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Case Report

Secretory Adenocarcinoma of the Endometrium

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ABSTRACT

I report a case of secretory adenocarcinoma of the endometrium. A premenopausal 53-year-old woman (gravida 2, para 2) who had no history of exogenous hormone use was found to have endometrial thickening on echography performed during an annual checkup. Dilatation and curettage was done and showed back to back or cribriform glandular proliferation and prominent subnuclear and supranuclear vacuolation. Endometrial hyperplasia, ranging from simple to atypical complex with subnuclear and supranuclear vacuolation, was also observed. The adjacent uninvolved endometrium was typically in a more advanced secretory phase. Dilatation and curettage was performed again and now showed atypical complex hyperplasia with mild secretory changes. Differentiating secretory adenocarcinoma from clear cell carcinoma is extremely important in view of the excellent prognosis of the former and unfavorable prognosis of the latter.

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Key words : secretory adenocarcinoma, endometrium, hyperplasia

INTRODUCTION

Secretory change is common in the endometrium of various physiological conditions. However, secretory changes associated with glandular proliferation, such as secretory carcinoma and atypical complex hyperplasia, are rarely observed[1-8]. I report a case of well-differentiated endometrioid adenocarcinoma with diffuse prominent secretory change in a premenopausal woman with no history of taking exogenous hormone.

CASE HISTORY

A 53-year-old premenopausal woman (gravida 2, para 2) was found to have endometrial thickening on echography performed during an annual checkup. She had no vaginal bleeding. She did not take any exogenous hormones. Her past history was unremarkable. Physical examination revealed a medium-sized uterus with a normal cervix. There were no palpable adnexal masses. The most recent menstruation had begun on December 19, 2000 and lasted for 10 days. Dilatation and curettage (D & C) was performed on January 25, 2001. Menstruation began 2 days later and lasted for 12 days. The patient underwent D & C again on February 15, 2001. The patient was well with no complains 8 weeks after the first D & C.

PATHOLOGIC FINDINGS

The first D & C specimen consisted of fragments of soft, pink-tan material measuring $2 \times 1 \times 1$ cm in aggregates. Microscopically, the endometrium showed crowding of the glands and epithelial hyperplasia with piling-up of various degrees. In some

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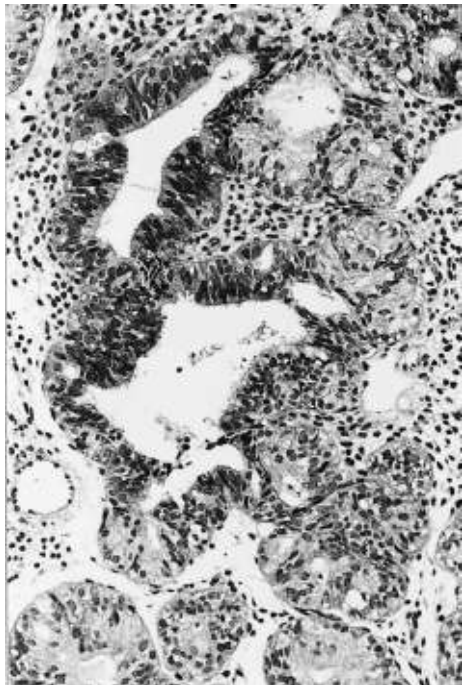

Fig. 1. First D & C specimen. Well-differentiated endometrioid adenocarcinoma. Note a cribriform glandular pattern with no residual intervening endometrial stroma (hematoxylin and eosin, ×200).

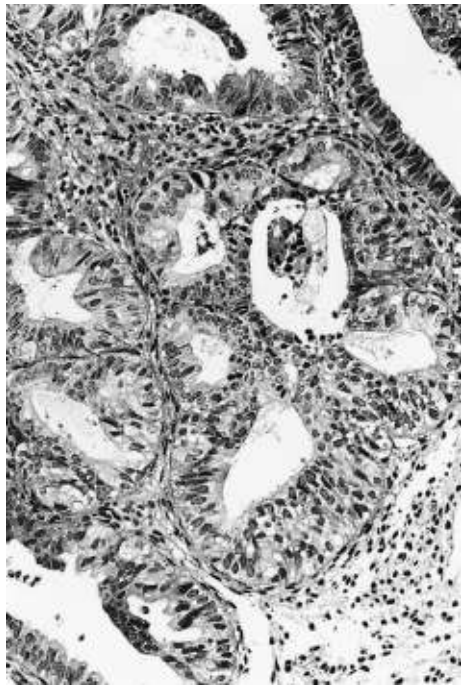

Fig. 2. First D & C specimen. Well-differentiated endometrioid adenocarcinoma with atypical complex hyperplasia. Note glandular crowding with a back to back pattern and subnuclear and supranuclear vacuolation (hematoxylin and eosin, ×200).

areas glands showed a back to back or cribriform pattern with no residual intervening endometrial stroma, indicating well-differentiated endometrioid adenocarcinoma (Figs. 1 and 2). The glands showed subnuclear and supranuclear vacuoles and occasional ciliated cells (Figs. 1 and 2). Other areas showed complex endometrial hyperplasia with atypia. They showed a proliferation of irregular glands, little intervening stroma, nuclear stratification, nuclear rounding and hyperchromasia, and prominent subnuclear and supranuclear vacuoles. The vacuoles were diastase-sensitive periodic acid-Schiff positive. Some areas showed simple endometrial hyperplasia that was characterized by tall columnar cells with subnuclear and supranuclear vacuoles and nuclear stratification (Figs. 3 and 4). The pattern was reminiscent of day-18 to 20 secretory endometrium. The adjacent uninvolved endometrium was typically in an advanced secretory phase (Fig. 4). The stroma was mildly edematous.

