Case Report

Myxoid High-Grade Endometrial Stromal Sarcoma: A Close Mimicker of Myxoid Leiomyosarcoma

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Abstract

Endometrial stromal sarcomas are rare malignant uterine tumors that make up approximately 10% of all uterine sarcomas, but only around 0.2% of all uterine malignancies. The high-grade category of ESS was reintroduced in the new World Health Organization (WHO) tumor classification system based on its distinct morphologic, immunohistochemical, and molecular characteristics. ZC3H7B-BCOR is a newly described subtype of high-grade endometrial stromal sarcoma that closely mimics the appearance of myxoid leiomyosarcoma. Although its frequency is reported as low, it may, in fact, be higher, as in the past these tumors were frequently misdiagnosed as leiomyosarcoma.

We hereby present a case report of a 45-year-old female who presented with disseminated peritoneal deposits of HG-ESS, which had initially posed diagnostic challenges due to its myxoid background and resemblance to leiomyosarcoma. Detailed case history and immunohistochemistry evaluation guided us to the final diagnosis.

Keywords:

ESS, hysterectomy, sarcoma, HG-ESS

Introduction

According to the 2014 World Health Organization (WHO) tumor classification system, Endometrial Stromal Tumor can be classified into four categories: Endometrial Stromal Nodule (ESN), Low-Grade Endometrial Stromal Sarcoma (LG-ESS), High-Grade Endometrial Stromal Sarcoma (HG-ESS), and Undifferentiated Uterine Sarcoma (UUS) [1]. High-grade endometrial stromal sarcomas are rare malignant uterine tumors that make up approximately 10% of all uterine sarcomas, but only around 0.2% of all uterine malignancies [2]. The two well-defined categories of high-grade endometrial stromal sarcomas recognized are: i) YWHAE-FAM22 (YWHAE-NUTM2) High-Grade Endometrial Stromal Sarcoma, and ii) ZC3H7B-BCOR High-Grade Endometrial Stromal Sarcoma [3].

ZC3H7B-BCOR is a newly described subtype of high-grade endometrial stromal sarcoma that closely mimics the appearance of myxoid leiomyosarcoma [4]. Although its frequency is reported as low, it may in fact be higher, as in the past, these tumors were frequently misdiagnosed as leiomyosarcoma. In the only series reported to date, typical tumors occur within a wide age range (28–71 years), but most frequently in the fifth decade. Patients present with non-specific symptoms, including vaginal bleeding and/or pelvic mass, and not infrequently have extrauterine disease at initial diagnosis. The clinical presentations in our case were pelvic mass, abdominal distension, and pain.

We hereby present a case of a 45-year-old woman who presented with extrauterine manifestation of HG-ESS, which is rare, particularly in middle-aged women. A case report of this rare entity is, therefore, necessary to better understand its clinical course and to differentiate it from its closest mimicker, myxoid leiomyosarcoma.

Case Report

A 45-year-old female presented with abdominal distension and a mass. A CT scan of the abdomen showed a heterogeneous hypoechoic lesion measuring 10 x 8 x 4 cm in the pelvis, involving the bladder and bowel walls (Fig. 1). Laparoscopic debulking of the tumor was performed, and the tissue was sent for histopathological examination.

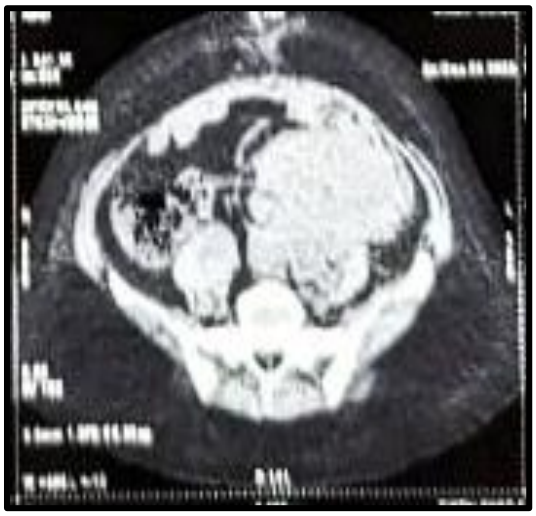

Figure 1: CT scan Abdomen & pelvis showing heterogenous hypoechoic lesion involving bowel and bladder

Grossly, the specimen consisted of multiple tissue pieces aggregating to 11 x 10 x 8 cm. The cut surface showed gelatinous, mucoid, and slimy areas, with a few grey-white regions noted (Fig. 2C).

