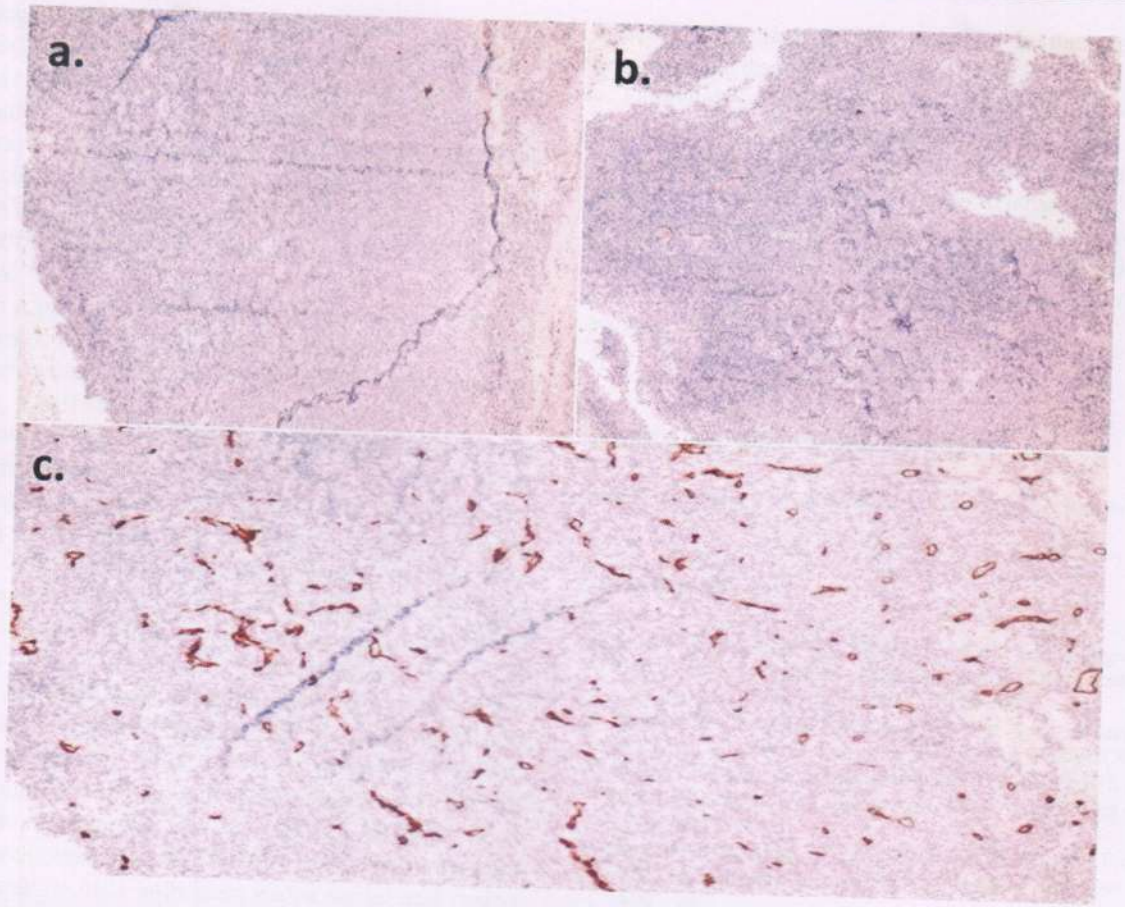

Fig. 4 Tumour cells were negative for: **a** desmin, **b** S-100, and **c** CD34. Magnification: **a**–**c** ×10

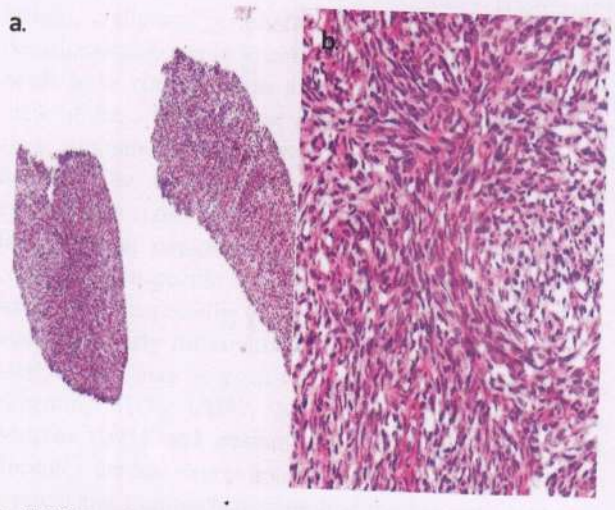

Fig. 5 H&E-stained sections from the thigh swelling revealed: **a**, **b** monophasic spindle cell sarcomatous morphology. Magnification: **a** ×4, **b** ×40

