DIFFUSE UTERINE LEIOMYOMATOSIS (DUL) COEXISTENT WITH INTRA-VASCULAR LEIOMYOMATOSIS MASQUERADING AS AN ENDOMETRIAL STROMAL TUMOR: A REPORT OF AN EXTREMELY RARE CASE

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ABSTRACT

Case Report: We present a 38 year old female with coexistent diffuse leiomyomatosis as well as intravascular leiomyomatosis of the uterus masquerading as an endometrial stromal tumor. A strong positivity for Desmin and Progesterone receptor (PR) favoured DUL while negative immunoreactivity for CD-10 helped in excluding endometrial stromal tumor.

Conclusion: DUL is a distinct entity from the uterine leiomyomas in terms of varied gross and microscopic features. To the best of our knowledge, this is the first report of coexistence of two rare variants of leiomyoma- diffuse and intravascular leiomyomatosis.

Keywords: diffuse uterine leiomyomatosis, leiomyoma, endometrial stromal tumor

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INTRODUCTION

Diffuse uterine leiomyomatosis (DUL) also referred to as complete fibromyomatosis, myomatosis, diffusemyomatous tendency is a rare condition characterized by symmetric enlargement of the uterus due to numerous poorly defined, confluent nodules almost completely replacing the myometrium.[1]

Baschinsky et al[2] have proposed that diffuse leiomyomatosis of the uterus is an exaggerated proliferation of multiple leiomyomas budding into each other and merging imperceptibly so that discrete nodules could not be readily noticeable by gross examination. Intravascular leiomymatosis (IVL) is a rare variant of leiomyoma characterised by smooth muscle proliferation within the lumen of blood vessel with attachment to the vessel walls.[3]

The clinical presentation of DUL is indistinguishable from uterine leiomyomas with patients usually presenting with abdominal pain, abnormal uterine bleeding or infertility. Although microscopic features of leiomyomatosis include haphazardly arranged fascicles of smooth muscle cells, it may exhibit a histological overlap with multiple leiomyomas andendometrial stromal sarcoma thereby posing a diagnostic challenge to the pathologist.[4,6] To the best of our knowledge, we present the first report of coexistent diffuse and intravascular leiomyomatosis, mascerading as an endometrial stromal tumor.

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CASE REPORT

A 38-year-old woman (gravida 2, para 2) presented to the Gynaecology clinic with abnormal uterine bleeding, dysmenorrhea and pelvic pain for last 6-8 months. Complete blood count revealed haemoglobin 10 g%, total leucocyte count 8,500/µl with differential leucocyte count within normal limits, platelets 1.6 lacs/µl and erythrocyte sedimentation rate of 12mm/hr.

Biochemical investigations were within the normal reference range. Pelvic ultrasound revealed a symmetrically enlarged uterus measuring 13x10x6 cm with multiple intramural fibroids, smallest being 0.5 cm while large discernable one was 3.5cm in diameter. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed.

Grossly, uterus was uniformly enlarged and on serial sectioning had a multinodular appearance due to almost complete replacement of myometrium by many intramural and subserosal nodules coalescing into each

other. Cut surface of nodules was greyish white with a whorled/ trabeculated appearance. The other pelvic organs, parametrium and ovaries were normal. Histologically, the nodules were composed of interlacing bundles of smooth muscle cells which had multifocal areas of hyalinization and degeneration (Figure 1). The nodules blended with each other and amalgamated imperceptibly with the surrounding normal myometrium. Proliferating small vessels resembling the endometrial spiral arterioles were observed, and there were bands of hyaline connective tissue separating islands and clusters of bland neoplastic stromal cells similar to ESS (figure 2). No cellular pleomorphism or abnormal mitotic figures were noted. Immunohistochemistry revealed strong positivity for smooth muscle actin (SMA), desmin, progesterone receptor-PR (figure 2) and a 3-5% Ki-67 labelling index.

A negative immunoreactivity for CD-10 helped in excluding endometrial stromal tumor. Extensive sampling was done which revealed focal areas where a proportion of the fibroid was seen within blood vessels at places attached to their walls. So, a final diagnosis of diffuse leiomyomatosis with a component of intravascular leiomyomatosis was rendered.

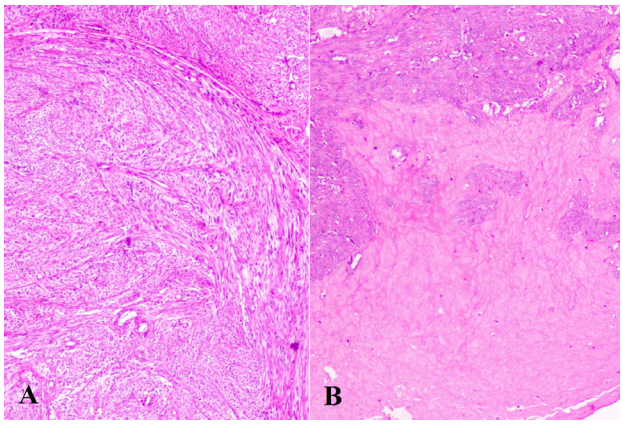

Fig 1: Photomicrograph showing A)the tumor nodules composed of interlacing bundles of smooth muscle cells, B) Areas of hyalinization and degeneration (H&E, 200X)

