## Case report:

# Leiomyoma with Lymphoid Infiltration: An Extremely Rare Histological Variant

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#### **Abstract**

**Background:** Uterine leiomyoma with lymphoid infiltration is an extremely rare variant of leiomyoma. To the best of our knowledge, only 20 cases have been reported till date in the literature. Pathogenesis of this entity is not very clear. The various hypotheses which have been proposed to explain the etiopathogenesis include reactive alterations due to intrauterine pessaries, hormonal therapy or immune response dysregulation. **Case report:** We hereby report a case of a 44 year old female who presented with abnormal uterine bleeding. A small intramural leiomyoma was found which on pathological examination turned out to be leiomyoma with lymphoid infiltration. **Conclusions:** The importance of recognition this peculiar histological variant is to avoid possible misinterpretation as malignant lymphoma, inflammatory pseudotumororpyomyoma. In our case the lymphoid infiltration was reactive which was confirmed on immunohistochemistry

**Keywords:** leiomyoma, leiomyoma with lymphoid infiltration, lymphoma, pseudo tumor, pyomyoma.

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#### Introduction

Leiomyoma is the most frequent benign tumor in the females of reproductive age group. Diagnosis of a leiomyoma is very simple, however, when unusual features are observed in some rare variants of leiomyoma, the differential diagnosis with leiomyosarcoma and other benign and malignant tumors becomes challenging. Leiomyoma with lymphoid infiltration (LLI) is a rare histologic variant with only a handful of reports in the literature 1-10. LLI sometimes creates a diagnostic dilemma for the pathologist as it may be mistaken for a lymphoma. The pathogenesis of this entity is not very clear. We report a case of leiomyoma with lymphoid infiltration observed in a 44 year old female who underwent hysterectomy for abnormal uterine bleeding.

## **Case Report**

A 44 year old female presented with abnormal uterine bleeding for the last 3 months. There was a past history of tuberculosis involving ovary and

fallopian tube. Ultrasound revealed a bulky uterus with a small intramural fibroid and left ovarian cyst. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed. Grossly, the uterus and cervix measured 10x8x5 cms. On serial sectioning an intramural fibroid, 1 cm in diameter identified. Cut surface was grey white and showed whorling (figure 1).

Microscopically, the fibroid comprised of interlacing bundles of smooth muscles. Interspersed within the leiomyoma were collections of lymphoid cells with formation of germinal center in some of them (figure 2,3). No lymphoid cells were seen in the adjoining myometrium. No atypical lymphoid cells/ blasts were seen. Endometrium was in proliferative phase with chronic cervicitis. Bilateral ovaries showed corpus luteum.

Immunohistochemistry revealed positivity for CD3 (T cells), CD20 (B cells), $\lambda$  and  $\kappa$  light chains indicating a reactive infiltrate.

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Figure 1. Gross specimen showing a small intramural leiomyoma

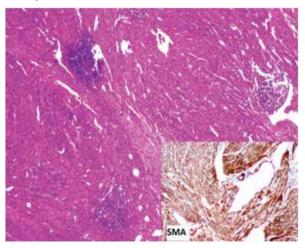


Figure 2. Photomicrograph showing interlacing smooth muscle bundles with interspersed collections of lymphoid cells (Hematoxylin& Eosin, 100x)

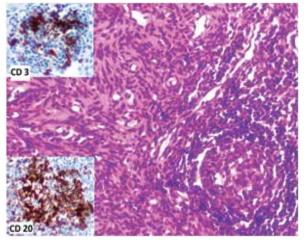


Figure 3. Photomicrograph showing collection of lymphoid cells with germinal center within the leiomyoma (Hematoxylin& Eosin, 400x)

#### Discussion

Uterine leiomyoma are the most frequent tumors of female genital tract occurring in approximately 20% women in the reproductive age group. Leiomyomas are estrogen dependent and tend to regress after menopause<sup>1,6</sup>. Many histologic variants have been described namely, lipoleiomyoma, myxoid leiomyoma, cellular leiomyoma, epithelioid leiomyoma, bizarre leiomyoma, leiomyoma with lymphoid infiltration<sup>8,9</sup>. Some of these variants may create a great diagnostic dilemma for the pathologist.

Leiomyoma with lymphoid infiltration (LLI) is an extremely rare histologic variant. On extensive search of literature, only around 20 cases have been reported till date 1-10. This entity was first reported by Ferry et al 2 who considered it to be a reactive process as in some cases intrauterine pessary was present. Many of these cases have been reported in patients following GnRH agonists which are administered to induce a state of artificial menopause prior to surgery to bring about reduction in size of the leiomyoma1. On the contrary, several authors have reported LLI without any history of intake of GnRH agonists <sup>3,5</sup>. The importance of this entity lies in the fact that it may be mistaken for a lymphoma. The features against a lymphoma include lymphoid infiltrate confined to leiomyoma, presence of predominantly small and large lymphocytes with a few plasma cells, histiocytes, formation of lymphoid follicles and absence of atypical lymphoid cells. Moreover, immunohistochemistry (IHC) helps in establishing the polymorphous/reactive nature of the lymphoid infiltrate utilizing T cell (CD3, CD4, CD8), B cell (CD20,  $\lambda$  and  $\kappa$  light chains) and histocytic (CD 68) markers. Other differential diagnoses for a leiomyoma with lymphoid infiltration include granulocytic sarcoma, pyomyoma and infiltrating pseudotumor. Granulocytic sarcoma comprises of collection of myeloid blasts which are not seen in LLI. Pyomyoma is seen in postpartum period and the infiltrate is composed of an admixture of neutrophils, lymphocytes, bacterial colonies and pus which may infiltrate into the adjoining myometrium unlike LLI. Inflammatory pseudotumor is a spindle cell tumor comprising of myofibroblasts, macrophages and mixed inflammatory infiltrate and may involve the adjacent tissues 4,5.

Pathogenesis of this entity is still unclear. Crow et al <sup>7</sup> suggested it could be due to immunological response to the alteration in cell surface antigen.

Lymphocytic infiltrate could be due to cell death as a result of ischemia or estrogen withdrawal <sup>6</sup>. Another proposed hypothesis is that there is a link between LLI and autoimmune process induced by hormone related changes in leiomyoma <sup>4</sup>. Belevejdov et al <sup>3</sup> reported elevated expression of lysosome associated membrane proteins (LAMP1 and LAMP2) implying enhanced autophagy, an indirect sign of degenerative changes.

Botsis et al <sup>5</sup> studied the frequency, histologic and IHC properties of massive inflammatory lymphocytic infiltration of leiomyomas over a 4 year period and encountered 5 such cases. They observed that gross, ultrasonographic and color Doppler findings were similar to a typical

leiomyoma. IHC revealed positivity for desmin, leucocyte common antigen,  $\lambda$  and  $\kappa$  light chains indicating a polyclonal nature of the lymphoid infiltrate.

Abraham et al <sup>9</sup> in their observational study on morphological variants and secondary changes in uterine leiomyomas, found 2 cases of LLI out of a total of 41 variants of leiomyoma. In another such study, Manjula et al <sup>8</sup> observed leiomyoma variants in 4.55% of all leiomyoma cases with only a single case of LLI.

The significance of recognition of this distinct histological variant of leiomyoma lies in avoiding misdiagnosis as a lymphoma, inflammatory pseudotumor or a pyomyoma.

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