tract involve elderly women and arise in the uterus but may spread to involve the vulva or vagina. In carcinosarcoma, both the epithelial and mesenchymal elements are typically of a higher grade and more anaplastic than in most synovial sarcomas, although there may be an overlap. In both the tumours, there is typically a sharp demarcation between the two components and there may be an immunohistochemical overlap. Heterologous mesenchymal elements in the form of malignant cartilage, bone, or skeletal muscle are a feature of some carcinosarcomas; however, cartilaginous or osseous elements are also rarely present in synovial sarcoma [15]. Mixed tumour of the vagina (spindle cell epithelioma) may also enter the differential diagnosis of biphasic synovial sarcoma [16]. This lesion typically occurs in premenopausal women and arises close to the hymenal ring in the lower vagina. Mixed tumour of the vagina is composed of an admixture of well-differentiated epithelial elements, often of both squamous and glandular types, and spindle-shaped cells. The spindle cell component usually predominates over the epithelial elements, and both components are usually bland without atypia or mitotic activity. In most instances, the spindle cell element in the mixed tumour of the vagina shows diffuse immunoreactivity with cytokeratin markers [17].

Endometriosis may be considered in the differential diagnosis of a biphasic synovial sarcoma in the

vulvovaginal region [18], although the glands in synovial sarcoma do not typically resemble endometrioid glands. Moreover, endometriosis in this region rarely forms a mass of significant size and the stromal element in synovial sarcoma is typically composed of plumper, more mitotically active cells than in endometriosis. ER and PR positivity of both the epithelial and stromal elements is usual in endometriosis and would not be expected in synovial sarcoma.

With a purely monophasic synovial sarcoma involving the vulva or vagina, the differential diagnostic possibilities are much wider. Given the morphologic appearances and the site, a cellular smooth muscle tumour is likely to be considered as well as a variety of other spindle cell lesions that characteristically or almost exclusively arise in the vulvovaginal region [19, 20]. The latter include aggressive angiomyxoma, angiomyofibroblastoma, cellular angiofibroma, and superficial myofibroblastoma of the lower female genital tract [21, 22]. The morphologic features of all these lesions differ significantly from monophasic synovial sarcoma in that they are typically of lower cellularity and show less mitotic activity. The immunophenotype of synovial sarcoma has been discussed, but most of the aforementioned lesions and the majority of smooth muscle tumours in the vulva and vagina are diffusely positive for desmin, ER, and PgR [19–22]. As stated, in our case, desmin was negative. Smooth muscle tumours usually contain spindle cells with blunt-ended nuclei and eosinophilic cytoplasm, the morphology differing from the case we describe. In cases of overtly malignant spindle cell lesions, malignant peripheral nerve sheath tumour, which occasionally occurs in lower female genital tract sites, also needs to be considered as a diagnostic possibility [12]. In view of the wide range of differential diagnoses at these sites, immunohistochemistry evaluation is often most helpful. Our case showed focal immunostaining with cytokeratins and/or EMA in the spindle cell element and in the epithelial components. However, these markers are obviously not specific for synovial sarcoma, and moreover, some cases, especially of monophasic type and in particular, the poorly differentiated variants, may be negative. Markers that may be positive in synovial sarcoma include vimentin, S100, CD99, bcl-2, and calponin [23–26], whereas CD34 and desmin are typically negative [27]. Recently, nuclear expression of TLE1 has been proposed as a promising immunohistochemical marker with high sensitivity and specificity in distinguishing synovial sarcoma from its histologic mimics [28].

Factors that are predictive of a worse outcome include tumour size greater than 5 cm, age above 20 years, proximal location, extensive tumour necrosis, and in particular, poorly differentiated morphology [5]. Since few cases of synovial sarcoma have been reported in the vagina, the prognosis for these is uncertain.

Pathologists should avoid misdiagnosing it for other more common primary lesions developing in the vagina. Every attempt must be made to differentiate between primary and metastatic tumours as the treatment options and prognosis are entirely different in these two scenarios. Thorough clinical workup, high degree of suspicion, and complete relevant IHC profile are helpful in reaching accurate diagnosis.

Compliance with Ethical Standards

Conflict of interest The authors have no conflict of interest to declare.

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41557, 41558
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Ref. No. KH/C-17/ 196 /2000. Date 2.2.2000.

