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Case Report

Case report: Identification of endometrial adenosarcoma on conventional Papanicolaou smear

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Adenosarcoma is a distinctive biphasic tumor of low malignant potential that accounts for 1–2% of uterine sarcomas. It usually presents as a large mass that protrudes into the cervical canal. Due to its rarity, cytopathologists may overlook it on Papanicolaou (Pap) smear. Here, we report a case presenting with enlarged vaginal mass. She was treated with surgical excision. There was recurrence after three months. Pap smear showed atypical stromal cells. However, they were not detected by cytopathologists the first time. We provide a brief summary of the cellular features of stromal cells and suggest immunocytochemistry with cell transfer smear for differential diagnosis of adenosarcoma on Pap smear.

Keywords: adenosarcoma, endometrium, Pap smear.

Introduction

Adenosarcoma is a rare entity in uterine neoplasm. It is characterized by benign epithelial components and low grade malignant stromal components. It is difficult to diagnosis in endometrial sampling or biopsy specimen due to tissue fragmentation and failure of capture of pathological diagnostic areas. Our case had an erroneous diagnosis in Pap smear and D&C specimen at first time. We reviewed the pathological specimens, and found characteristic stromal cells in Pap smear. We use cell transfer technique to confirm the nature of stromal cells in Pap smear. Since atypical stromal cells in pap smear is not usually found, we gave a brief review and differential diagnosis of the cell features and suggested cell transfer technique to perform immunocytochemistry for assisting diagnosis.

Case Report

A 51-year-old female visited our gynecological department due to irregular vaginal bleeding. Sonographic examination revealed a 4.6cm cervical mass, and surgical excision was performed.

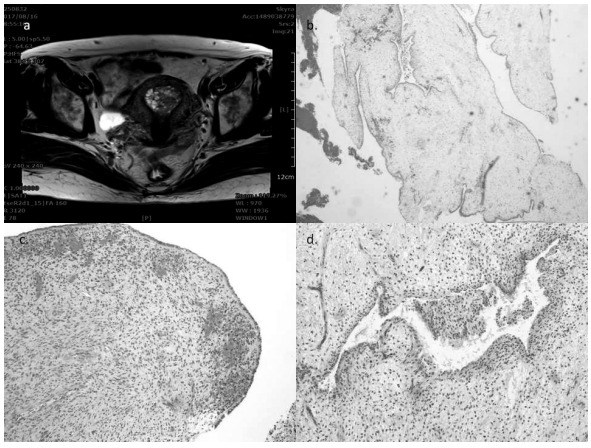

Figure 1: A: multiseptated cystic and solid enhancing components with lattice-like appearance in MRI. B: polypoid tumor in with rigid cyst formation (hematoxylin-eosin, original magnification, 40X). C: leaf-like polypoid appearance of adenosarcoma ((hematoxylin-eosin, original magnification, 100X).. D: High-power view of hyperchromatic stromal cells with increased mitosis (hematoxylin-eosin, original magnification, 200X).

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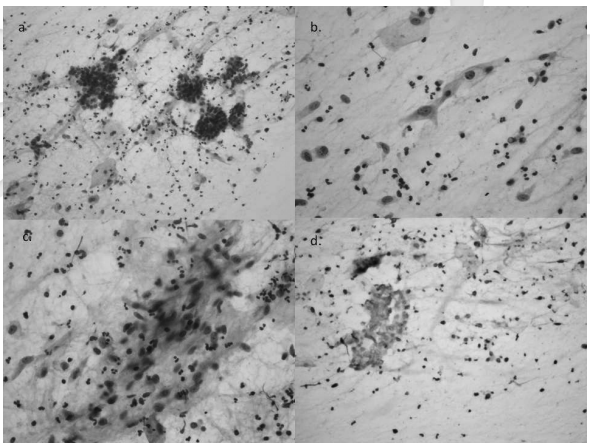

Figure 2: a: Loose clusters and individual hyperchromatic stromal cells surroundded with bland-looking endometrial fragments (pap smear, original magnification 200X). b. Hyperchromatic stromal cells with oval shaped nuclei and tapered cytoplasm with comet-like appearances(pap semar, original magnification 400X) . C: Loose clusters of stromal cells with mild necrotic background (pap semar, original magnification 400X). D: positive nuclear staining of WT-1 of endometrial stromal cells (cell transfer cytology smear, original magnification 400X)

