# STROMAL CELL SARCOMA OF THE UTERUS

by

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## *Introduction*

Stromal cell sarcomas form an uncommon group of tumours of the uterus. Their rarity and varying histological grades make their biological behaviour unpredictable and thus lead to a variety of names to connote their uncertain behaviour, such as stromal endometriosis, stromatosis, and endolymphatic stromal myosis, (Novak, 1974). To the best of our knowledge, a total of 7 cases of stromal cell sarcoma, and 8 cases of malignant mixed mesodermal tumours of uterus have been reported in the Indian literature during the period from 1960 to 1975 with a variety of terminology.

In the files of department of Pathology, Lady Hardinge Medical College and Hospitals, New Delhi, 8 cases of stromal cell sarcoma, including 2 of malignant mixed tumours of the uterus were encountered over a period of 15 years (1960 to December 1975) and are presented in this report. An attempt has been made to simplify the connotative terminology, its grading on the basis of mitotic activity and to depict possible source of origin in these cases.

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## *Material and Methodology*

### *Diagnostic criteria and classification adopted*

The cases diagnosed histologically as stromal cell sarcoma, endometroid sarcoma, endometrial sarcoma, and carcinosarcoma of the uterus were selected out from the files of the department of pathology during the period from 1960 to December, 1975. All the microslides were studied and the microscopic configuration described by Koss, *et al* (1965) was taken into cosideration for the diagnosis of stromal cell sarcoma which included endolymphatic stromal myosis. The general terminology and classification adopted was that of Ober and Tovell (1959) and also accepted by Williamson and Christopherson (1972) and Saksela *et al* (1974) with slight modification in grading of the tumours.

These stromal tumours were classified into stromal cell sarcoma, including low grade stromal cell sarcoma, moderately differentiated type, and malignant mixed mesodermal sarcoma. The mixed mesodermal sarcomas were separated into Homologous type (Carcino-sarcoma) wherein the carcinomatous and sarcomatous components were of regular mullerian origin and into Heterologous type where additionally tissues such as bone, cartilage or striated muscle were present.

Mitiotic counts were performed in the different most active and cellular parts of the tumour and the degree of polymorphism assessed. On the basis of cytologic criteria, the general pattern of differentiation, and number of mitotic activity per 10. High Power Fields (HPF x 6 x 40), a rough grading of tumours was attempted.

*Observations*

*Clinical*

*Age*: As shown in Table I, patients with stromal cell sarcoma with an age range of 20 to 50 years were comparatively younger than those of carcino-sarcoma average age 56 and 57 years respectively.

*Symptoms*: Excessive irregular vaginal bleeding was the most frequent complaint for which patients attended the hospital. Three patients out of 6 cases of stromal cell sarcoma additionally complained of pain in the lower abdomen. Both the cases diagnosed as carcino-sarcoma were post menopausal. The mean interval from menopause to diagnosis was 7.5 years.

*Pathologic Findings*: *Stromal cell sarcoma.*

*Gross*: Uterus was enlarged in all the cases except one (case 5) wherein the

TABLE I

*Distribution of cases with Presenting symptoms*

| No. | Age | Symptoms | Histologic Diagnosis |
|---|---|---|---|
| 1. | 30 yrs. | Irregular excessive vaginal bleeding —2 yrs. | Stromal cell Sarcoma. |
| 2. | 20 yrs. | Excessive vaginal bleeding —6 months. | Stromal cell Sarcoma. |
| 3. | 28 yrs. | Excessive irregular vaginal bleeding 1 month. Pain in lower abdomen—1 yr. Whitish discharge per vaginum —2 months | Stromal cell Sarcoma. |
| 4. | 25 yrs. | Excessive vaginal bleeding off & on 1 month | Stromal cell Sarcoma. |
| 5. | 40 yrs. | Excessive bleeding per vaginum — 1½ yrs. Pain in lower abdomen— | Stromal cell Sarcoma. |
| 6. | 50 yrs. | Irregular excessive bleeding per vaginum—3 months. | Stromal cell Sarcoma. |
| 7. | 56 yrs. | Menopause—for 9 yrs. Blood stained discharge—3 months Pain in lower abdomen —3 months. | Carcino-sarcoma. (Homologous mixed sarcoma) |
| 8. | 57 yrs. | Menopause—for 6 yrs. Blood stained discharge —5 months. | Carcino-Sarcoma. (Homologous mixed sarcoma). |