: C E R T I F I C A T E :

This is to certify that Dr. Vikas Gosavi worked in this hospital from July 1982 to June 1983 as Asst. Surgeon (Lecturer) & from July 1983 to October 1984 as Associate Surgeon.

His work was good and he was sincere and hard working.

These posts were teaching posts - initially for the National Board of Examinations (NBE) & the Nursing School here and then for the Medical College to which this hospital is attached.

DR. H.R. TATA,
MEDICAL DIRECTOR

HRT/nrs.

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(Government of Maharashtra)

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Office : 2695
Resi : 2675
Gram : Medical College, Miraj.

Ref. : GMCM/ 2838/ VIII/ 3946

Date : 28/12/1986.

C E R T I F I C A T E

Certified that Dr. V.S.Gosavi, has worked as Lecturer in Surgery at Govt. Medical College, Miraj & General Hospital, Sangli for the period from

1) 28-10-1984 to 25-10-1985
2) 28-10-1985 to 24-2-1986

Dean,
Govt.Medical College, Miraj.

To,
Dr. V.S.Gosavi,
796, Near Dr.Limaye's Hospital,
VISHRAMBAG SANGLI.

No.MMC/SS/RP/VKG/4045 of 198

Office of the Dean,
Miraj Medical College, Miraj.
Dated:- 23rd February, 1981.

24

CERTIFICATE.

THIS is to certify that DR. V. S. GOSAVI has done the following House Posts/Registrar Post :-

Sr. No.	House Post/Registrar Post.	Hospital where he has done the Post.	Period.
1)	House Post in Gen.Surgery. (on strike from 5-6-78 to 13.6.78.)	General Hospital, Sangli.	1-1-78 to 30-6-78.
2)	House Post in ~~Plastic Surgery~~ E.N.T. (on strike from 16-10-78 to 26-10-78).	Wanless Hospital, Miraj.	1-7-78 to 31-12-78.
3)	House Post in Plastic Surgery.	-do-	1-1-79 to 30-6-79.
4)	House Post in Genl.Surgery.	-do-	1-7-79 to 31-12-79.
5)	Registrar in E.N.T.	-do-	1-7-80 to 31-12-80.

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for DEAN,
MIRAJ MEDICAL COLLEGE, MIRAJ.

To
Dr.V.S.Gosavi,
Miraj Medical College,
Miraj, with ref.to his application dt.19/2/81.

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Phone: 0253-2539199 / EPABX: 0253-2539100 - 300 / Fax: 0253-2539200
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MUHS/ PG/E-1/1206/Honorary/ 185 /08 10/03/2008

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अधिष्ठाता

To

The Dean,
Government Medical College,
Pandharpur Road, Miraj
Dist-Sangli-416410

Sub: - Recognition as Honorary Post-Graduate Teacher...

Ref: - Govt. of India Letter no. V-11025/41/95-ME(UG)/P-1 Dated -11/02/2008

Sir / Madam,

With reference to the above cited subject & letter, I am directed to inform you that in view of the norms prescribed as per provision under the section 29 (2) (*l*) of the MUHS Act, 1998 Hon'ble Vice-Chancellor is pleased to grant recognition as Post-Graduate Teacher to the following Honorary teachers of your College **subject to the terms and conditions of appointment order & as per the letters from Government of India vide reference No. V-11025/41/05-MI/(UG) dated 23rd Oct 2005 and No. V-11025/41/95-ME(UG)/P-1 dated 11th Feb 2008** for imparting instructions to the Post Graduate Degree, Diploma course(s) in the subject mentioned against their name.

Sr. No.	Name of the Teacher	Subject	Period of Recognition
1	Dr. Sumant H. Kulkarni	Obst & Gynae	20/04/2007 to 22/10/2011
2	Dr. Sudhakar S. Jadhav	Gen Surgery	20/04/2007 to 22/10/2011
3	Dr. Vikas S. Gosavi	Gen Surgery	20/04/2007 to 22/10/2011
4	Dr. Avinash H. Patil	Gen Surgery	20/04/2007 to 22/10/2011
5	Dr. Sharad S. Sawant	Gen Surgery	15/03/2007 to 22/10/2011
6	Dr. Anand P. Kulkarni	Obst & Gynae	20/04/2007 to 22/10/2011

Kindly note that the recognition given by the University is valid till the above said teacher is in services of the said Medical College or attains 65 years of age, whichever is earlier. You are requested to handover the copy of letter to the concerned teacher(s).