Microscopic examination of the tumor revealed a cellular mass with a destructive pattern of invasion into the adipose tissue, composed of spindle cells arranged in haphazard fascicles. The background displayed abundant myxoid stroma, with few areas of necrosis and atypical mitoses (Fig. 3A-D).

Individual tumor cells exhibited pleomorphic vesicular nuclei and scant to moderate eosinophilic cytoplasm. The mitotic count was 20-25 per 10 high-power fields (HPF), with focal areas of tumor necrosis and lymphovascular tumor emboli (Fig. 3A-D).

Considering the above histomorphological features, the differential diagnoses of retroperitoneal sarcoma were considered, including dedifferentiated liposarcoma, myxoid endometrial stromal sarcoma, and myxoid leiomyosarcoma. A subsequent immunohistochemistry (IHC) panel was conducted for confirmation.

The tumor cells were diffusely and membranously positive for CD10 and focally, patchily positive for Cyclin D1, while negative for SMA, Desmin, H-caldesmon, S100, MDM2, ER, and PR. Mib1 highlighted 80% of tumor nuclei (Fig. 3E-G).

The IHC workup confirmed the diagnosis of high-grade endometrial stromal sarcoma (HG-ESS). Further clinical details of the patient were sought, revealing that she had undergone a hysterectomy at a peripheral hospital for a uterine mass lesion, which was diagnosed as leiomyosarcoma on H&E stained slides (Fig. 2A, B). Upon retrieving the paraffin blocks from that peripheral hospital, the sections showed tumor morphology similar to the peritoneal mass received at our center (Fig. 4A-E). Thus, it was inferred that the peritoneal mass was the metastatic spread of the primary uterine HG-ESS. Unfortunately, the patient succumbed within two weeks of diagnosis.

Figure 2: (A) Cut surface of the uterus showing obliteration of the entire endometrial cavity by a bulky, fleshy mass with areas of necrosis. (B) Gross image showing a bulky, globular uterus with a few nodular areas on the serosa. (C) Gross image of a retroperitoneal mass showing multiple tissue pieces with slimy, mucoid, hemorrhagic areas.

Discussion

The differential diagnoses primarily included dedifferentiated liposarcoma, myxoid endometrial stromal sarcoma, and myxoid leiomyosarcoma. Although the histomorphology was suggestive of liposarcoma, as per dictum, dedifferentiated liposarcoma does not present as a retroperitoneal mass. Due to the presentation at an uncommon site and the negative IHC markers (S100 and MDM2), the possibility of dedifferentiated liposarcoma was ruled out. Metastasis of myxoid endometrial stromal sarcoma and myxoid leiomyosarcoma were the differentials considered further. As all the IHC markers for smooth muscles (i.e., SMA, H-caldesmon, and Desmin) were negative, the possibility of myxoid leiomyosarcoma was also ruled out. The rapid clinical progression—tumor involving bowel and bladder with compression symptoms like constipation, urinary incontinence, and dribbling—and a past history of being operated on for a uterine mass, along with the IHC profile, supported the diagnosis of H-ESS.

