ENDOMETRIAL ADENOSARCOMA

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Endometrial cancer is a common disease of perimenopausal and postmenopausal women. The common histologic type is endometrioid adenocarcinoma. Adenosarcoma is among the rarest type of endometrial cancer, and is by definition a malignant tumor composed of morphologically malignant stroma and benign glandular epithelium. Here, we report two uncommon cases of endometrial adenosarcoma. The clinical course, treatment and histopathologic features of the tumors are reviewed and discussed.

In the first case, a 46-year-old married Taiwanese woman, gravida 0, para 0, with a history of diabetes mellitus presented with vaginal bleeding for 1 month. A thickened endometrium, measuring up to 3.14 cm, was noted on sonography. Diagnostic dilatation and curettage was done with subsequent radical surgery composed of total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and bilateral para-aortic and pelvic lymph node dissections. Histopathologic examination showed a tumor exhibiting exophytic growth from the endometrium, consisting of polypoid cleft-like glands surrounded by a cuff of cellular parenchyma. The epithelial component was cytologically bland and the mesenchymal component exhibited significant cytologic atypia and frequent mitoses (> 5 mitoses per 10 high-power fields) (Figures 1 and 2). Immunohistochemical study of the malignant mesenchymal tumor cells was positive for vimentin, focally positive for estrogen receptor, and negative for progesterone receptor, desmin, CD10, Her-2/neu, CD117 and epidermal growth factor receptor (EGFR). An endometrial adenosarcoma was diagnosed. The postoperative course of the patient was smooth and she was still being followed up regularly at the outpatient department after 6 months.

In the second case, a 64-year-old woman presented with postmenopausal bleeding for a period of time. A uterine mass, measuring 4 × 4 × 2 cm, was noted during sonographic examination. Diagnostic dilatation and curettage was performed. Microscopic examination of the tumor revealed hypercellular stroma with marked atypia, leaf-like appearance and periglandular stromal cuffing (Figures 3 and 4). The tumor cells were positive for estrogen receptor and progesterone receptor but

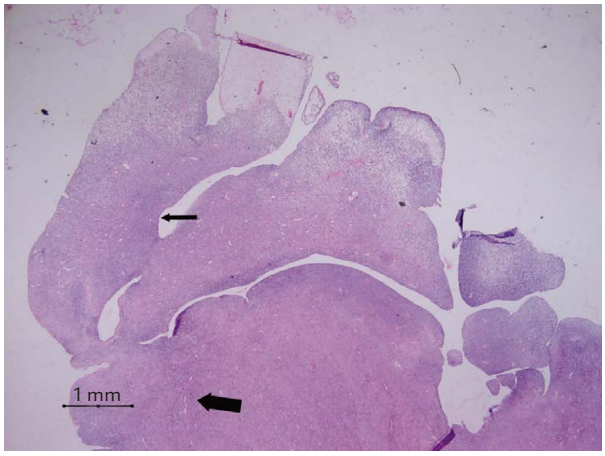

Figure 1. Histopathologic examination showing polypoid cleft-like glands surrounded by a cuff of cellular parenchyma (low-power field). Small arrow: epithelial component; large arrow: stromal component.

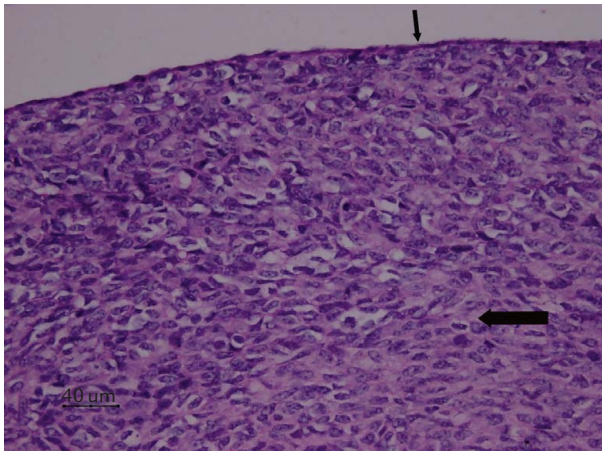

Figure 2. Histopathologic examination showing the epithelial component is cytologically bland, and the mesenchymal component exhibits significant cytologic atypia and frequent mitoses (> 5 mitoses per 10 high-power fields). Small arrow: epithelial component; large arrow: stromal component.

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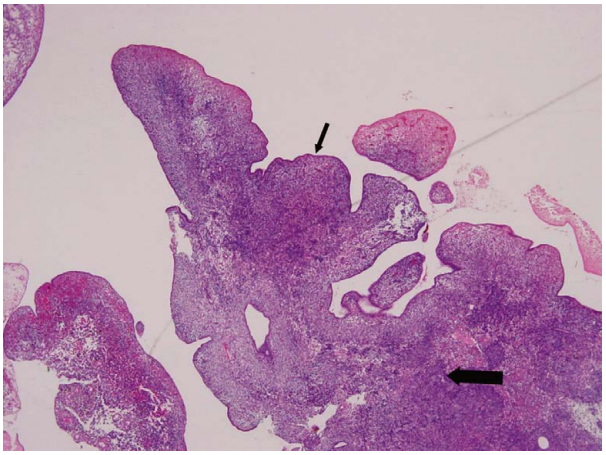

Figure 3. Histopathologic examination showing leaf-like appearance and periglandular stromal cuffing (low-power field). Small arrow: epithelial component; large arrow: stromal component.