The second D & C specimen consisted of fragments of soft, pink-tan material measuring 3×1×1

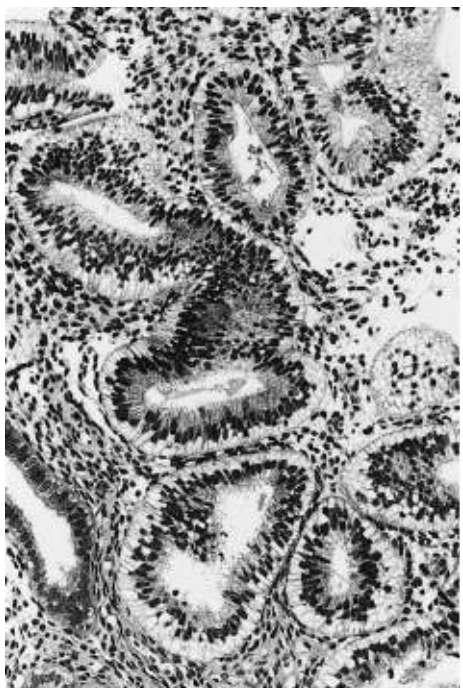

Fig. 3. First D & C specimen. Note epithelial stratification and prominent subnuclear vacuoles reminiscent of secretory endometrium day 18-20 (hematoxylin and eosin, ×200).

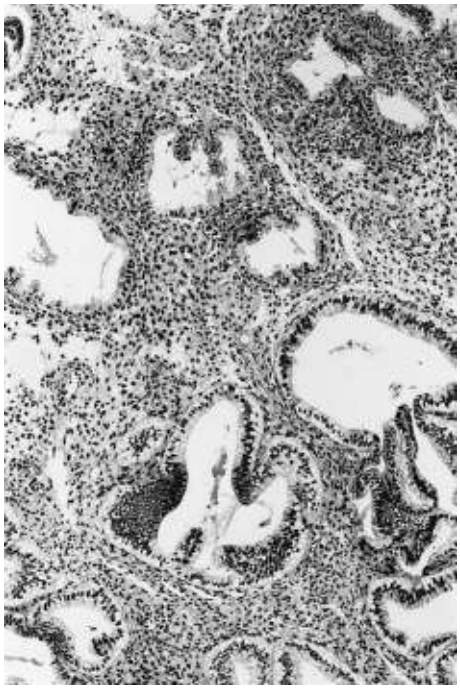

Fig. 4. First D & C specimen. Note mild glandular crowding with nuclear stratification and prominent subnuclear vacuoles (bottom) and adjacent uninvolved endometrium with more advanced secretory features (top) (hematoxylin, ×100).

cm in aggregates. It showed atypical complex endometrial hyperplasia with subnuclear and supranuclear vacuoles in mild degree.

Discussion

Secretory effect is characterized by columnar cells with subnuclear or supranuclear vacuoles containing clear glycogenated cytoplasm resembling the glandular cells of early secretory endometrium. The secretory pattern may be present diffusely or focally in well-differentiated endometrial adenocarcinoma. Secretory adenocarcinoma, in which most cells exhibit subnuclear or supranuclear cytoplasmic vacuoles, is a variant of well-differentiated endometrioid adenocarcinoma in the WHO classification[9] which represents only 1-2% of endometrial carcinoma[4]. The endometrial changes of the first D & C in the present case ranged from simple to complex and atypical hyperplasia with focal presence of adenocarcinoma. The lesion was considered to be secretory adenocarcinoma arising from atypical complex hyperplasia. Interestingly, both carcinomatous and hyperplastic areas contained prominent secretory vacuoles (glycogen) and the adjacent uninvolved endometrium had more advanced secretory features. The same phenomenon was described by Kurman and Scully[2]; in all cases in which the ovaries were available for examination, a corpus luteum was present and indicated the role of progesterone in this pattern. The second D & C of the current case revealed atypical complex hyperplasia with mild secretory changes, which suggest secretory activity. On the other hand, in a reported case of secretory carcinoma secretory change was observed in the first curettage specimen but not in a later hysterectomy specimen[1].

In rare cases, especially in patients whose anovulation is associated with polycystic ovarian disease, persistent endometrial hyperplasia is seen along with secretory changes of the glands and stroma. In a small number of such cases, there is atypical glandular hyperplasia with a cribriform pattern and even overt neoplasia[10]. The possibility that the present patient was associated with polycystic ovarian disease is very low. Secretory features were frequently observed in endometrioid adenocarcinoma in patients taking oral contraceptives[11]. Although secretory change can result from progestational stimulation, there is no such association. Secretory carcinomas in postmenopausal women are not uncommon[1]. Because the patient had not received any exogenous hormones and the menstrual cycle and the endometrial histologic features were disaccord, I assume that that this secretory adenocarcinoma was a response to the internal abnormal hormonal environment, including abnormalities of both estrogen and progesterone.

The differential diagnosis in this case includes clear cell carcinoma and atypical complex hyperplasia with secretory change. Differentiating secretory adenocarcinoma from clear cell carcinoma is extremely important in view of the excellent prognosis of the former and unfavorable prognosis of the latter. Clear cell carcinoma usually has a papillary or solid pattern; a well-formed glandular pattern is unusual. The cells of secretory adenocarcinoma are columnar with subnuclear or supranuclear vacuoles.

In contrast, the cells in clear cell carcinoma are more rounded with a centrally located nucleus ; hobnail cells are characteristic. Nuclear atypia is more marked in clear cell carcinoma[4]. The distinction of secretory adenocarcinoma from atypical hyperplasia with secretory change is based on the presence of stromal invasion in the carcinoma[8].

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