UTERINE LEIOMYOSARCOMA — CLINICOPATHOLOGIC FEATURES AND REVIEW OF LITERATURE†

by

CHANDRALEKHA P. SHROFF,* M.D.
CUSSUMA M. CHODANKAR,** M.D.

and

R. M. SARAOGI,*** M.D.

Introduction

Leiomyosarcoma of the uterus is a rare tumour. The reports on its frequency vary from 0.22% to as high as 6% (Parsons, 1978 and Kempson and Bari, 1970). As it is uterine sarcomas are rare tumours which constitute 1-3% of all uterine cancers. Nevertheless, these tumours represent the most intriguing and perhaps the most malignant of all uterine tumours. In a decreasing order of frequency, the three histologic variants are mixed mesodermal sarcoma (50%), leiomyosarcoma (30%) and endometrial stromal sarcoma (15%) (Salazar *et al* 1978).

This study was taken up with the view of detecting the possible aetiological factors, clinical features and histopathological characteristics in all myomatous tumours received over a period of eleven years from the year 1969 to 1979 in this institute.

Material and Methods

Two hundred and ninety-nine myomatous tumours of the uterus were reviewed on the basis of cellularity, pleomorphism and mitotic counts. The tumours were divided into leiomyomas, bizarre leiomyomas, cellular leiomyomas, metastastizing leiomyomas and leiomyosarcomas (after Kempson and Bari 1970; Christopherson *et al* 1972). Out of which leiomyomas numbered 276 (92.58%), cellular leiomyomas 11 (3.6%), bizarre leiomyomas 3 (1%), metastasizing leiomyoma 1 (0.30%) and leiomyosarcoma 8 (2.52%).

Observations

Tables I and II show the age incidence, parity, menstrual status and presenting symptoms in the patients.

TABLE I

Distribution of Leiomyosarcoma According to Age group and Parity

Age Range	No. of patients	Parity
40-50 yrs.	4	Multiparous*
50-60 „	2	„
60-70 „	1	„
70-80 „	1	„

* Only 1 patient presented with menorrhagia (D & C done). The remaining 7 were menopausal.

*Associate Professor, Pathology.
**Reader, Pathology.
***Reader, Obstetrics and Gynaecology, L.T.M. Medical College, Sion, Bombay-400 022.

†This Paper was Presented at the Annual Conference of Indian Association of Pathologists and Microbiologists held at Trivandrum in December 1981.

Accepted for publication on 16-6-82.

TABLE II
Presenting Symptoms in Patients With Leiomyosarcoma

Symptoms	No. of patients
1. Vaginal bleeding	3 (2 patients post menopausal 1 patient came with menorrhagia (D & C done)
2. Leucorrhoea	5
3. Abdominal mass	5
4. Gastrointestinal symptoms constipation—vague abdominal pain	6
5. Genitourinary symptoms—burning micturition	3

Investigations

Routine investigations like Hb, CBC, urinalysis and X-ray chest were within normal limits. Vaginal cytology collected in 2 patients showed abundant polymorphonuclears, bacterial clumps, atrophic vaginal epithelial cells and few degenerate spindle shaped cells.

Blood Group

Five cases belonged to group A-Rh positive, 1 B-Rh positive and remaining 2 to O-Rh positive.

Estimation of serum alkaline phosphatase and CEA (Carcinoembryonic antigens) levels was not done in any of these cases.

Operation Notes

Six patients were subjected to exploratory laparotomy. Three cases showed enlarged nodular uteri with friable pseudopapillary projections on the external surface. One of these showed peritoneal seedlings with effusion and adhesions between the loops of intestine and other pelvic viscera (only biopsy from the tumour was taken in this case). Out of the remaining 3, 2 had multiple fibroids and 1 had solitary myoma with haemorrhagic areas (Fig. 1). Panhysterectomy was performed in 5 cases. One case presenting with an ulcerated mass in the endocervical canal was biopsied, while in 1 dilatation and curettage was done. All specimens were subjected to pathologic study.

Pathologic features are presented in Table III, (Fig. 2).

