Minimal Deviation Endometrioid Adenocarcinoma of the Uterine Cervix
- A Case Report -

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Minimal deviation adenocarcinoma (MDA) of the cervix was first described by Gusserow in 1870 as a well differentiated adenocarcinoma in which most of the glands are impossible to be distinguished from the normal endocervical mucosa, although the MDA invades deep into the cervical stroma. At first, MDA was restricted to the mucinous type, but the definition of MDA has been expanded to other cell types, including the endometrioid, clear cell and nonspecific cellular types of differentiation. Minimal deviation endometrioid adenocarcinoma (MDEA) is a variant of MDA, and it is characterized by the proliferation of infiltrative, mildly atypical endometrioid glands with no or minimal stromal reaction. Only 17 cases of cervical MDEA have been reported in the English literature. In this current report, we describe our recent experience of a patient with MDEA and we compare this case with the previous reports.

CASE REPORT

A 39-year-old woman (gravida 5, para 2) was admitted for a cone biopsy because of an abnormal pap smear that showed atypical glandular cells, and this was suggestive of neoplasia. Four years previously, she had undergone a cone biopsy of the cervix for cervical intraepithelial neoplasia (CIN) III at our hospital, and subsequently she was closely followed up with a pap smear in every 6 months. Otherwise, she was in good health and she had received no hormone therapy. The histologic finding of the first cone biopsy was focal squamous cell carcinoma in situ with clear resection margins. No tubo-endometrioid glands, endometriosis or glandular neoplasia were observed at that time. The follow-up pap smears were all normal, except the most recent one that revealed many neoplastic glandular cells in monolayered sheets, rosettes, and clusters with palisading and feathering borders. The tumor cells had oval, hyperchromatic nuclei, with chromatin clumping and small nucleoli. Histologic examination disclosed endometrial-type glands with a bland, isolated, mainly rounded appearance and these glands were widely scattered deep into the cervical stroma with only scant stromal reaction. An association of MDEA with tubo-endometrioid metaplasia or cervical endometriosis has been suggested by identifying the tubo-endometrioid glands in the vicinity of the MDEA.
ly reached the base of the resection margin. The maximum invasion depth was 7 mm (Fig. 2A). The glands were scattered singly (Fig. 2B) with the occasional formation of complex glands by the fusion of two or more glands (Fig. 2C). The glands were lined by cuboidal to columnar epithelium with mild nuclear enlargement and hyperchromasia, but the nucleoli were not prominent. The number of mitotic figures ranged from 0 to 3 per gland (15-20 per ten high-power fields) (Fig. 2D). Little desmoplastic stromal reaction or chronic inflammatory infiltrate was observed around the invasive glands, and there were no signs of a squamous intraepithelial lesion or squamous cell carcinoma. The patient subsequently underwent a radical hysterectomy and bilateral pelvic lymph node dissection for curative resection. The uterus weighed 110 g when it was freshly resected and it measured 11.5 × 7.5 × 4 cm. No gross abnormality was seen, except for the cone biopsy defect in the cervix, and the endomyometrium was unremarkable. Residual MDEA was focally observed in 2 of 24 slices of the cervix. The maximum depth of invasion of the residual MDEA was 4 mm. Tubo-endometrioid metaplasia and endometriosis were detected around the MDEA (Fig. 3), but no evidence of malignancy was observed in the endomyometrium, parametrium or the pelvic lymph nodes. The patient is alive with no evidence of the disease 18 months after the radical hysterectomy.