diagnosis was made on endometrial curettings. Endometrial cavity was dilated and its lower portion or whole of it was filled with pale gray-white, fleshy, irregular polypoidal mass of soft tissue. The cut surface was homogenous and solid. Three cases (Cases 3, 4, 6) in addition showed areas of necrosis and hemorrhage. In addition to it at places the tumour surface was covered with friable yellowish purulent material.

*Carcino-sarcoma*

*Gross*: Both the cases presented grossly as fungating polypoidal soft mass of tissue in the endometrial cavity with extensive areas of necrosis and hemorrhage. One was arising from the lateral wall and the other in the lower posterior part of the uterus.

*Microscopic*: All the 6 cases of stromal cell sarcomas showed a general make up of sheets of somewhat spindle, oval or polyhedral cells with fairly abundant eosinophilic cytoplasm, growing as irregular mass towards the uterine lumen and also penetrating the interstitial tissue of myometrium forming sharply defined irregular islands (Fig. 1). Polypoidal intralymphatic growth was seen in 3 cases and blood vessel invasion in 2.

*Mitotic activity*: In the 2 tumours of stromal cell sarcoma showing morphologically benign looking makeup, the mitotic activity was found to be nil and also showed no blood vessel invasion or areas of necrosis. In further 2 cases (Case Nos. 2 and 3) microscopic examination revealed mild hyperchromatism associated with areas of necrosis and hemorrhage and mitotic activity of 1 and 2/10 HPF respectively. Thus 4 cases were labelled as low grade stromal cell sarcoma. The lone case with 13 mitotic figures per IOHPF (Cast No. 6) showed moderate nuclear hyperchromatism, polymorphism with multinucleated giant cells, increased number of vascular invasion and extensive areas of necrosis (Table 2).

TABLE 2
*General Morphological Makeup of Stromal Cell Sarcoma*

| Case No. | Myometrial invasion | Lymphatic invasion | Blood vessel invasion | Necrosis and hemorrhage | Nuclear polymorphism | No. of mitotic figures per 10 HPF. |
|---|---|---|---|---|---|---|
| 1. | Positive | Negative | Negative | Negative | Benign looking | Nil |
| 2. | Positive | Positive | Negative | Negative | Benign looking | Nil |
| 3. | Positive | Positive | Positive | Positive | Mild degree | 2. |
| 4. | Positive | Negative | Negative | Positive | Mild degree | 1. |
| 5. | Endometrial | curettings | | Positive | Moderate degree | tissue was scanty |
| 6. | Positive | Positive | Positive | Positive | Moderate degree | 13. |

Both the cases of mixed mesodermal sarcoma showed variable admixture of carcinomatous and spindle celled sarcomatous components (Fig. 2). No heterologous tissue was found. Extensive areas of necrosis and hemorrhage were seen surrounding freshly thrombosed vessels. In the most cellular areas there was an average of 20 mitotic figures per 10 HPF. One case (No. 8) revealed bilateral adenexal extension of the tumour predominantly comprising of carcinomatous component.

*Endometrium*

It was available for study in 4 cases of stromal cell sarcoma and was of proliferative type, thinned in 2 instances and of normal thickness in other 2. The common denotation among these 4 cases was variable degree of abnormal focal stromal cell hyperplasia with widely apart endometrial glands. In 2 cases there were even multiple polypoidal excrescences of proliferating stromal cells without accompnying glands (Fig. 3).

In carcinosarcoma no uninvolved portion of the endometrium was left out. In areas, a characteristic patchy malignant transformation of either glandular component or of stromal tissue or both together was seen, which merged with more wide, cellular and anaplastic areas. The surface epithelium wherever preserved also showed marked nuclear atypia.