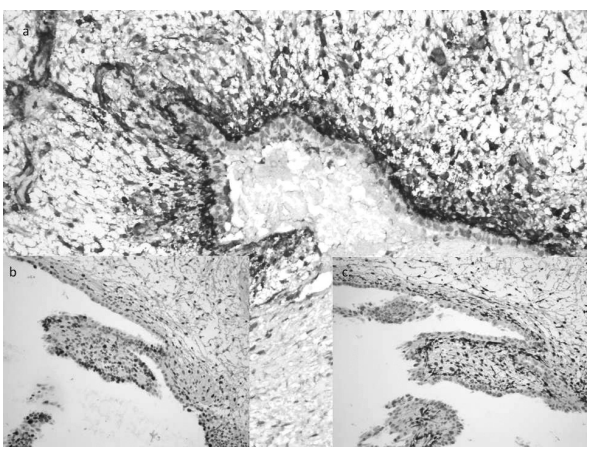

Figure 3: a. Immunohistochemical demonstrate the endometrial stromal cells of periglandular cuffing with WT-1 positive (original magnification 400X). b. Immunohistochemical study revealed increase Ki- 67 of stromal cells (original magnification 200X). c. CD10 positive of stromal cells (original magnification 200X).

Pathologically, it revealed polypoid mass with bland-looking stromal cell proliferation due to absence of mitotic counts and periglandular cuffing. After three months, recurrent vaginal bleeding was found, and a 3cm cervical polypoid mass was found again. MRI study revealed the septate mass, admixed solid components with lattice-like appearance in the endometrial cavity (Fig 1a). At the same time, pap smear was performed but signed out as negative finding. Endometrial curetting was performed. Pathologically, it reveals several intraglandular stromal cells protruding and proliferations and rigid cystic formation focally (Fig 1b-d). Because of not very salient appearance of periglandular stromal condensation, but focal increase of mitotic counts, adenosarcoma was suspected. We reviewed the Pap smear, atypical mesenchymal cells were neglected. The atypical mesenchymal cells showed two cytological pattern: individual cells and stromal cell fragments. The stromal cells reveal mild to moderate hyperchromatism with oval shaped nuclei and tapered cytoplasm with comet-like appearances. Occasionally, several nucleoli and nuclear grooving were seen. Indistinct cell borders were seen especially in loose cell clusters. Bland glandular cells clusters or nests were seen associated to these atypical mesenchymal cells. The background was necrotic (Fig 2a-d). In order to search the nature of atypical mesenchymal cells on pap smear, we make a cell transfer smear to perform immunocytochemistry (BenchMark XT model automated staining platform:Ventana Medical System). The atypical mesenchymal cells demonstrates CD10 (supplier: Biocare; clone 15E2E2; dilution 1:100, catalog number: 062218) positive and WT-1 (supplier: ThermoFisher; clone CALP; dilution 1:800, catalog number: 1168P1611F) positive (Fig 3a-c). It was the same as immunohistochemical result. Finally, we signed out the case as adenosarcoma.

Discussion

Adenosarcoma is a rare entity of uterine malignancy, first described in 1974 by Scully and Clement, was a biphasic tumor composed of benign epithelial fragments and maligant stromal components. Pathological differential diagnosis vary with the morphological spectrum of adenosarcoma. At the very low grade of the spectrum, adenofibroma, adenomyoma, and atypical polypoid adenomyoma would be included in the differential diagnosis. In actual situation, endometrial biopsy, sampling and curettage specimen, the polypoid mass may be very

Table 1. Differential diagnosis in conventional pap smear (paper review)