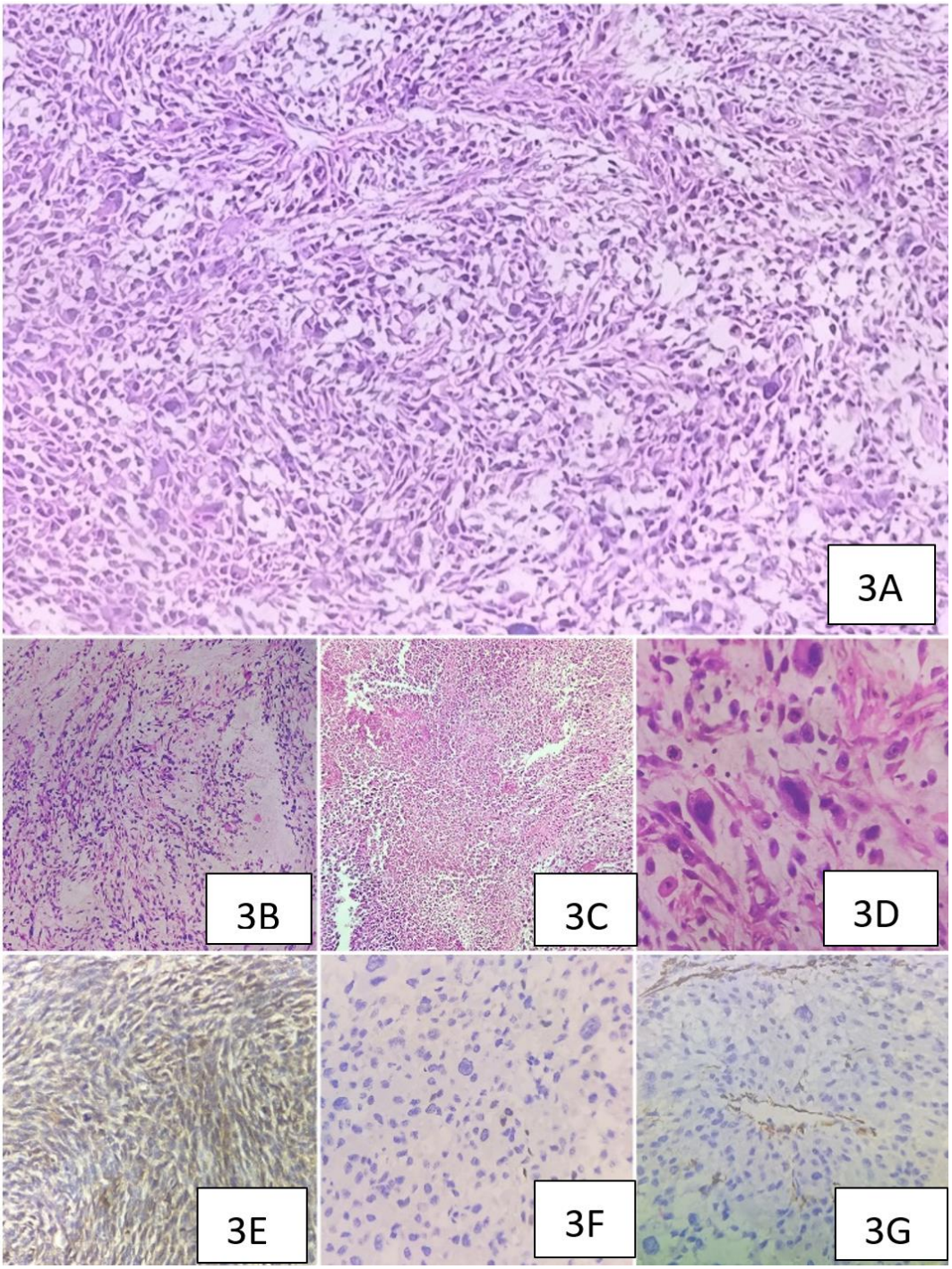

Figure 3: (A) Microphotograph from retroperitoneal mass showing haphazardly arranged fascicles of spindle cells with cytological atypia and tumor giant cells (H&E, 100X). (B) Microphotograph showing fascicles of spindle cells against an abundant myxoid background (H&E, 400X). (C) Microphotograph showing geographical areas of tumor cell necrosis (H&E, 100X). (D) Microphotograph showing bizarre cells with pleomorphic nuclei (H&E, 400X). (E) Microphotograph showing diffuse, membranous positivity of CD10 (IHC, 400X). (F) Microphotograph showing focal and patchy positivity of Cyclin D1 (IHC, 400X). (G) Microphotograph showing negative Smooth Muscle Actin (IHC, 400X).