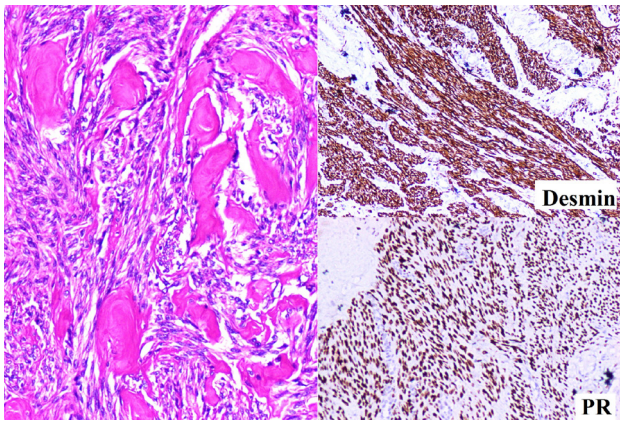

Fig 2: Photomicrograph showing bands of hyaline connective tissue separating islands and clusters of bland neoplastic stromal cells similar to ESS (H&E, 400X), Immunohistochemistry for desmin and PR showed strong positivity.

DISCUSSION

Diffuse uterine leiomyomatosis is a benign, extremely unusual condition with uniform enlargement of the uterus on account of nearly complete replacement of the myometrium by many poorly defined leiomyomatous nodules coalescing into each other.[1] Intravascular leiomymatosis is another rare variant of leiomyoma characterised by smooth muscle proliferation within the lumen of blood vessel with attachment to the vessel walls.[3]

Leiomyomas are clonal neoplasms with consistent cytogenetic alterations. It is postulated that various tumors within the diffuse uterine leiomyomatosis arise from different clones, implying that DUL may be an exuberant growth of multiple uterine leiomyomas budding into each other and blending imperceptibly so that it becomes difficult to separately identify individual nodules grossly.[2]

The most common presentation of DUL patient is abdominal pain and abnormal uterine bleeding which is akin to most uterine leiomyomas.[1] Patients usually belong to third and fourth decades of life with complaints of menorrhagia, dysmenorrhea, infertility, and pelvic pressure.[2,5] Several authors have reported cases of DUL with coexistent pregnancy, although complications like premature rupture of membranes, cervical incompetence, intrapartum haemorrhage necessitating hysterectomy have been documented. [7,8] Few cases of benign metastasizing leiomyomatosis have also been reported in the literature.[9]

The characteristic histopathology of DUL reveals nodules blending with each other as well as moulding inseparably with the surrounding myometrium. The nodules comprise of benign smooth muscle cells in compact fascicles and interweaving bundles. Histologically, the differential diagnosis of leiomyomatosis includes multiple leiomyomas, intravascular leiomyomatosis and endometrial stromal sarcoma (ESS).[1,2,4,5]

Uniform symmetrical involvement of the entire myometrium by smooth muscle nodules without well-defined borders between the nodules favours DUL while multiple leiomyomas are well circumscribed with asymmetrical involvement of the uterus.[2,5] Endometrial stromal sarcoma is characterized by its invasive growth with a clear cut transition with the normal myometrium, and a sheet like arrangement unlike DUL which shows a fascicular growth pattern. Moreover, microscopically ESS has small tumor cells with round to oval nuclei and scant cytoplasm separating the thick walled vessels and intravascular growth.[5,6] Immunohistoreactivity for CD-10 favours ESS over DUL. Salient features of intravascular leiomyomatosis include a creamy to yellowish colour grossly with intravas-

cular extensions of wormlike smooth muscle tumor with multinodular indistinct margins and the presence of some or all of the neoplastic smooth muscle within the vascular channels, microscopically as was observed in the present case.

Nisolle et al[10] concluded that diffuse leiomyomatosis lesions may be under the influence of progesterone as progesterone receptors (PRs) were significantly higher in leiomyoma than in the adjacent myometrium similar to our case. Antiprogestin agents may serve as alternative mode of treatment DUL.

Two theories have been proposed for the occurrence of intravascular leiomyomatosis- primary growth within the vessel or an extension of pre-existing leiomyomas. The definitive treatment of IVL includes total hysterectomy with possible oophorectomy and removal of tumors from within venous and cardiac systems. GnRH analogues and anti-estrogens may be used as a conservative approach.[11]

The treatment of choice still remains hysterectomy, even though the patients are young in the third or fourth decades of life, as the numerous confluent nodules are not amenable to myomectomy. No recurrences have been reported following hysterectomy for DUL. Various treatment modalities like uterine arterial embolization, GnRH analogues, hysteroscopic resection for early-stage diffuse uterine leiomyomatosis have been proposed as an alternative to hysterectomy for the treatment of DUL.[6]

To conclude, diffuse uterine leiomyomatosis is a clinically distinct entity from the uterine leiomyomas in terms of varied gross and microscopic features as well as possibly pathogenesis and their treatment. DUL may on occasion be diagnostically challenging for the pathologists.

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