Discussion

Leiomyosarcomas of the uterus are infrequent neoplasms characterized by aggressive behaviour and early pattern of dissemination and death. These tumours constitute 30% of all uterine sarcomas. They tend to occur in comparatively younger age between fourth to fifth decades of life. (Salazar *et al* 1978; Hart and Billman, 1978). In the past, lack of uniformly accepted histologic criteria for the diagnosis of leiomyosarcoma of the uterus made it difficult to determine the prognosis and to evaluate the results of therapy. This is clearly demonstrated by the discrepancy in the reported incidence that varies from 0.22% to as high as 6% of all uterine smooth muscle tumours and disparity in 5 year survival figures which range from 3%-75% (Kempson and Bari 1970). Leiomyosarcoma is rarely diagnosed preoperatively or at operation. It is occasionally recognized at gross pathologic examination, though frequently, it is an unexpected finding on microscopic examination. Ideally, every myomatous uterus should be opened in the operating room, but sectioning every portion of a large multinodular uterus is not possible. Myoma in post menopausal women with rapid growth, bluish softenning, haemor-

TABLE III

Gross and Histopathologic Appearances With Follow-up in Cases of Leiomyosarcoma

	Gross appearances	Histologic appearances*	Follow up
a.	5 Panhysterectomy specimens 2 Showed complete distortion of uterus with necrotic haemorrhagic friable growths. 3 were myomatous uteri: 2 multiple fibroids with occasional foci of necrosis. 1 solitary myoma with haemorrhage and necrosis. (Fig. 1).	3 poorly differentiated leiomyosarcoma 1 moderately dfferentiated leiomyosarcoma 1 well differentiated leiomyosarcoma	One case died one month after operation. 4 cases were lost to follow up.
b.	2 cases of biopsy: 1 from ulcerated growth protruding out of the cervix 1 from laparatomy (open biopsy)	Moderately diffeerntiated leiomyosarcoma	The case of open biopsy died and was autopsied with widespread intraperitoneal seedling. Cervical case was lost to follow up.
c.	D & C material fleshy, necrotic on gross D & C done for menorrhagia)	Poorly differentiated leiomyosarcoma (Fig. 2)	Lost to follow up.

* Classified according to Hendrickson & Bari (1980)

rhages and necrosis that cuts more readily should suggest malignant change and the surgeon may then plan surgery accordingly (Gudgeon 1968; Parson 1978).

The main problem for the pathologist is to differentiate between benign myoma and low grade sarcoma. It is necessary to study the individual cell carefully. The degree of cellular atypism appears to be of limited value in determining the malignancy of smooth muscle tumour. Tumours with 5-9 mitosis/h p f usually behave aggressively and metastatize, while uterine smooth muscle tumours with less than 5 mitoses/10 h p f are usually benign. Ideally, most active mitotic areas should be evaluated. It is often difficult to distinguish mitotic figures from pyknotic folded bizarre or hyperchromatic nuclei and in such situations the help of mucicarmine stain should be sought since it gives more satisfactory nuclear details, (Gallop and Cordray 1979; Norris 1976). Biochemical studies also help in the diagnosis. There is elevated alkaline phosphatase level in the blood preoperatively which declines to normal post operatively (Bodon and Mijangos 1972).

Likewise, elevated CEA levels in the presence of leiomyosarcomas have been used as indicators of tumour activity and

have served as useful aid in management of the disease. This may be of value in signalling persistence and recurrence of the disease (Parente *et al* 1979).

History of previous pelvic irradiation for benign conditions such as dysfunctional uterine bleeding has been implicated as aetiologic factor for uterine sarcomas (Gudgeon 1968; Salazar *et al* 1978). Oestrogens may induce uterine myomas and leiomyosarcomas, whereas progesterone and androgens help in decreasing the size (Gallup and Cordray 1979), Eilber and Moton 1970; Goldenberg et al (1975) suggest that viral aetiology in the genesis of tumours leiomyosarcoma should not be disregarded.

