Case report

Atypical Leiomyoma: a rare histologic variant - A Diagnostic Challenge

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Abstract:
Bizarre or atypical leiomyoma (LM) is defined as "leiomyoma containing giant cells with pleomorphic nuclei and little or no mitotic activity." Due to the ominous and worrisome microscopic appearance (many large giant cells with hyperchromatic, pleomorphic, malignant looking nuclei), this variant maybe misdiagnosed as a sarcoma. It, therefore presents a diagnostic challenge to the pathologist to accurately diagnose such a tumor while ensuring that a true malignancy is not overlooked. We report a case of a atypical leiomyoma of the uterus in a 40 year old female presenting with irregular menstrual bleeding. This highlights the need for extensive tissue sampling in such dubious cases to help arrive at a correct diagnosis.

Keywords: atypical leiomyoma; bizarre leiomyoma; symplastic leiomyoma

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Introduction:

Atypical or symplastic leiomyoma is a rare variant of leiomyoma (LM) which contains cells with moderate to severe cytological atypia in the absence of necrosis and a low mitoses (<10 MF/10 HPF).[1] Despite its worrisome histologic appearance comprising of bizarre multinucleated giant cells and large, pleomorphic, hyperchromatic nuclei, atypical LM usually follows a benign clinical course with rare instances of recurrence, which is in contrast to a sarcoma. Therefore, it is very crucial to accurately diagnose such tumors to prevent overenthusiatic and overzealous treatment and in the meantime preventing the underdiagnosis of a malignant tumor. We report a case of atypical leiomyoma of the uterus in a 40 year old female to highlight the importance of a correct pathological diagnosis in such dubious cases.

Case Presentation:

A 40 year old female presented with irregular menstrual bleeding and lower abdominal pain for the last 3-4 months. Her cycles ranged from 16 to 24 days with heavy menstrual flow associated with dysmenorrhea. She had three children and last child birth was 10 years back. There was no history of discharge per vaginum. Her medical, surgical and family history was not significant. On examination, uterus was 18 weeks size, uniformally enlarged mobile soft and non tender with normal adnexa.

Her haemoglobin was 9.8gm% with microcytic hypochromic red cell picture. Rest of haematological and biochemical investigations were within normal limits. On sonography, an echogenic mass measuring 9.5x9.8 cm was observed in posterior wall of the uterus, suggestive of fibroid. Hysterectomy was performed. On gross examination, a specimen of uterus and cervix was received measuring 15x13x10cm. On serial sectioning, a large circumscribed intramural mass measuring 9x8.5x7cm was observed distorting

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the endometrial cavity. Cut surface was grey white and showed whorling.

Microscopically, the tumor was composed of bundles of smooth muscle cells, many of which showed nuclear enlargement, pleomorphism and hyperchromasia. Bizarre multinucleated giant cells were also seen scattered in between. Mitotic activity was low (2-3 MF/10 HPF). Taking into account the alarming histological appearance of cells, extensive sampling of the tumor was done to rule out leiomyosarcoma. However, there were no areas of necrosis, hemorrhage or increased mitoses. Finally, a diagnosis of atypical or bizarre variant of leiomyoma was rendered.

Discussion:

Bizarre or atypical leiomyoma (LM), according to World Health Organization (WHO) classification is defined as "leiomyoma containing giant cells with pleomorphic nuclei and little or no mitotic activity." It was first brought to attention in 1909 when it was thought that it contained cells suggestive of "sarcomatous degeneration". Thereafter, various synonyms have been used to describe this rare variant of a common uterine tumor like leiomyosarcoma in situ (not favoured), atypical leiomyoma, bizarre leiomyoma, pleomorphic leiomyoma or symplastic leiomyoma.[1]

Clinically, the patients belong to reproductive age group and usually present with pelvic pain, abdomino-pelvic mass or heavy/irregular menstrual bleeding. Grossly, tumor can range from 1 to 14cm in diameter with a mean of 4.2cm approximately. The leiomyoma may be intramural, subserosal or submucosal. Cut surface of bizarre LM is similar to conventional LM with a firm, solid, grey white, whorled appearance. Occasionally, areas of cystic change, hemorrhage, yellow/tan discoloration or myxoid change maybe encountered.[2]

Microscopically, atypical LM is characterised by bizarre spindle cells with pleomorphic, hyperchromatic nuclei and scattered multinucleated giant cells. Occasional atypical mitosis may also be observed. These bizarre giant cells may be distributed uniformly throughout the tumor or focally or form discrete aggregates. Cells may show prominent intranuclear eosinophilic inclusions resembling macronucleoli.[1,2]

Bell et al[3] studied a substantial number (n=213) of problematic uterine smooth muscle neoplasms. From a wide variety of LM features assessed, the important predictors that emerged were: mitotic index, degree of cytological atypia and coagulative necrosis. Despite worrisome histological features, most of the atypical LM displayed benign behaviour.[3]

Downes et al[2] analysed 24 bizarre leiomyomas to determine their spectrum of pathological features and to establish their clinical behaviour. They followed certain inclusion criteria for atypical leiomyoma in their study, namely: 1) tumor should originate in uterus, 2) should undoubtedly be of smooth muscle type, 3) presence of pleomorphic, bizarre multinucleated giant cells accounting for atleast 5% of tumor and 4) mitosis <10MF/10HPF in most mitotically active areas of the tumor. On follow up, all patients were alive with none developing any recurrence or metastasis. Their study firmly established the benign behaviour of bizarre LM despite high cellularity, bizarre cells and 2-7mitoses/10HPF.[2]

The behaviour of atypical LM treated with myomectomy alone is still not very clear. To analyse this, Sung et al[4] studied 13 cases of atypical LM treated by myomectomy alone with long term follow up results. None of the patients developed metastasis and only one developed a local recurrence. Authors suggested that if atypical LM is discovered on myomectomy, careful follow up should be done and hysterectomy could be recommended.