DISCUSSION

Minimal deviation endometrioid adenocarcinoma of the cervix is a very rare neoplasm, and this was first described by Kaminski and Norris in 1983. Since that time, only 17 cases have been reported in the English literature and there have been no such reports in the Korean literature. The tumor is a well differentiated cervical adenocarcinoma with a deceptively benign appearance. The endometrial-type glands have a bland, isolated, mainly rounded appearance and they are widely scattered deep in the cervical stroma with scant stromal reaction. This innocuous histological appearance may easily result in a misdiagnosis of a benign condition such as tubo-endometrioid metaplasia or cervical endometriosis. The presence of glands predominantly lined by ciliated epithelium similar to that of the fallopian tube, or by columnar epithelium resembling that of the endometrium without any surrounding stroma within the cervix is referred to as tubo-endometrioid metaplasia. Under low power, the glands resemble endocervical dysplasia or even adenocarcinoma in situ, while a high-power examination shows an absence of major cytologic atypia and mitotic activity. The diagnosis of benign tubo-endometrioid metaplasia is easy to make when ciliation of the epithelial cells is seen. In addition, the glands in tubo-endometrioid metaplasia have an arrangement similar to normal endocervical glands and they often extend down to the normal endocervical glands. Cervical endometriosis is considered rare, although recent studies have demonstrated an increased incidence that’s associated with a patient having undergone a previous cone biopsy. The glands are lined by pseudostratified columnar epithelium with abundant eosinophilic cytoplasm and there is a surrounding endometrial type stroma. Some cells are ciliated, while others show secretory apical snouting. The pathogenesis of endometriosis is uncertain, although it has been postulated to occur via the implantation of shed endometrial cells or metaplasia as a consequence of injury such as surgical trauma. In 1991, Ismail reported the cervical findings of 42 hysterectomies that were done from 1 to 91 months (mean; 12.2 months) following conization.
None of the 42 prior cone biopsies indicated tubo-endometrioid metaplasia or endometriosis. However, 29 (69%) cervices from post-conization hysterectomies showed tubo-endometrioid glands accompanied by a varying amount of endometrial type stroma,
which suggests the possible effects of posttraumatic regeneration on the endocervix. Our patient also exhibited post-conization changes such as tubo-endometrioid metaplasia and cervical endometriosis. Therefore, aberrant differentiation following trauma may be the correct proposed mechanism for post-conization cervical endometriosis and tubo-endometrioid metaplasia. Tubo-endometrioid metaplasia or cervical endometriosis can be distinguished from MDEA by its orderly arrangement and the lack of major nuclear abnormalities that do not extend beyond the depth of the normal endocervical glands.

The histologic pattern in our patient was similar to those of the previously reported cases of MDEA. The tumor was well differentiated and it had a deceptively benign appearance with bland, isolated, mainly rounded, endometrioid type glands that were widely scattered within the cervical stroma, and this was beyond the limit of the normal endocervical glands. We saw little stromal response to the invasive glands and 15-20 mitotic figures were observed per 10HPF. The cytologic features of our patient overlapped those of cervical adenocarcinoma in situ and well differentiated endometrioid adenocarcinoma, and the cytologic features were similar to those of a previous report. Exfoliated columnar cells were arranged in monolayered sheets with nuclei in a palisade at the periphery and in rosettes.

The pathogenesis of MDEA is uncertain. Young et al. identified tubo-endometrioid glands in the vicinity of the tumors in three of five cases of MDEA, and this supports an MDEA origin from benign tubo-endometrioid glands. Our patient underwent a cone biopsy for CIN III 4 years earlier and no evidence of tubal metaplasia or cervical endometriosis was seen at that time. In contrast, the recent cone biopsy and hysterectomy specimen revealed tubo-endometrioid metaplasia and cervical endometriosis around the tumor. This finding supports the possibility that MDEA originates from tubo-endometrioid metaplasia or endometriosis.

The prognosis of MDEA is uncertain because so few cases have been reported and most of those had a limited period of clinical follow-up. Of the 17 reported cases, 14 patients were well and alive 3-14 years after hysterectomy. Of the remaining three patients, one died of unrelated causes after 9 years, the second patient died 14 years afterward, and the third died of the disease 6 years after her hysterectomy. Our patient is currently in good health with no evidence of recurrence. Therefore, this tumor appears to have a relatively favorable prognosis.

REFERENCES