INTRODUCTION

According to World Health Organization [WHO] classification, Bizarre leiomyoma is defined as “Leiomyoma containing giant cells with pleomorphic nuclei and little or no mitotic activity”. In 1909, Kelly and Cullen in their monograph on myomata of uterus described several tumors that macroscopically had the usual appearance of myomata but histologically contained cells suggestive of “sarcomatous degeneration” including large multinucleated tumor cells. In 1961 Przybora introduced the term “leiomyosarcoma in situ” for a group of 15 uterine smooth muscle tumors in which distinctly atypical cells, especially multinucleated giant cells were found within otherwise simple myoma. The designation “leiomyosarcoma in situ” never gained favor for these tumors instead, the terms “atypical leiomyoma”, “bizarre leiomyoma”, “pleomorphic leiomyoma” and “symplastic leiomyoma” became popular. The notion that myomatous tumors with bizarre nuclei represent a stage in the development of leiomyosarcoma was discarded. Instead tumors were regarded as histologic variant of otherwise ordinary leiomyoma. In 1972, Christopherson et al specifically described 17 bizarre leiomyomas that were called from a large group of uterine tumors with a prior diagnosis or suspicious of sarcoma. In subsequent classification developed for WHO, Christopherson’s term “bizarre leiomyoma” was adopted and “symplastic leiomyoma” and “Pleomorphic leiomyoma” were acknowledged as synonymous designations. Bizarre [symplastic] leiomyoma have a frightening microscopic appearance because of the many large giant cells with very large, cytologically malignant looking nuclei, which may be multiple. These lesions, which occur at premenopausal age, lack the mitosis that characterize leiomyosarcoma and have proved to be benign. It is composed of tumor cells with variation in size and shape, hyperchromatic nuclei and multinucleated forms but no coagulative necrosis or increased mitotic activity. It may occur spontaneously but is often seen in patients taking progestin compounds. A recent trend in classification of uterine smooth muscle neoplasms into clinically benign and clinically malignant groups has been to move from exclusive reliance upon mitotic index [MI] to an approach that incorporates additional histopathologic characteristics.

CASE REPORT

A 40 year old female presented with mass per abdomen over a period of 2 years (fig 1).
Per abdominal examination revealed uterus of 20 weeks size, firm in consistency and easily mobile. Per speculum examination revealed greenish yellow discharge. With the above findings clinical diagnosis of fibroid uterus was made. Hematological investigations revealed anemia with hemoglobin of 11.4g%. Urine microscopy showed 3-5 per cells / high power field. Blood group was B positive. ECG revealed left ventricular hypertrophy with systolic overload. Thyroid function test, renal function test and blood sugars were within normal limits. A clinical diagnosis of a fibroid uterus was made. Abdominal ultrasound scan showed uterus measuring 18x10x15cm with multiple fibroids. The patient was put on intravenous antibiotic and intramuscular analgesics 5 days prior to surgery. Total abdominal hysterectomy with bilateral salpingoophorectomy was done. The specimen of uterus and cervix with bilateral adnexa was sent for histopathological examination. Post operative stay of the patient was uneventful. The patient was discharged seven days after the surgery. The patient is currently under regular follow-up. Grossly we received specimen of uterus with cervix with bilateral adnexa weighing 1,100 grams. Uterus and cervix measured 14x10x10 cm. Right and left ovaries measured 6x2x1 cm. Cut section through uterus and cervix showed multiple grey-white intramural fibroids largest measured 3x2cm (fig 2, 3, 4). Cystic areas were seen within intramural fibroids.

Microscopy revealed endometrial glands in secretary phase.
Myometrium showed intramural leiomyoma composed of bizarre spindle shaped cells with vesicular nuclei showing moderate to severe pleomorphism arranged diffusely and in fascicles (fig 5). Presence of bizarre giant cells was the most striking feature (fig 6). Good number of cells showed prominent nucleoli (Fig.7). Few cells showed intranuclear inclusion bodies (Fig.8). Tumor cells showed mitotic activity. Mitosis was less than four / ten High Power Field (HPF) by highest count method and less than one / ten HPF by average count method. One percent toludine blue stain was used to demonstrate mast cells (Fig.9) which ranged from as high as 9 / HPF to 2 / HPF with an average of 3.4 / HPF. Most of the mast cells showed degranulation.

**Figure 5**
Fig 5. Photomicrograph of tumor tissue showing diffusely arranged bizarre spindle shaped cells [H&E, x200].

**Figure 6**
Fig 6. Photomicrograph of tumor tissue showing bizarre multinucleated giant cells (arrows) [H&E, x200].

**Figure 7**
Fig 7. Photomicrograph of tumor tissue showing tumor cells having vesicular nucleus with prominent nucleoli (arrows) [H&E, x400].

**Figure 8**
Fig 8. Photomicrograph of tumor tissue showing intranuclear inclusion in the tumor cell (arrow)[H&E, x400].
**DISCUSSION**

Bizarre leiomyomas are infrequently encountered in surgical pathology. Bizarre leiomyoma have a wider range of morphologic changes and mitotic activity than has been recognized. Patients age ranged from 25 to 51 years [mean 40.7] in the study conducted by KA Downes et al. RE Fechner reported a series of 5 cases of atypical leiomyomas in age group of 32 to 47 years. KA Downes et al observed pelvic pain, enlarged uterus and irregular or heavy menstural bleeding as the presenting signs and symptoms. The presenting complaints included Dysmenorrhea and menstrual irregularity [three cases] and pelvic pain [three cases] in the study conducted by RE Fletcher. In the present case, middle aged female presented with mass per abdomen of two year duration.