*Discussion*

*Classification and terminology*

While reviewing the Indian literature a variety of terminology was encountered among the published cases of stromal cell sarcoma, viz., uterine sarcoma and coexistent adenocarcinoma (Reddy and Sarojini, 1962), which included 4 cases of sarcomatous change in fibromyoma, one stromal cell sarcoma and one collision tumour; Malignant tumour of the body of uterus (Gharpure, 1968); Sarcoma of uterus (Giri,, 1968; and Gosh, 1971), Endometrial stromal sarcoma (Srivastava and Kishore, 1971) and Round cell sarcoma of the uterus (Gosh, 1973).

There was not much of variation in the terminology of malignant mixed tumours of the uterus. These were mainly expressed as Mixed tumours of the uterus by Sarojini (1962), Kshirsagar *et al* (1970), Reddy *et al* (1970), Phadke *et al* (1973) and Madhwan *et al* (1974) and Collision tumours by Patwardhan and Gadgil (1969); but to separate them in to homologous or heterologous types was sparingly attempted. Reddy *et al* (1975) have reported malignant mixed tumours of uterus as endometrial sarcoma.

Hunter (1953) and Hunter and Latting (1958), Over and Tovell (1959) and Koss *et al* (1965) referred the stromal cell sarcoma irrespective of benign looking proliferation of stromal cells on the basis that they have the notable propensity of growth in the interstitial spaces, lymphatics and vessels of myometrium. Lymphatic invasion to label the tumour as endolymphatic stromal myosis according Norris and Taylor (1966) was noticed in 50% of our cases. Hunter, Nohlgren and Lancefield (1956) and Neelson and Hagerty (1962) are of the consensus that endolymphatic stromal myosis is a low grade stromal cell sarcoma which may occasionally show a more aggressive and sarcomatous progression. Williamson and Christopherson (1972) classified the malignant mixed tumours of the uterus into homologous type (carcino-sarcoma) and heterologous type. Saksela, Lampinen and Procope (1974) accepted the classification as proposed by Ober and Tovel (1959) and are also of the view that

endolymphatic stromal myosis and stromal cell sarcoma represent only two different modes of the growth of one and the same process. We have also adopted the same with slight modification and it facilitated to include all the histological gradations of stromal cell sarcoma from completely benign looking histological makeup of stromal cell proliferation in the myometrium with or without intralymphangial growth (endolymphatic stromal myosis). The tumours associated with less than 10 mitosis/IOHPF were labelled, low grade stromal cell sarcoma to moderately differentiated stromal sarcoma with more than 10 mitotic figures/IOHPF and poorly differentiated stromal cell sarcoma showing more than 20 mitosis per 10 HPF.

*Age*

In the present study the patients of stromal cell sarcoma were between 20 to 50 years of age, with a mean age of 32.1 year. The cases published in the Indian literature were in the age range of 20 to 73 years with a mean age of 48 years. The cases in our study belonged to comparatively younger age group. It was surprising to come across a solitary case of malignant mesodermal mixed tumour in a girl of 18 years reported by Kshirsagar *et al* (1970) whereas all the other cases were beyond 40 years of age (Table III).

TABLE 3

*Number of cases of stromal cell sarcoma and malignant mixed mesodermal tumours of the uterus reported in the Indian Literature from* 1960 *to* 1975

| S. No. | Authors | Year | Age | No. of cases |
|---|---|---|---|---|
| | Stromal cell sarcoma | | | |
| 1. | Reddy and Sarojini | 1962 | 35 yrs. | 1. |
| 2. | Gharpure | 1968 | 46 yrs. | 1. |
| 3. | Giri | 1968 | 54 yrs. & 60 yrs. | 2. |
| 4. | Srivastva and Kishore | 1971 | 20 yrs. | 1. |
| 5. | Gosh | 1971 | 46 yrs. | 1. |
| 6. | Gosh | 1973 | 73 yrs. | 1. |
| | Total | | | 7. |
| 7. | Present series | | | 6. |
| | Mixed mesodermal sarcoma | | | |
| 1. | Reddy and Sarojini | 1962 | 45 yrs. | 1. |
| 2. | Patwardhan and Gadgil | 1969 | 55 yrs. | 1. |
| 3. | Kshirsagar, *et al* | 1970 | 18 yrs. | 1. |
| 4. | Reddy et al | 1970 | 54 yrs. | 1. |
| 5. | Phadke *et al* | 1973 | 40 yrs. | 1. |
| 6. | Madhvan et al | 1974 | 50 yrs. | 1. |
| 7. | Reddy *et al* | 1975 | 65 yrs. & 60 yrs. | 2. |
| | Total | | | 8. |
| 8. | Present series | | | 2. |

