

Cellular Leiomyoma versus Endometrial Stromal Sarcoma: A Report of a Rare Case Presenting a Diagnostic Challenge on Intraoperative Frozen Section

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Abstract

Endometrial stromal sarcomas (ESSs) account for approximately 0.2% of all uterine malignancies. Cellular leiomyoma (CL) often simulates low-grade ESS due to similar cytology. We report the case of a 34-year-old female with a mass per abdomen. Frozen sections showed a tumor with many thin- and thick-walled vessels along with hyaline material. A differential diagnosis of CL and endometrial stromal tumor was suggested. The index case was diagnostically challenging to pathologists. Paraffin sections supplemented by immunohistochemistry (smooth muscle actin, CD10, and beta-catenin) favored CL. Frozen section sometimes leads to over/underestimation of tumor in view of small sampling area of tumor.

Keywords: Cellular leiomyoma, endometrial stromal tumor, frozen section, immunohistochemistry

INTRODUCTION

Endometrial stromal tumors (ESTs) are rare uterine mesenchymal neoplasms and on occasion pose a diagnostic dilemma for pathologists.^[1] According to the current WHO classification, they have been categorized into endometrial stromal nodule, low-grade endometrial stromal sarcoma (LG-ESS), high-grade ESS, and undifferentiated uterine sarcoma.^[1] Among EST, ESSs are very rare accounting for approximately 0.2% of all uterine malignancies.^[2]

Although frozen section plays a very crucial role in intraoperative diagnosis of gynecological pathology, it may lead to over- or underestimation of tumor in view of small sampling area of tumor. Cellular leiomyoma (CL) often simulates LG-ESS due to increased cellularity. It becomes all the more difficult to distinguish ESS from CL on frozen sections. The index case presented a

diagnostic challenge to pathologists on frozen section which was later resolved by histopathology supplemented by immunohistochemistry (IHC).

CASE REPORT

A 34-year-old female came to a gynecology clinic with a mass per abdomen associated with dull pain. No menstrual irregularities were reported. On abdominal examination, the uterus appeared enlarged up to the size of 14 weeks, and per vaginal examination revealed a large firm mass but the cervix could not be appreciated. Ultrasonography showed a uterine mass measuring 10.2 cm × 7.8 cm × 10.9 cm, suggestive of degenerated fibroid with no other lymph node or organ involvement.

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The patient was nulliparous and was being investigated for infertility; moreover, in view of uncertain nature of large uterine mass, a frozen section was requested keeping in mind the need for conservative approach.

Intraoperative findings revealed a normal-appearing uterus with a large mass measuring approximately 15 cm overlying the cervical region. On opening, the mass came out in bits and pieces which were sent for frozen section. We received multiple gray-brown friable soft-tissue pieces measuring 6 cm × 5 cm × 1 cm. Frozen sections showed a tumor composed of round-to-oval cells with mild nuclear pleomorphism and minimal mitosis. Many thin- and thick-walled vessels were also seen along with deposition of hyaline material interspersed between the tumor cells [Figure 1]. A differential diagnosis of CL and EST was suggested. In view of lack of a definitive opinion on the nature of the tumor and the necessity to conserve the uterus, complete excision of the mass was performed. Grossly, a large partially encapsulated globular soft-tissue mass measuring 8 cm × 7 cm × 4 cm was received along with multiple grey-white friable pieces [Figure 2]. Cut surface of the mass was solid, gray-white, and friable. Hematoxylin- and eosin-stained sections showed a highly cellular tumor composed of oval-to-spindle cells arranged in fascicles and sheets interspersed with many thick-walled blood vessels. Even on extensive sampling, mitosis was sparse (1–2/10 high-pass filter) with mild nuclear atypia and no evidence of necrosis. Histological features were suggestive of CL. IHC was advised to rule out EST. Smooth muscle actin (SMA) showed diffuse strong positivity, progesterone receptor (PR) showed focal positivity, while CD10, beta-catenin, inhibin, and estrogen receptor were negative [Figure 3]. Thereby, a final impression of CL was given. The patient was kept on follow-up, and no further surgical intervention was required.

DISCUSSION

ESS and CL can exhibit marked similarity in architectural and cytological characteristics, thereby creating a diagnostic dilemma which is furthermore exaggerated by ESS with smooth muscle differentiation.

Clinically, patients with ESS present with abnormal uterine bleeding, pelvic pain, or dysmenorrhea.^[2] Patients with CL have chief complaints of menstrual irregularities, pelvic mass, abdominal pain, and pelvic pressure. However, our patient presented with mass and dull pain in the abdomen without menstrual irregularities.

ESS usually occurs in the 4th–5th decade.^[3] Uterine imaging in cases of ESS is not reliable and can lead to faulty diagnosis of adenomyosis or uterine leiomyoma.^[2] CL are well-circumscribed, tan, or yellow nodules that tend to

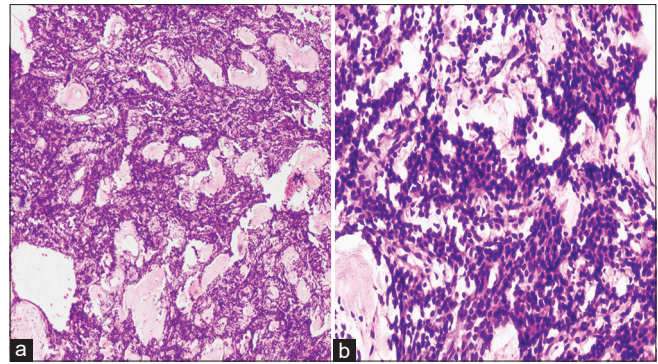


Figure 1: Frozen sections – a) cellular tumor with many thin and thick-walled vessels (Rapid H&E, ×200) b) round to oval cells with mild nuclear pleomorphism and minimal mitosis along with deposition of hyaline material interspersed between the tumor cells (Rapid H&E, ×400)