RE Fechner observed that the uterus weight ranged from 160 grams to 140 grams with a mean of 191.2 grams. Grossly, the maximum dimension of bizarre leiomyoma ranged from 1 to 14 cm with a mean of approximately 4.2cm in the study conducted by KA Downes et al. In their study, location of tumor in the uterus was evaluable in 17 cases. Ten were intramural, six were submucosal and one was subserosal. The gross description of the tumors was generally that of an ordinary leiomyoma (firm, whorled, white, pink or gray cut surface). Descriptions included notations of a yellow or tan coloration [eight cases], hemorrhagic [two cases], focal softening [one case], cavitation [one case] and myxoid change [one case]. In the present case, uterus weighed 1,100gm. Cut section showed multiple grey-white intramural fibroids largest measuring 3cm in the longest dimension. Cystic areas were appreciated within the tumor.

Microscopy revealed intramural leiomyoma with bizarre spindle cells with vesicular nuclei showing moderate to severe pleomorphism. Cells were arranged diffusely and in fascicles at places. KA Downes et al had observed bizarre cells being distributed diffusely throughout the tumor in 12 tumors [50% cases]. In the other 12 [50% cases], tumors bizarre cells formed defined aggregates or discrete nodules. The cells often had prominent intranuclear invaginations so called inclusions of brightly eosinophilic cytoplasm mimicking macro nuclei. KA Downes et al made similar observations in their study. Mast cells were 3.4/HPF in the present case. A Ori et al observed that mast cells were significantly higher in bizarre and cellular leiomyomas than in ordinary leiomyoma and leiomyosarcoma.

KA Downes et al had following four criteria for inclusion of case in their study: [1] origin of the tumor in the uterus, [2] Unquestionable smooth muscle cell type, [3] Presence of readily evident pleomorphic bizarre multinucleated tumor giant cells comprising a minimum of 5% of the tumor and [4] Mitotic <10MFs/10 HPF by highest count method in the most mitotically active areas of the tumor. Similar criteria were used in the work up of the present case. KA Downes et al observed 19 tumors (79%) contained giant cells with more ominous appearing nuclei in which there were coarsely granular or clumped chromatin with areas of clearing, sometimes with enlarged true nucleoli. Similar features were appreciated in our case. The cardinal and definitional feature of all 24 tumors was the obvious presence of bizarre pleomorphic tumor cells with atypical nuclei. This feature was prominent in the present case.

In the present case, mitotic figure was <4/10 HPF by highest count method and <1/10 HPF by average count method. When KA Downes et al used highest count method in their study, the mean mitotic count was 1.6 MF/10 HPF/tumor and it was 0.8 MFs/10 HPF/ tumor by average count method. KA Downes et al had observed cogulative necrosis which had the typical features of healing infarction or so called hyalin necrosis.

SW Bell et al classified problematic uterine neoplasms into five groups. Group I constituted uterine smooth muscle neoplasms [USMNs] with insignificant atypia without coagulative tumor cell necrosis [CTCN] and with high MI. Group II consisted of USMNs with diffuse significant atypia without CTCN with variable MI. Group III constituted USMNs with diffuse significant atypia with CTCN with a variable MI. Group IV included USMNs with insignificant
atyria with CTCN and with a variable mitotic index. Finally Group V included USMNs with focal or multifocal significant atypia, without necrosis and with a variable MI. The present case corresponds to group II of Bell’s categories of USMNs. CTCN was considered as ominous finding particularly when accompanied by significant atypia.

The diagnostic approach to each USMN is as follows: First the tumor was examined under low magnification to determine the degree of atypia mild [insignificant] or moderate to severe [significant]. The sections were then evaluated for presence or absence of necrosis. If the atypia is significant and there is no necrosis or only hyalin necrosis, the tumors are interpreted as leiomyoma irrespective of mitotic activity. This approach also helps to avoid over diagnosis of leiomyomas with unusual histological patterns as malignant. If atypia is significant, a search is made for necrosis. If CTCN is present, tumor is leiomyosarcoma regardless of mitotic counts. If necrosis is absent or is of hyalin type, a mitotic count is made and further classification is based on MI. A Bivariate rule employing MI and Cytological feature performed better than either MI or atypia. Trivariate approach that used MI, degree of atypia and CTCN tends to ameliorate interpretive difficulties.

RE Fechner had reported series of five cases of atypical leiomyomas in patients on synthetic progestin therapy but concluded that these atypical changes could be due to chance alone. Emphasis is placed on differentiating atypical leiomyomas from leiomyosarcoma. In the present case, patient was not on any hormonal therapy. This supports the conclusion aspect of RE Fechner.

CONCLUSION

Bizarre Leiomyoma is a rare tumor of uterine smooth muscles. It requires careful evaluation of various microscopic features as it closely mimics its malignant counterpart. Considering constellation of microscopic features, a systematic approach is needed to exclude malignancy.
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