



ENDOMETRIAL STROMAL NODULE MASQUERADING AS UTERINE LEIOMYOMA - A CHALLENGING DIAGNOSIS IN FROZEN SECTION

Oncopathology

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ABSTRACT

Endometrial stromal tumors (EST) are rare, and endometrial stromal nodules (ESN) are the least common. We present a case of a 71-year-old woman, who presented with urinary retention, constipation, and a lower abdominal mass of 16 weeks- size. Radiologically, the uterine mass was reported as leiomyoma with mitotic degeneration. She underwent a hysterectomy. Frozen section examination revealed uniform small mononuclear cells in a loose fibrous stroma. Histopathology and immunohistochemistry reports confirmed ESN. Endometrial stromal tumors are challenging to diagnose in frozen section examination. The appropriate diagnosis is possible only after a complete gross and microscopic examination. Thus, hysterectomy is the treatment of choice in benign and malignant tumors. The non-infiltrative border of stromal tumors is the most important criterion for diagnosing EST. The distinction between them is mandatory because of the significant difference in their clinical prognosis.

KEYWORDS

Endometrial stromal tumors, endometrial stromal nodule, endometrial nodule in frozen section, leiomyoma mimicker.

INTRODUCTION

Endometrial Stromal Tumors (EST) account for 3% of all uterine neoplasms. The World Health Organization recognizes four categories of endometrial stromal tumors based on clinical and pathologic features: (a) endometrial stromal nodule (ESN), (b) low-grade endometrial stromal sarcoma (LGESS), (c) high-grade endometrial stromal sarcoma (HGESS), and (d) undifferentiated uterine sarcoma (UUS) (1,2). These categories are defined according to their distinct translocations, tumor morphology, and prognosis(3). However, differentiating between the subtypes is difficult in specimens obtained after curettage. A complete gross and histological examination of the uterus is the most accurate method of diagnosis, and the recommended therapy for an endometrial stromal neoplasm is a total hysterectomy(4). However, the ESN is difficult to diagnose because of its similarity to low-grade endometrial stromal sarcomas. The ESN is a non-invasive and clinically benign type of EST(5). High-grade endometrial stromal sarcomas can be differentiated from LGESS by gross appearance, microscopic features, mitotic state, and immunohistochemistry(2). In this case report, we present a patient with a stromal nodule who has undergone a total abdominal hysterectomy. We insist on the fact that endometrial stromal nodule is a rare disease, yet to be carefully differentiated from other stromal sarcomas, which have varying prognoses.

CASE PRESENTATION

A 71-year-old postmenopausal woman presented to the gynecology outpatient department with complaints of urinary retention and constipation for the past three days. She had dull pain and discomfort in the lower abdomen for the past several weeks. She was on treatment for hypertension, hypothyroidism, and coronary artery disease (CAD). A painless pelvic mass reaching above the level of the umbilicus was palpated on examination. Ultrasound of the abdomen and pelvis showed a well-circumscribed mass in the uterus with heterogeneous (cystic and solid components) echo texture. Magnetic resonance imaging (MRI) revealed a large posterior wall fibroid measuring 7 x 6.8 x 6 cm with mitotic degeneration, without parametrial infiltration and hydronephrosis. It was reported as leiomyoma with mitotic degeneration of size 7X6.8X6 cm with patchy restricted diffusion and low apparent diffusion coefficient (ADC). Laboratory investigations revealed anemia (Hemoglobin of 10 gm/dL (ref: 12-14 g/dL), and the rest of the parameters were within normal limits. She received a packed red blood cell transfusion and subsequently underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy. The surgical specimen was sent to the frozen section for a primary diagnosis. A gross examination of the surgical specimen (Figure 1) showed a fairly circumscribed globular solid cystic lesion measuring 9 x 7.5 x 5cm within the myometrium, pushing the endometrial cavity. Endometrium appeared unremarkable. The cystic area had septations

and was filled with hemorrhagic fluid, while the solid area displayed a soft to firm, fleshy tan-brown to granular red cut surface that bulged above the surface. The lesion was 1 cm away from the serosa. Bilateral adnexae were unremarkable.



Figure 1: Gross appearance showed a fairly circumscribed globular solid cystic lesion measuring 9 x 7.5 x 5cm within the myometrium, pushing the endometrial cavity. Endometrium appears unremarkable. The cystic area had septations and was filled with hemorrhagic fluid while the solid area displayed a soft to firm, fleshy tan brown to granular red cut surface that bulged above.

The frozen section examination (Figure 2) demonstrated monomorphic small mononuclear cells in a loose fibrous stroma. Few cells were eosinophilic. These were considered changes secondary to ischemia hence, a definite opinion could not be provided.