Thanking you,

Yours faithfully,

Dy. Registrar
I/C Academic Section (PG)

Copy to: 1) The Concerned teacher(s),
2) Controller of Examinations, M.U.H.S., Nashik

(Note:- 1. In case , if it is found at later stage that information furnished in Post Graduate Recognition form by any teacher is incorrect, PG Recognition / UG approval granted by the University will stand cancelled.

2. The recognition for Honorary teachers shall cease automatically after the completion of period of recognition without any intimation from the University.)

No.GMCM/SS/H/5568-73/08.
Office of the Dean,
Govt. Medical College, Miraj.
Date: - /04/2008.

Copy forwarded to –

1) Dr. Sumant H. Kulkarni. and Dr. Anand P. Kulkarni, Hon. Asstt. Professor of Obst. & Gynaecology, through the Professor and Head of the Department of Obst. & Gynaecology, Govt. Medical College, Miraj and P.V.P. Govt. Hospital, Sangli.

2) Dr. Sudhakar S. Jadhav, 3) Dr. Vikas S. Gosavi, 4) Dr. Avinash H. Patil, 5) Dr. Sharad S. Sawant, Hon. Asstt. Professor of Surgery, through the Professor and Head of the Department of Surgery, Govt. Medical College, Miraj and P.V.P. Govt. Hospital, Sangli for information and further necessary action.

Dean,
Govt. Medical College, Miraj.

S. U. Press : 3:2(1,200)/A-1/11-2002

SHIVAJI UNIVERSITY, KOLHAPUR

SU/PG/Affl./Recog/ 2854 Date :

To
Dr. Gosavi Vikas Sadashiv
798, Vishrambag,
Sangli.

12 1 JUN 2003

Sub. : Permanent recognition as a Post-graduate Teacher for ~~M. Phil/Ph. D./~~Post-graduate courses.

Sir/Madam,

With reference to your application for recognition as a Post-Graduate Teacher of this University, and on the recommendation of the concerned Recognition Committee, I am to inform you that the University authorities are pleased to grant you permanent recognition as a Post-graduate Teacher for Post-Graduate course/~~M. Phil./Ph. D.~~ (By Papers/~~By research~~) of this University for imparting instructions in the following subject and at the examination stated below :

Subject	Examination
General Surgery	M. S. By papers

Please note that this recognition is valid till you are in the regular services of the College / Institution affiliated to this University only and eligible for Post-Graduate teaching as per the rules made in this respect by the University authorities.

Yours faithfully,

~~Dy~~ Registrar.

Copy forwarded with compliments to The Principal / ~~Director~~. Government Medical College, Miraj, Dist. Sangli

Associate Professor of P...
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Admissions Office : 2639

February 17, 1981

CERTIFICATE

This is to certify that Dr. V.S. Gosavi worked in this institution as Junior Medical Officer in Cardiothoracic Surgery Department from 1st January 1980 to 30th June 1980.

M.V. Rajapurkar

(DR. M.V. RAJAPURKAR)
MB, M.Sc.(Med)D.Phil(Med)
Medical Administrator

MVR:Jps.

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एनेस्थीसियोलॉजी
की उपाधि
अंकिता लपालोकर
(टाटा स्मारक केंद्र)
को विधिवत् रूप से इसके योग्य पाने पर
प्रदान करता है।

Homi Bhabha National Institute
hereby confers the degree of
Doctor of Medicine in
Anaesthesiology
on
Ankita Lapalikar
(Tata Memorial Centre)
the student having been found duly
qualified for the same.

परिणाम के अनुमोदन की तारीख Date of approval of result : October 18, 2017

अध्यक्ष, विद्या परिषद् Chairman, Academic Council

अध्यक्ष, प्रबंधन परिषद् Chairman, Council of Management

Enrolment No. HLTH09201409019

HBNI is a University established under Section 3 of the UGC Act, 1956 vide Notification No. F.9-5/2004-U.3, dated 3rd June, 2005 of Government of India
Regd. Office: Training School Complex, Anushaktinagar, Mumbai-400 094

Result Notified in: July, 2017

ISCCM

INDIAN COLLEGE OF CRITICAL CARE MEDICINE
INDIAN SOCIETY OF CRITICAL CARE MEDICINE

PROVISIONAL CERTIFICATE

Indian Diploma In Critical Care Medicine

This is to Certify that Ankita Lapalikar has completed the training requirement and passed the written and practical examination for the award of Indian Diploma in Critical Care Medicine (IDCCM) which was held in April, 2019.

Date:6th May, 2019

Dr. Sumit Ray
Controller of Examinations
Indian College of Critical Care Medicine