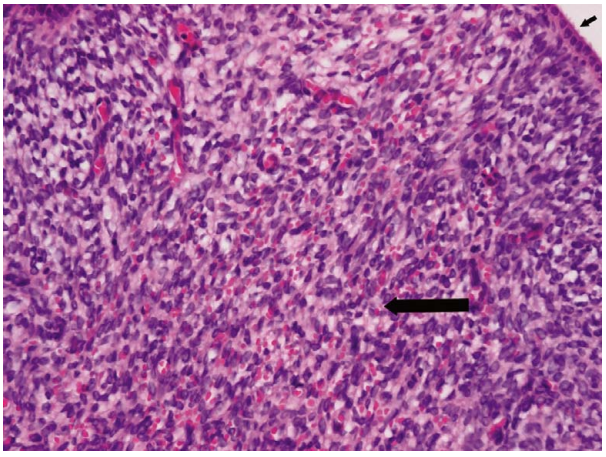

Figure 4. Histopathologic examination showing hypercellular stroma with marked atypia (high-power field). Small arrow: epithelial component; large arrow: stromal component.

negative for Her-2/neu, CD117 and EGFR. The fluorescence *in situ* hybridization of Her-2/neu was not overexpressed (Figure 5). The final pathologic diagnosis was adenosarcoma of the endometrium. Further treatment was performed at another hospital with a smooth postoperative course, and the patient was still free of disease after 4 years' follow-up, according to medical records.

Adenosarcoma of the uterine body was first described by Clement and Scully in 1974 [1]. The tumor is composed of epithelial and stromal components. The stromal component is malignant, but the epithelial component is benign. Adenosarcoma is a rare tumor; only 10 cases of uterine body sarcoma, other than endometrial stromal sarcoma, leiomyosarcoma and malignant mixed müllerian tumor, were registered between 1996 and 2002, according to the annual report of the Taiwan Cancer Registry [2].

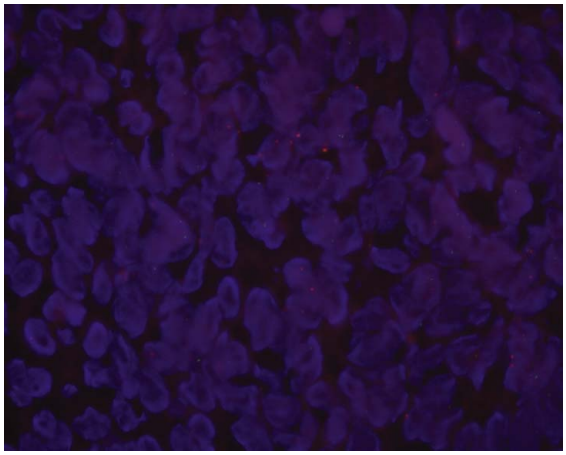

Figure 5. Fluorescence *in situ* hybridization stain of Her-2/neu showing no overexpression. Blue signal: DNA; green signal: centrioles; red signal: Her-2/neu.

The important differential diagnosis for adenosarcoma of the endometrium includes carcinosarcoma and adenofibroma. Adenofibroma consists of both bland stroma and epithelium. Carcinomatous and sarcomatous differentiation must be appreciated in carcinosarcoma. These two differential diagnoses cause no difficulty for experienced pathologists. Although endometrial adenosarcoma and carcinosarcoma are similar in management, distinction between adenosarcoma and carcinosarcoma is important owing to different prognoses and outcomes. They are difficult to differentiate with imaging alone, and a misdiagnosis may be made even on histologic examination if the specimen is too small or is signed out by an inexperienced pathologist.

The mainstay of treatment for primary endometrial adenosarcoma is complete surgical resection. The standard surgical method is radical or total hysterectomy, based on tumor stage, with bilateral salpingo-oophorectomy, bilateral pelvic lymph node dissection and omentectomy [3].

There is no standard recommendation for adjuvant therapy. The use of chemotherapy, radiotherapy or concurrent chemoradiotherapy is still under investigation because of limited experience with this malignancy.

A previous report showed overexpression of EGFR in 33% of adenosarcoma cases [4]. However, both of our cases were negative for EGFR, CD117 and Her-2/neu, so the current new therapy target of CD117, Her-2/neu and EGFR might have been useless for our patients.

The recurrence rate of uterine adenosarcoma is about 25–40% and distant metastases occur in 5% of patients [5–7]. The recurrences usually consist exclusively

of the sarcomatous component, but in rare cases, recurrences can consist of both epithelial and sarcomatous components [1,5,6]. The histologic features associated with poor prognosis include extrauterine spread at diagnosis, myometrial invasion, sarcomatous overgrowth of the mesenchymal component, lymphovascular permeation, and presence of a rhabdomyosarcoma element [1,7]. Long-term follow-up is necessary for the common delayed recurrence that occurs 3–5 years postoperatively [1]. Death from adenosarcoma is reported in about one-quarter of patients. The interval between initial diagnosis and death is often more than 5 years, if no obvious stromal overgrowth is noted [8].

In conclusion, primary endometrial adenosarcoma is rare. It should be carefully differentiated from adenofibroma and carcinosarcoma because of different clinical outcomes. Once the diagnosis of endometrial adenosarcoma is made, thorough preoperative imaging studies and postoperative pathologic examinations are important, since adenosarcoma with stromal overgrowth has a poorer prognosis. More clinical and pathologic experience is required with this uncommon entity.

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