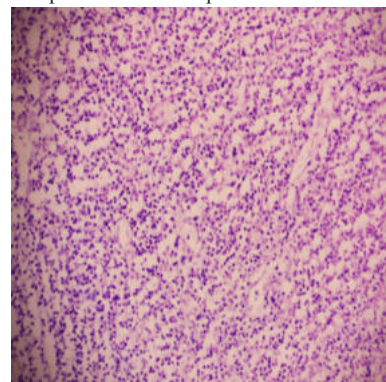


Figure 2: Frozen examination showed uniform small mononuclear

cells in a loose fibrous stroma. Few cells are eosinophilic (secondary to ischemia).

Microscopic examination showed (Figure 3) a circumscribed lesion composed of sheets of uniform mononuclear cells with scant cytoplasm intervened by amianthoid fibers- like and star-burst shaped collagen bands in a fibro hyalinised stroma with areas of ischemic necrosis. Focally, preserved spindle cells with elongated blunt-ended nuclei were seen. There were no permeative margins beyond 3 mm and lympho-vascular invasion. There is no evidence of thrombi in the adjacent vessels. High-grade features like mitosis, nuclear atypia/ pleomorphism, and coagulative necrosis were absent. Hence, a differential diagnosis of leiomyoma with secondary changes (like extensive lymphocytic infiltration) and superficial myofibroblastoma with secondary changes were considered, and immunohistochemistry (IHC) was advised.

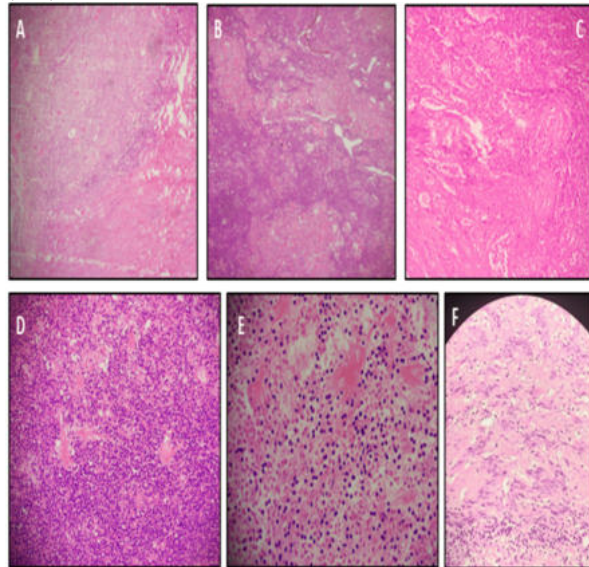


Figure 3: Microscopic appearance showed (A,B) a circumscribed lesion composed of sheets of mononuclear cells with scant cytoplasm, (C) Areas of ischemic necrosis, (D,E) Lesion intervened by amianthoid fibres like and star burst shaped collagen and bands of fibrohyalinised stroma.(F) Focal preserved spindle cells with blunt ended nuclei, arranged in stacks alternating with areas of fibro-hyalinization.

By IHC (Figure 4), the tumor was immuno-reactive to CD10 and desmin while negative for smooth muscle actin(SMA), h-Caldesmon, CD 45, D2-40, and CD 34. The Ki-67 proliferation index was low (5%). Based on the macroscopy, microscopy, and IHC findings, the tumor was diagnosed as an endometrial stromal nodule.

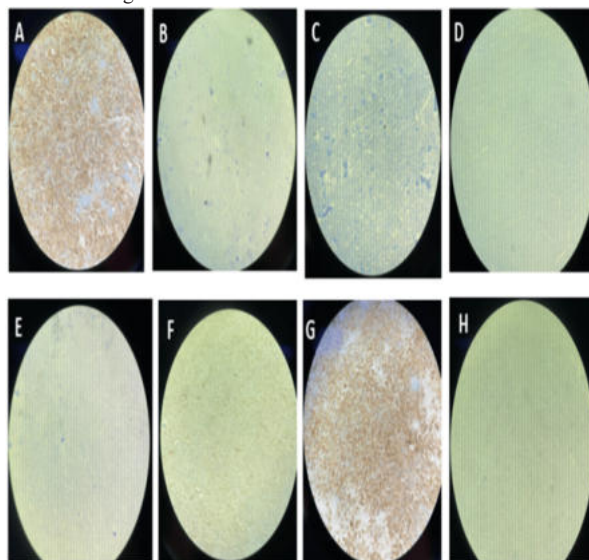


Figure 4: IHC examination showed (A) patchy Desmin positivity,

(B-F) Immunostaining for Smooth muscle actin (SMA), h-Caldesmon, CD 45, D2-40, CD 34 were negative. (G) diffuse CD 10 positivity, (H) ki-67 was low (5%)