Two cases that were subjected to vaginal cytology were negative for malignant cells due to immense attendant necrosis, cellular degeneration and haemorrhage. In the present study, the average age of patients with leiomyosarcoma was 57 years. All were multiparous with 7 of them being menopausal. Gudgeon (1968) and Bartisch *et al* (1968) in their studies concluded that there is no significant relationship between parity and leiomyosarcoma, we did not find any significant relationship in this respect either. In none of them leiomyosarcoma was suspected clinically, all were diagnosed on histopathological examination. In 1 patient, tissue obtained at curettage showed the presence of leiomyosarcoma. However, negative report following curettage does not always mean that a symptomatic patient does not harbour a leiomyosarcoma, especially when the situation is intramural or subserosal. In 3 cases, sarcomatous change was noted in pre-existing leiomyoma. Montague *et al* (1965) suggest that possibility of sarcomatous changes in a myomas may go unrecognised due to insufficient sectioning of the tumours. In their series, the incidence of sarcomatous change in myomas was 0.29%.

An interesting finding in this study is that 5 of the cases reported here belong to blood group 'A'. This finding is in accordance with Ghooi *et al* (1970) who demonstrated high frequency of blood group A2 in males with sarcoma.

Summary and Conclusion

Two hundred and ninety-nine myomatous tumours of the uterus are reviewed. Only 8 tumours fulfilled the criteria recommended for histologic diagnosis of leiomyosarcoma. Other notable features are as follow:

1. The incidence of leiomyosarcoma in our study was 2.52%.
2. The average age for leiomyosarcoma in our study was 57 years.
3. Three cases (37.5%) occurred in pre-existing leiomyomas.
4. Five cases (62.5%) belonged to blood group A.
5. There was no significant relationship between parity and leiomyosarcoma.

Hence we conclude that women with post menopausal bleeding and vague abdominal symptoms with myomatous uteri or otherwise should be suspected of having leiomyosarcoma. In addition to routine diagnostic measures like curettage radiologic investigations, these patients should also be subjected to cytologic screening and determination of serum alkaline phosphatase and CEA since these investigations have both diagnostic and prognostic significance.

Acknowledgement

We thank Dr. B. R. Kalke, M.S. Dean, L.T.M. Medical College, Sion, Bombay for allowing us to publish this paper.

References

1. Bartisch, E. G., Bowe, E. T. and Moore, J. G.: Obstet. Gynec. 32: 101, 1969.
2. Bodon, G. R. and Mijangos, J. A.: Am. J. Surgery, 124: 673, 1972.
3. Christopherson, W. M., Williamson, E. O. and Gray, L. A.: Cancer. 29: 1513, 1972.
4. Eilber, F. R. and Morton, D. L.: Cancer. 26: 588. 1970.
5. Gallup, D. G. and Cordray, D. R. Obstet. Gynec. Survey. 34: 300, 1979.
6. Ghooi, A. M., Kamalpuria, S. K., Jain, P. K. and Tandon, P. L.: Indian J. Cancer. 7: 296, 1970.
7. Goldenberg, G. J., Sparll, G. M., Hogg, G. R.: Can. Med. Assoc. J. 110: 49, 1974.
8. Gudgeon, D. H.: Obstet. Gynec. 32: 96, 1968.
9. Hart, W. R. and Billman, J. K.: Cancer. 41: 1902, 1978.
10. Hendrickson, M. R. and Kempson R. L. Surgical Pathology of the uterine corpus, (1980) Chapter 18, p. p. 469-418, (Vol. 12 in series major problems in Pathology. W. B. Saunders Philadelphia, London, Toronto (C).
11. Kempson, R. L. and Bari, W.: Human Pathol. 1: 331, 1970.
12. Montague, A. C. W., Swartz, D. P. and Woodruff, J. D.: Am. J. Obstet. Gynec. 92: 421, 1965. zz
13. Norris, H. J.: Editorial Mitosis counting III Human Pathol. 7, 483.
14. Parents, J. T., Axelrod, M. R., Levy J. L. and Chiang, C. E.: Am. J. Obstet. Gynec. 131: 812. 1978.
15. Parsons, L. and Sommers, S. C.: Gynaecology (2nd Edition) 1978, p. .p 1057-1063. W. B. Saunders Co. Philadelphia/London/Toronto.
16. Salazar, O. M., Bonfiglio, T. A., Patten, S. F., Keller, B. E., Feldstein, M., Dunne, M. E. and Rudolph, J.: Cancer. 42: 1152, 1978.

See Figs. on Art Paper I