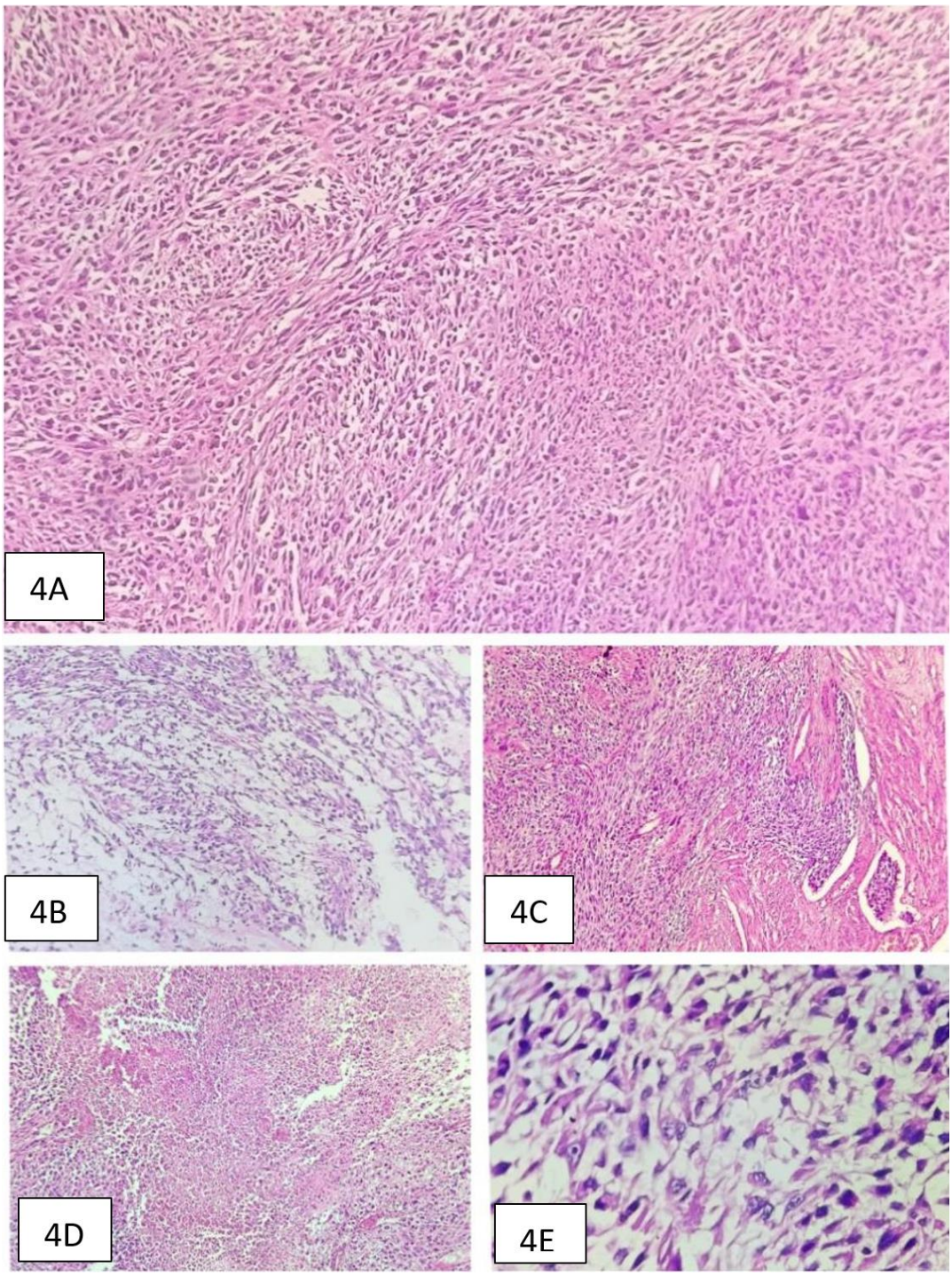

Figure 4: (A) Microphotograph from uterine mass showing fascicles of spindle cells with round to oval nuclei, inconspicuous nucleoli, and eosinophilic cytoplasm (H&E, 100X). (B) Microphotograph showing fascicles of spindle cells with cytological atypia against an abundant myxoid background (H&E, 400X). (C) Microphotograph showing lymphovascular tumor cell emboli (H&E, 100X). (D) Microphotograph showing geographical areas of tumor cell necrosis (H&E, 100X). (E) Microphotograph showing bizarre cells and tumor giant cells against a myxoid background (H&E, 400X).

This once again reiterates the fact that one should always consider metastasis from the uterus when dealing with high-grade mesenchymal lesions involving the retroperitoneum. HG-ESS has an aggressive clinical course and poor prognosis if detected at a later stage. The biologic behavior of high-grade ESS is intermediate between low-grade ESS and undifferentiated uterine sarcomas. However, their exact recognition has prognostic implications [5].

This report constitutes a rare case of high-grade ESS with myxoid differentiation in a 45-year-old woman. ZC3H7B-BCOR endometrial stromal sarcoma is a newly described subtype of high-grade endometrial stromal sarcoma that closely mimics the appearance of myxoid leiomyosarcoma.

Wagh and Menon [6] have also reported two cases of high-grade endometrial stromal sarcoma with similar histomorphological findings as in our case. They also confirmed the diagnosis through IHC studies. In their study, molecular studies like FISH were also carried out, but a few rare mutations could not be confirmed as the probes required were very expensive and unavailable at their center. In our present case, FISH was not done due to resource limitations.