	Endometriosis[2]	Adenomyoma[7]	adenosarcoma	#Low-grade ESS[5]	*MMMT[6]
Endometrial glandular cells	consisted of three-dimensionl tight clusters of cells with small round nuclei.	Clusters of crowded glandular cells exhibited irregularly branching.	Sheet of glandular cells with small round nuclei.	not present.	Irregular cohesive cluster; and three-dimensional cell balls.
background	Scanty histiocytes with hemosiderin.	clean background;	Bloody.	Bloody(42%); clean(50%)	necrotic(50%)
		dissociated cells are not present.		Necrotic(8%).	
Stromal cells	syncytial groups; with oval to spindled cells with indiscrete cytoplasmic borders.	Short fascicles of spindle cells within endometrial glandular clusters.	Spindle and epithelioid cells, indistinct cell border, mild hyperchromasia,	Epithelioid and spindle cells attached the vessles; single and clusters	not present.

note: # low grade ESS: low grade endometrial stromal sarcoma; *MMMT: malignant mixed mullerian tumor.

collagenous, without obvious periglandular cuffing and peripheral stromal condensation pathologically. In addition, the mitotic counts of the mesenchymal component may vary significantly, some areas may less than 1Mf per 10HPFs, such as our case. Furthermore, the specimen may only contains some nondiagnostic areas. Under these circumstances, combining Pap smear finding would be a good helpful tool. However, the entity is very rare, so the cytopathologists may not be familiar with their cytological features. Screen errors may be occurred. Pasternak S et al found five cases diagnosed with adenosarcoma with Pap smear performed before tumor resection, and four cases have abnormal mesenchymal cells found in Pap smear but failure to screen successfully1. This means the ratio of occurrence of these atypical stromal cells is not low in such cases, however, the detection rate is very low. We review the papers about the cellular features of adenosarcoma found in pap smear: bloody necrotic background, loose cohesive clusters or single isolated cells, composed of epithelioid, spindle- shaped cells with mild to moderate hyperchromatism are reported1,2,3. In our case, the stromal cells revealed marked malignant features in Pap smear with hyperchromatism, plemorphism and disordered arrangement of cell clusters. From paper review, we find the endometrial benign stromal cells in Pap smear generally in single or dense cohesive groups, with very scanty cytoplasm, round to oval nuclei and indistinct cytoplasmic borders4. If the stromal cells behave malignancy, the arrangement in cell clusters would be disordered, not even-spaced. The malignant single stromal cells are hyperchromatic, pleomorphic. The nucleoli are seen2. Sometimes, nuclear grooving would be present. The above findings offer a good hint to differential diagnosis from other benign stromal lesion, such as endometriosis and adenomyoma (Table 1). In our case, the endometrial glanadular cells are always surrounded with stromal cells. The benign endometrial glandular cells always presented with compact tridimensional groups of cells with cuboidal cells with scanty cytoplasm. It offers differential diagnosis between malignant mixed mullerian tumor. In addition, the three dimensional clusters of cervical adenocarcinoma is always composed of atypical columnar cells with peripheral feathering, different from cuboidal appearance of endometrial cell groups. In our case, the background is necrotic. Chiung-Ru Lai et al thought the background was due to endometrial origin3. Maria Luisa Policarpio-Nicolas et al denoted 50% cases of low grade stromal sarcoma presented with necrotic background in pap smear5. Mary B. Casey also denoted only 50% cases presented with necrotic

background even though cases of malignant mixed mullerian tumors in pap smear6.

However, in their study, no malignant stromal cells are seen in Pap smear. So, the presence of necrotic background would raise a red flag of the presence of malignant lesion not specific for adenosarcoma.

Chiung-Ru Lai et al suggested immunocytochemical stain as a auxiliary tool to define the stromal cells3. However, it is very difficult for immunocytochemical performing in conventional Pap smear. We suggested using the cell transfer technique. It is very simple technically and multiple immunostains can apply in a single cell smear by cell transfer technique.

In conclusion, to avoid of misdiagnosis, the cytopathologists should be alert to the presence of benign or malignant endometrial stromal cells in Pap smear. For pathological practice, since the mitotic counts and periglandular cuffing of adenosarcoma are not easily evaluated by histological curetting specimen or biopsy specimen, re-evaluate the presence of atypical stromal cells or not in pap smear and perform a immunocytochemical stain by cell transfer technique would be very helpful to avoid mis-diagnosis of the rare entity.

Discussion

To the Histopathology Laboratory personnel for the experiments.

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