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Uterine adenosarcoma: a case-based review of the diagnostic features

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Abstract

Uterine (Müllerian) adenosarcomas are rare malignancies which account for 5% of uterine sarcomas. Most presentations are postmenopausal, and with early stage disease. This report highlights these entities' diagnostic features, namely having a neoplastic benign or mildly atypical epithelial component, and sarcomatous (often low-grade) stromal component. Architecturally, they resemble Phyllodes tumour. Stromal projections are lined by benign or mildly atypical Müllerian-type epithelia. Heterologous elements may be present, or there may be sex cord-like differentiation. The stroma typically displays increased periepithelial cellularity (the characteristic 'cambium' layer) and a mitotic activity of 2 or more mitotic figures/10 high power fields. Immunohistochemical profile shows the stroma to be oestrogen receptor, CD10 and Wilm's tumour-1 positive, with strong immunoreactivity for P53 and Ki67 seen in cases with sarcomatous overgrowth, where CD10 and ER positivity is often lost.

Keywords: uterus, adenosarcoma, histology, immunohistochemistry

Introduction

Uterine (Müllerian) adenosarcomas are rare malignancies first described in 1974 which account for only 5% of uterine sarcomas (1,2) and 0.1-0.25% of uterine corpus cancers overall. Although these entities predominantly affect the uterus, they can occur elsewhere both in the gynaecological tract and outwith, such as in the gastrointestinal tract (3). The median age of presentation is 58 years, with a wide age range of 14-89 years. Women typically present with abnormal vaginal bleeding (4). On examination, the uterus is commonly enlarged with, occasionally, tissue protruding from the external cervical os. Macroscopically, these lesions appear as polypoid masses of variable size, frequently with a spongy cut surface (4). Most patients present with Stage 1 disease, in which 5 year survival is 60-80% (2). This report aims to highlight the diagnostic features of these uncommon entities.

Case report

Herein, we present the case of a 61 year old female presenting with post-menopausal bleeding. There was no significant past medical history. On vaginal examination the cervix was normal, but the uterus was bulky and retroverted. Ultrasound showed diffuse endometrial thickening of 27mm. At hysteroscopy, the cavity was full with a 14cm polypoidal growth from which curettings were taken. Macroscopically the specimen comprised of mucus and fragments of grey haemorrhagic tissue measuring 25 x 25 x 7 mm in aggregate.

Histologically, the curettings appeared to be polypoid fragments of oedematous stroma variably overlaid by a mixture of endocervical and ciliated columnar epithelium. Stromal

condensation was apparent beneath the epithelial surface, with a cambium layer identified in most tissue fragments. Stromal cells had a mixture of round and angular nuclei with minimal cytoplasm. They displayed moderate nuclear pleomorphism, occasional nucleoli, multinucleate forms and scattered mitotic figures (up to 4 in 10 high power fields). Stromal cellularity decreased away from subepithelial areas, where the tissue appeared to be more myxoid and oedematous (Figure 1). In addition, some of the fragments contained xanthoma cells. There was no evidence of epithelial atypia, presence of heterologous elements, lymphovascular space involvement or necrosis.

Immunohistochemical staining showed positivity with vimentin, Ki67 (20-30% of stromal nuclei), oestrogen receptor (ER), Wilm's tumour (WT)-1 (cytoplasmic), CD10 (focal), p53 (focal) and desmin (focal). There was negative staining with SMA and MyoD1. Overall, the appearances were those of a low-grade adenosarcoma.

The patient was discussed at a tertiary referral centre MDT and underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy. The histology from the resection specimen confirmed the diagnosis. This sarcoma was Stage 1a, with no myometrial invasion, sarcomatous overgrowth or lymphovascular invasion.

Discussion and Conclusion

Histologically, uterine adenosarcomas comprise a neoplastic benign or mildly atypical epithelial component, and sarcomatous (most often low-grade) stromal component (3). At low power the architecture is reminiscent of a Phyllodes tumour, with leaf-like architecture. Stromal projections can be lined by any type of benign or mildly atypical Müllerian-type epithelia, with or without squamous metaplasia. Intraglandular stromal protrusions are characteristic. The stroma is usually low-grade and of endometrial stromal or fibroblastic-type. In some cases, however, it may be high grade and have the appearances of an undifferentiated sarcoma (3). Heterologous elements may be present, or there may be sex cord-like differentiation (1).

Although the stroma can be uniformly cellular, it typically displays increased cellularity around the epithelium, giving the characteristic 'cambium' layer (3,4). WHO diagnostic criteria define adenosarcoma as having a stromal mitotic activity of 2 or more mitotic figures/10 high power fields, as suggested by Clement and Scully (4). However, the diagnosis can be made if the characteristic low power architecture, cambium layer or marked stromal atypia are present (3,4). Immunohistochemical profile shows the stroma to be ER, CD10 and WT-1 positive (2,3), with strong immunoreactivity for P53 and Ki67 seen in cases (33%) with sarcomatous overgrowth, where CD10 and ER positivity is often lost (5).Important differential diagnoses include adenofibroma, carcinosarcoma, endometrial stromal sarcoma and embryonal rhabdomyosarcoma.

Management is usually by total hysterectomy and bilateral salpingo-oophorectomy. Negative prognostic factors include presence of myometrial invasion, sarcomatous

overgrowth, lymphovascular invasion, necrosis and the presence of heterologous elements (1). Although uterine adenosarcomas are capable of local recurrence, both lymph node and distant metastases are rare. Radiotherapy is not recommended, and there is only limited evidence for the use of neo-/adjuvant or adjuvant chemotherapy and hormonal therapy. There may be a potential future therapeutic target as the PIK3/AKT/PTEN pathway is mutated in approximately 70% of cases (2).

References:

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Practice Points

- A striking feature of adenosarcoma is the Phyllodes-like architecture, best appreciated at low power.
- Look for the condensed stromal area surrounding the epithelium, the *cambium layer.*
- The WHO defines adenosarcoma based upon a stromal mitotic activity of 2 or more mitotic figures per 10 high power fields.

Multiple Choice Questions

1. Which of the following type of epithelia can be found within an adenosarcoma?

A: Endometrioid

B: Ciliated

C: Mucinous

D: Squamous

E: All the above

2. A 17 year old female presents with abnormal vaginal bleeding. On examination there is a polypoid mass protruding through the os. Macroscopically, this appears as a polypoid, grape-like mass with a homogenous tan cut surface. Histologically, there is a densely cellular zone of small blue cells below the normal surface epithelium, with adjacent alternating hypo- and hypercellular stroma. What is the most likely diagnosis?

A: Adenosarcoma

B: Carcinosarcoma

C: Embryonal rhabdomyosarcoma

D: Adenofibroma

E: Polypoid endometriosis

3. Which of the following is the best indicator of recurrence and poor survival in adenosarcoma?

A: Deep myometrial invasion

B: Sarcomatous overgrowth

C: Lymphovascular invasion

D: Necrosis

E: Presence of heterologous stromal elements

Figure 1: Adenosarcoma displaying characteristic variability in stromal cellularity, x4 (A); cambium layer, x10 (B); and nuclear atypia, x20 (C).