*Symptoms*

The commonest complaint was of irregular excessive vaginal bleeding. Koss, *et al* (1965) in their study found the similar common complaint along with abdominal discomfort and awareness of increasing abdominal girth. Among our cases in 6 out of 8, enlargement of uterus of approximately 12 to 14 weeks size was detected on clinical examination, but these patients did not complain of increase in abdominal girth, possibly the Indian women are not generally figure conscious.

*Microscopic Pathology*

*Stromal cell sarcoma*

Myometrial invasion by proliferating sheets of stromal cells was seen among all the cases. In one instance multifocal hyalinization of the interstitial connective tissue of the tumour was seen and similar finding was also encountered on one occasion by Koss *et al* (1965) which is not so commonly seen.

*Mitotic activity*

In the present study number of mitotic activity per 10 HPF could well be correlated with frequency of blood vascular invasion, nuclear hyperchromatism and its variabilities and extent of necrosis. It was directly propotional to the above factors, (Table 2). Norris and Taylor (1966) stated that patients with tumours having fewer than 10 mitotic activity per 10 HPF had an actuarial survival of 100% at 10 years i.e. slow clinical progression. He referred to these cases as stromal myosis. In the same study 15 patients labelled as stromal cell sarcoma had 10 or more mitosis per 10 HPF and showed 55% survival at 5 years.

*Malignant Mixed mesodermal sarcoma*

In this study both the cases belonged to homologous type (Carcino-sarcoma) and one case showed 20 mitosis per 10 HPF with one atypical mitosis and bilateral adenexal metastasis predominantly of carcinomatous element which correlated with the statement of Novak (1974).

*Histogenesis*

Krupp, *et al* (1961), Chabon, *et al* (1963) and Bartsich, *et al* (1967) advocated the theory that mixed mullerian tumours originate from totipotential cells in the endometrium and usually these totipotential cells are identified as adult endometrial cells, Willis (1962), Norris, *et al* (1966) and Norris and Taylor (1966). It was stated by Koss, *et al* (1965) that if the stroma surrounding intact endometrial glands showed changes identical to those proliferating within the myometrium, origin from the endometrium would seem most likely. In the present study, 4 cases of stromal cell sarcoma showed abnormal focal proliferation of stromal cells in the uninvolved portions of endometrium. At places these focal hyperplastic points merged with wide areas composed of streams of proliferating spindle cells morphologically akin to those infiltrating the myometrium. This gives ample support of origin of stromal cell sarcoma from the endometrial stroma. None of the tumours in the study was found to be arising from adenomyosis and this was consistent with the observations of Norris and Taylor (1966).

In the case of carcinosarcoma, at places there were multifocal malignant transformation of either glandular or stromal component or of both together which merged with more wide areas of malignant tissue of both components. It appeared as if there might be a factor or factors operating on endometrium with

an outcome of carcinosarcoma. The heterologous element if present can be explained on the basis that these totipotent ectopic or adult stromal cells (Willis, 1962) may just represent varying stages of differentiation (Williamson and Christopherson, 1972), or it a metaplastic tissue (Saksela *et al* 1974).

*Prognosis*

It being a retrospective study, all the patients in the report could not be followed up and no relavent information could be elicited from the case records. However recently diagnosed patients are alive but it needs further study.

*Summary*

A collection of 8 cases of stromal cell sarcoma of uterus including 2 mixed mesodermal sarcoma (carcinosarcoma) is presented in this report on account of their rarity. A variability in its connotative terminology published in the Indian literature has been discussed and the cases briefly reviewed. An attempt has been made to grade the stromal cell sarcomas on the basis of number of mitotic figures per 10 high power fields. A possible source of origin of these tumours in endometrium is discussed.

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*See Figs. on Art Paper IV*