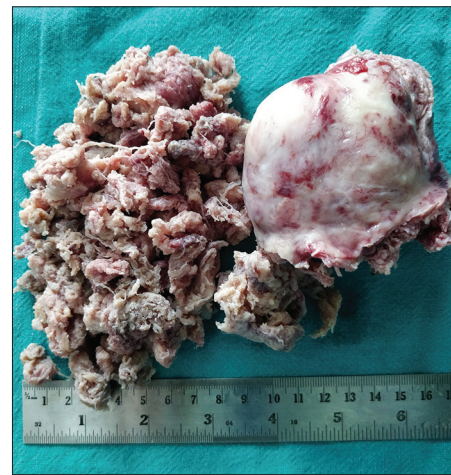


Figure 2: Gross - large partially encapsulated globular soft tissue mass along with multiple grey-white friable pieces

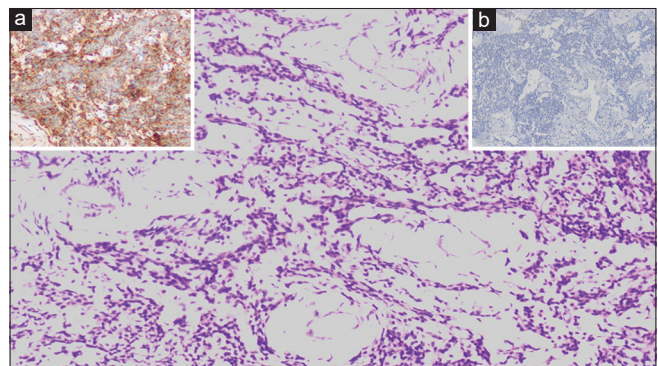


Figure 3: Paraffin sections - highly cellular tumor composed of oval to spindled cells arranged in fascicles and sheets interspersed with many thick-walled blood vessels (H&E, ×200). Inset a) IHC: SMA - diffuse positivity (×200) Inset b) IHC: CD10 – negative (×200)

have a softer consistency than the usual type of leiomyoma, however, histologically, they have an irregular border. They have markedly increasing cellularity and can mimic low-grade ESS.^[3] Grossly, LG-ESS usually involves

endometrium, forming a soft, tan, to yellow polyp, which may be infarcted or hemorrhagic.^[4] However, the present case received tissue mostly in bits and pieces for frozen.

The histogenesis of ESTs is still a matter of controversy. It has been proposed as differentiation of epithelial, sex cord, and smooth muscle elements by a variety of immunohistochemical and ultrastructural studies.^[5] Due to the tendency of endometrial stromal cells to differentiate into well-developed smooth muscle cells, it becomes all the more difficult sometimes to differentiate EST from CL.^[6] The endometrial stroma occasionally gives rise to neoplasm that may resemble stromal cells cytologically and architecturally. The authors have found that ESTs are composed of cells that have a resemblance to endometrial stromal cells of proliferative endometrium.^[2,7]

CL is a benign smooth muscle proliferating tumor composed of densely cellular fascicles of smooth muscle with scant intervening collagen with the presence of large thick-walled blood vessels. Endometrial stromal proliferations show predominantly delicate arborizing vessels. Oliva *et al.*^[8] emphasized large thick-walled blood vessels as an important feature to distinguish CL from stromal proliferation. However, the presence of many thin- and thick-walled vessels along with deposition of hyaline material interspersed between the tumor cells on frozen lead to the confusion in the present case.

ESTs show heterogeneous morphological features, with LG-ESS being a clinically indolent malignant neoplasm with minimal cytological atypia, infrequent mitotic figures, and numerous thin-walled small arteriolar type vessels.^[5] The current case, showed sparse minimal atypia along with presence of thick and thin walled vessels and hyaline material. This created a dilemma on frozen section examination which was later resolved on studying the paraffin sections and immunohistochemistry (IHC), later. Frozen section is limited by small area of sampling which may lead to over- and underestimation of tumor.

IHC plays a major role in differentiation of CL and ESS. Strong and/or diffuse positivity of CD10 favors ESS. ESSs are almost always positive for both estrogen and PRs. However, CL shows positivity for h-caldesmon and desmin.^[3] Rajendran observed in his study (2020) that leiomyomas are more progesterone dependent than estrogen dependent as seen in the present case.^[9] Inhibin positivity is seen in uterine tumors resembling ovarian sex cord tumors.^[10] In the current case, SMA showed diffuse strong positivity while CD10, beta-catenin, and inhibin were negative.

The main tumor of ESS is always intramural, but most of them involve endometrium and uterine curettage may be helpful in

such cases, however, definitive diagnosis can only be made on hysterectomy specimen.^[2] Distinguishing ESS from CL is essential in view of different prognosis and treatment plan. Total hysterectomy with bilateral salpingo-oophorectomy is the main line of management for ESS.^[2]

CONCLUSION

Distinguishing ESS from CL can be problematic on frozen section, however, in view of differing prognosis and treatment, it is a very crucial task for both pathologist and clinician. However, histopathology coupled with IHC remains the gold standard.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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