Ly et al[5] analysed the clinicopathological characteristics of 51 cases of atypical LM of uterus. Average follow up was 42 months (range 0.3 to 121.8 months). Of those treated with hysterectomy, 1 had recurrence, 1 died of other causes and remaining 94% were free of disease. While among those treated by myomectomy, 82% had no evidence of recurrence, 2 had residual atypical LM in subsequent hysterectomy specimen and 1 underwent second myomectomy for atypical LM. They concluded that atypical LM has a low rate of extrauterine, intra abdominal recurrence (<2%) with a negligible risk for distant metastasis. Patients may be treated with myomectomy alone but should be monitored for local intrauterine residual/ recurrent disease.

Deodhar et al[6] studied 21 cases of Smooth muscle tumors of uncertain malignant potential (STUMP) and atypical leiomyomas and concluded that there is a considerable overlap in the terminologies- STUMP, atypical LM, atypical LM with low risk of recurrence and atypical LM with low malignant potential. Although most of these behave in a benign manner, followup without adjuvant therapy is recommended. They stressed upon the critical evaluation of coagulative tissue necrosis in such tumors.

Due to the ominous and worrisome microscopic appearance (many large giant cells with hyperchromatic, pleomorphic, malignant looking nuclei), this variant maybe misdiagnosed as a sarcoma. Inspite of such an alarming histological picture, atypical LM follows a more or less benign clinical course, contrary to a leiomyosarcoma. It, therefore presents a diagnostic challenge to the pathologist to accurately diagnose such a tumor while ensuring that a true malignancy is not overlooked. This highlights the need for extensive tissue sampling in such dubious cases to help arrive at a correct diagnosis.

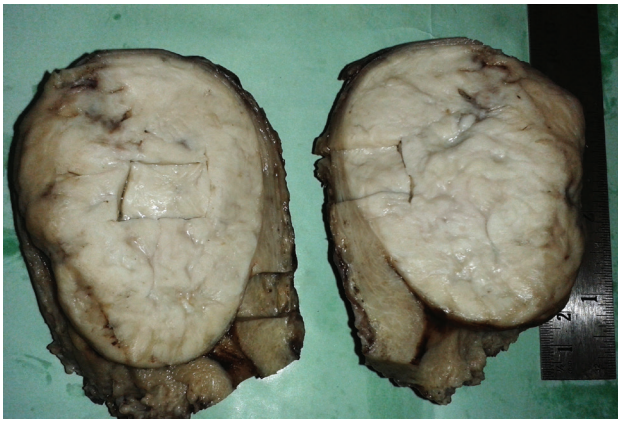

Figure 1: Gross specimen of uterus showing a large intramural leiomyoma with grey white cut surface showing a whorled appearance

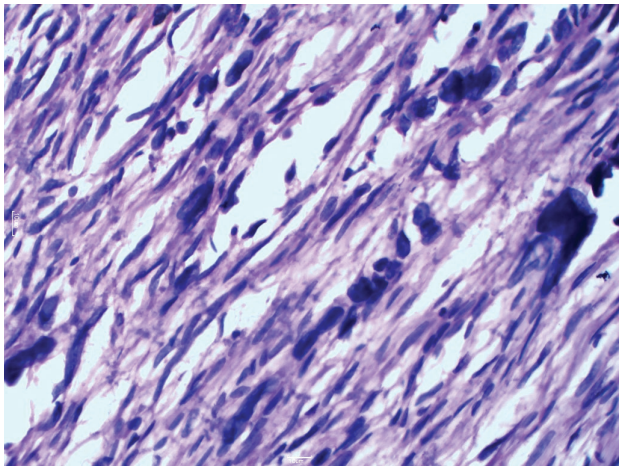

Figure 3: Photomicrograph showing smooth muscle cells with nuclear enlargement, pleomorphism and hyperchromasia (Hematoxylin and Eosin, 400x).

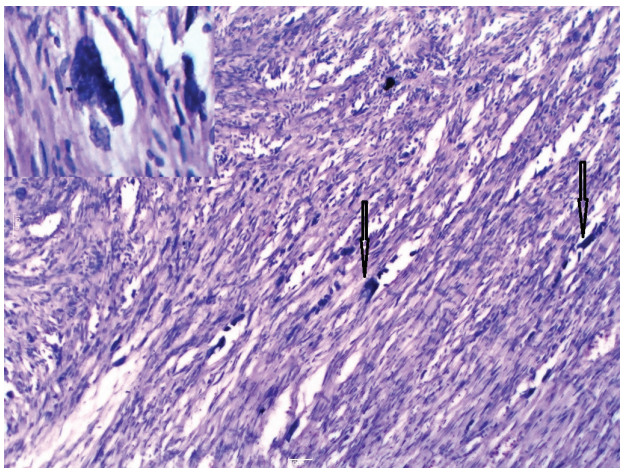

Figure 2: Photomicrograph showing bundles of smooth muscle cells, many of which showed nuclear atypia (arrow) (Hematoxylin and Eosin, 100x). Inset top left - Bizarre multinucleated giant cells (Hematoxylin and Eosin, 400x)

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