ZC3H7B-BCOR endometrial stromal sarcoma presents with nonspecific symptoms, including vaginal bleeding and/or a pelvic mass, and not infrequently has extrauterine disease at initial diagnosis. These tumors tend to be uniformly cellular, growing in haphazard fascicles of spindle cells without overt pleomorphism. Cells have scant to relatively abundant gray to eosinophilic cytoplasm and oval to spindle nuclei with inconspicuous nucleoli and evenly distributed chromatin. The background stroma is either myxoid, including variably sized pools of basophilic material, or collagenous. The present case had a myxoid background and was not associated with a conventional or variant component of low-grade endometrial stromal sarcoma, thus ruling out YWHAE-NUTMT2 high-grade endometrial stromal sarcomas. The immunohistochemical profile of typical ZC3H7B-BCOR tumors and those with BCOR-ITD closely overlap, except for CD10 expression, which is typically positive, often with a diffuse and strong pattern of staining in typical ZC3H7B-BCOR tumors but negative or only focally positive in BCOR-ITD tumors. The diffuse positive CD10 expression in the present case further suggests the diagnosis of ZC3H7B-BCOR high-grade endometrial stromal sarcoma [6].

Hysterectomy and bilateral salpingo-oophorectomy with adjuvant chemotherapy is the standard treatment. Although experience with these tumors is limited, patients with ZC3H7B-BCOR high-grade endometrial stromal sarcomas have a prognosis that parallels that of patients with YWHAE-NUTMT2 high-grade sarcomas, as both are associated with a higher stage at presentation (including lymph node metastases) and frequent recurrences and metastases.

Limitations of our study: Molecular studies would have confirmed the diagnosis of ZC3H7B-BCOR endometrial stromal sarcoma.

Conclusion

ZC3H7B-BCOR endometrial stromal sarcoma closely mimics myxoid leiomyosarcoma and should be considered in the differential diagnoses when dealing with a sarcoma with a myxoid background.***Funding: Not applicable.***

Consent: Written informed consent was obtained.

Ethical Clearance" Not applicable, as this is a case report.

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