DISCUSSION

Endometrial stromal tumors are among the least common neoplasms of the uterine corpus, with an annual incidence of about 2 per million women. The benign endometrial stromal nodule is a rare subtype that accounts for about one-fourth of the endometrial stromal tumors, that constitute less than 5% of uterine tumors (6). ESN usually occurs at premenopausal age but can be observed over a wide age range, from 31 to 86 years, with a mean of 53 years(7). Patients may be asymptomatic or may have abnormal bleeding and lower abdominal or pelvic pain (3). Our patient had urinary retention, constipation, and lower abdominal discomfort. The preoperative diagnosis of ESN is difficult. ESN cases are generally diagnosed preoperatively as leiomyoma. The most important differential diagnoses are LGESS and cellular/ highly cellular leiomyoma. The non-infiltrative border of stromal tumors is the most important criterion for the diagnosis. Histological examination of the uterus is the most accurate method to make an appropriate diagnosis and thus hysterectomy is the treatment of choice in benign as well as malignant tumors (8).

ESNs are well-circumscribed masses with a soft consistency and yellow-to-orange color (2,9). ESN is differentiated from LGESS by its expansile but non-infiltrative and smooth margins in contrast with an irregular nodular growth in the endometrium with varying degrees of myometrial permeation as well as extension to extrauterine veins and lymphatics seen in the latter (8). Cyst formation, ischemic necrosis, and hemorrhage may also be present (2). This patient also had a well-circumscribed mass without parametrial infiltration and hydroureteronephrosis. Gross examination revealed a circumscribed globular solid cystic lesion measuring 9 x 7.5 x 5cm within the myometrium, pushing the endometrial cavity. Endometrium appeared unremarkable. The cystic area had septations and was filled with hemorrhagic fluid, while the solid area displayed a soft to firm, fleshy tan-brown to granular red cut surface that bulged above the surface. The lesion was 1 cm away from the serosa.

The cytomorphology of ESN is similar to low-grade sarcomas. Both are composed of a diffuse growth of uniform small blue cells with scant cytoplasm and oval to spindle nuclei that resemble endometrial stromal cells of proliferative endometrium, that grow in sheets and focally whorl around arterioles (8).

Microscopically, myometrial infiltration if present, can be seen as protrusions less than 3 in number, 3 mm or less with no angiolymphatic invasion and minimal mitotic activity (<3/10 HPF) 3 in a stromal nodule. Tumors with myometrial infiltration >3 mm and >3 in number would be categorized as LG-ESS. HGESS and UUS show destructive infiltrative growth into the endometrium, myometrium, or both. Microscopically, marked nuclear atypia is characteristic of high-grade ESS and UUS with a mitotic rate of >10/10 HPF (8). Smooth muscle differentiation in ESN can be confusing as one may misinterpret the interdigitating metaplastic smooth muscle as myometrial invasion (7).

Delineating the actual tumor border during gross examination is extremely helpful. Extensive sampling of the tumor margin is mandatory for the prompt diagnosis of these tumors. Although ESNs are benign tumors, hysterectomy is the gold standard to rule out malignancy.

Immunohistochemical expression of ESN includes CD10 positivity, SMA, h-caldesmon, and desmin negativity (or weakly positive) (3). In our case, the tumor expresses diffuse CD10 and patchy Desmin positivity. The nodule was immunonegative with SMA (Smooth muscle actin), h-Caldesmon, CD 45, D2-40, and CD 34. Though the immune profile of an ESN practically matches that of an ESS, it is crucial to identify and categorize them accurately. This is because of the difference in their clinical prognosis. ESN portends an excellent prognosis, while the prognosis of ESS is significantly worse.

High-grade endometrial stromal sarcomas can be differentiated from LGESS by gross appearance, microscopic features, mitotic state, and immunohistochemistry(1). Like GESS, t(7;17) resulting in JAZF1-SUZ12 gene fusion is the most common chromosomal rearrangement in conventional and variant ESNs(7). This case is unique in that it is associated with significant areas of infarct type/ ischemic necrosis. This made us think of leiomyoma with secondary changes at the first

look. Considering the huge differences in therapeutic options and clinical outcomes, it is essential to differentiate endometrial stromal nodules from ESS and other mesenchymal tumors.

CONCLUSION

The diagnosis of endometrial stromal tumors with secondary changes is challenging on frozen section examination. There is no reliable preoperative diagnostic procedure to identify this tumor. The therapeutic strategy is surgical. The histopathology diagnosis is critical, which has its pitfalls. Immunohistochemistry and extensive tumor sampling are required to distinguish endometrial stromal nodules (benign) from low-grade endometrial stromal sarcoma (indolent malignant tumor). Recognition and classification of endometrial stromal tumors are necessary as they have different molecular profiles and prognoses.

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