

Pitfalls of Frozen Section in Gynaecological Pathology: A case of endometrial tumor with sex- cord- like elements

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Precis:

Endometrial stromal tumors with sex cord- like elements are rare tumors which can pose a diagnostic dilemma on frozen section.

Keywords: Endometrium; endometrial stromal sarcoma, sex-cord-like elements; frozen section; pathology

Abstract:

Endometrial stromal tumor with sex cord- like elements (ESTSCLE) is a rare entity which shares similar histological features with uterine tumors resembling ovarian sex cord tumors (UTROSCT). Differentiating the two entities involves ample sampling of the tissue to distinguish the percentage of sex- cord components within the tissue, genetic studies and immunohistochemical staining. Frozen section provides limited information for exclusion of either tumor; and the tumor is rare enough that the diagnosis may not be considered with the limited sampling; therefore deferral of diagnosis to permanent sections may be appropriate.

Introduction:

The use of frozen section in the intraoperative consultation of gynecologic pathology is very useful in providing a probable diagnosis, aiding the staging of tumors and guiding the surgeon as to the need for further surgical intervention, for example, lymph node dissection. Whereas determining the degree of myometrial invasion may be a straightforward task, differentiating unusual tumors can be problematic. Frozen section is limited to sampling a small area of tumor, which may over- or underestimate tumor elements and there are many artifacts which may be created during freezing which may distort the architecture and morphology of the tissue. Endometrial stromal tumors with sex cord-like elements (ESTSCLE) and uterine tumors resembling ovarian sex cord tumors

(UTROSCT) are rare uterine stromal tumors which bear similar morphological features but have different genetic profiles and immunohistochemical staining patterns. In 1976, Clement and Scully (3) described these two entities and classified them based on the percentage of sex-cord component admixed with stromal elements. Endometrial stromal tumors with sex cord-like elements (ESTSCLE) contain <50% sex- cord components whereas uterine tumors resembling ovarian sex cord tumors (UTROSCT) contain 50-100% sex cord components. The following case presented a diagnostic challenge at frozen section because of the appearance and percent of tubular elements seen, as well as the rarity of the lesion.

#### Case report

The patient was a 79 year old female who presented with a 5 month history of pelvic pressure and pain and difficulty with micturition and defecation. Transvaginal sonogram demonstrated a 12.7cm uterus with a heterogenous mass occupying the uterus and cervix (10.6 x 9.7 x 9cm) and CT PET scan demonstrated 3 bibasilar lung nodules. A total hysterectomy and bilateral salpingoophorectomy was performed. Intraoperative consultation of a 627g uterus (figure 1) revealed an 11 x 10 x 4.6cm tan/brown well circumscribed intramural mass which extended to the endocervical canal and distorted the anatomy of the specimen. Cut sectioning revealed a fleshy tan/brown tumor with focal areas of necrosis and hemorrhage. A section of tan tissue was submitted for frozen section which revealed numerous microfollicles with colloid- like material interspersed with focal solid areas of spindle-like cells with scant cytoplasm. The microfollicles made up the majority of the frozen section (figure 2), with stromal elements not recognized until permanent section, and a deferral was issued pending permanent sections.

On permanent section, extensive sampling revealed that most of the tumor was actually of low grade endometrial stromal sarcomatous morphology (figure 3), with only focal sex- cord- like areas (10%). It was purely by chance that the sex- cord- like areas was sampled at the frozen section, leading to the difficulty in rendering a diagnosis.

Immunohistochemical staining was positive for CD10 , AE1/3 cytokeratin, rare cells for calretinin , focally for inhibin and CD99 (mostly in sex- cord areas). Cytogenetics was performed which showed a gain of chromosome 1q through isochromosome formation and loss of chromosome 22 which is the most frequent copy number changes found in low- grade endometrial stromal sarcoma(10). A diagnosis of endometrial stromal tumors with sex- cord-like elements (ESTSCLE) based on the presence of predominance of low grade endometrial stromal sarcoma, a sex cord component of <50% immunohistochemical staining and cytogenetics. Biopsy of one of the lung nodules revealed metastatic disease, and the patient has been offered hormonal therapy.

#### Discussion:

Endometrial stromal tumors with sex cord like elements (ESTSCLE) are a subgroup of low grade endometrial stromal sarcomas. This tumor is comprised of cells resembling endometrial stromal cells that are spindle- like to epithelioid with scant cytoplasm. They stain positively for CD10 and frequently have a t(7;17) (p15;q21) translocation resulting in JAZF1-jjAZ1 fusion (5). The stroma resembles proliferative phase endometrial stroma with prominent vessels, as in usual low grade endometrial stromal sarcoma. Tumor cells can be located in large nests or as tongue-like infiltrates. Mitoses are infrequent (<10per hpf) in low grade cases. Myometrial invasion and lymph vascular involvement distinguishes this tumor from a stromal nodule. Sex- cord components constitute between 10-50% of the tumor population in ESTSCLE. Numerous cases have been described where these tumors also stain for inhibin (2), CD99, pankeratin, vimentin, prolactin (1), ER, PR, desmin & caldesmon.

Uterine tumors resembling ovarian sex cord tumors (UTROSCT) microscopically have a variety of patterns including anastomosing trabeculae, microfollicular, macrofollicular, tubular, retiform, solid, plexiform cords and diffuse patterns. These sex cord components usually comprise >50% of the tumor population. The individual cells

are spindle shaped with round to ovoid nuclei, with minimal pleomorphism, inconspicuous nucleoli and scant cytoplasm. Like endometrial stromal tumors with sex cord like elements (ESTSCLE), the stroma resembles proliferative endometrial stroma. Mitoses are also infrequent. It is to be noted that there should be no endometrial stromal neoplastic cells within the sex- cord- regions. No genetic abnormalities have been described for this entity; however the immunohistochemical profile can help in the diagnosis. Calretinin and at least three of the following should be positive to make the diagnosis: CD99, inhibin (5) and melan-A. This tumor can also be positive for pankeratin, epithelial membrane antigen, WT-1, smooth muscle actin, desmin(5), CD10, estrogen receptor, progesterone receptor and CD117.

Macroscopically both UTROSCT and ESTSCLE can present as tan, well circumscribed intramural masses with pushing or infiltrating borders. These two tumors are reported to behave in a similar pattern with a prognosis which depends upon the stage at presentation. Complete excision confers a good prognosis; however recurrence has been well documented.

In summary, there is limited use of frozen section in the diagnosis of endometrial stromal tumors with sex- cord- like elements (ESTSCLE).Confirmation of diagnosis should be deferred until adequate sampling, immunohistochemistry and genetic studies are performed.

Legend

Figure 1- Cut section of uterus showing well circumscribed tan/ brown intramural mass extending to endocervix.

Figure 2- Frozen section of mass showing sex- cord- like elements in a microfollicular pattern

Figure 3- Permanent section of intraoperative consultation demonstrating sex- cord- like elements interspersed within areas of low grade endometrial stromal sarcoma

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