CASE REPORT

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A young woman with clear cell adenocarcinoma of the uterine cervix

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Abstract In May 1999, an 18-year-old woman visited a physician because of vaginal bleeding and the excretion of large clots from the vagina. A vaginal tumor was discovered and the patient was referred to our outpatient department. Vaginal examination showed a bleeding, tumor, approximately 6 cm in size, protruding from the cervical os and filling the vagina. The cytological finding of the uterine cervix was class V, and the histological diagnosis by punch biopsy was clear cell adenocarcinoma (CCAC) of the uterine cervix. The patient initially received neoadjuvant chemotherapy (NAC) with intraarterial injections of 8 mg/m² of mitomycin, 270 mg/m² of etoposide, and 380 mg/m² of carboplatin. Although the NAC reduced the size of the tumor, it failed to produce favorable pathological changes and was therefore deemed ineffective. A radical abdominal hysterectomy and pelvic lymphadenectomy were performed on October 12. Macroscopic findings showed a tumor, 6 cm in diameter, growing from the right side of the uterine cervix, with a fragile, necrotic surface. Pathological diagnosis was CCAC of the cervix (pT2a, N0, M0). The patient was discharged from our hospital without any postoperative chemotherapy or radiation therapy. No signs of recurrence have been detected since. We reviewed the literature on CCAC patients in Japan up to the present and compared the data with the data reported in a review of CCAC in the Netherlands. While there were similarities between the patients in the two countries in the patients’ pattern of growth and the poor prognosis of the tumors, there was a significant difference between the countries in the patients’ history of diethylstilbestrol (DES) exposure. Results suggest that menarche and menopause may play roles in promoting carcinogenesis, or alternatively, that a subpopulation of women are subject to genetic or exogenous risk factors other than DES.

Key words Clear cell adenocarcinoma · Neoadjuvant chemotherapy · Intraarterial chemotherapy · Uterine cervix · Young woman

Introduction Clear cell adenocarcinoma (CCAC) of the uterine cervix is a rare disease accounting for only 4% of all adenocarcinomas of the uterine cervix. CCAC is refractory to chemotherapy and radiation therapy, and its prognosis is poor in comparison with that of squamous cell carcinoma of the same organ. Several studies have linked the occurrence of cervical or vaginal CCAC in young women with intrauterine exposure to diethylstilbestrol (DES), a synthetic nonsteroidal estrogenic hormone prescribed to pregnant women as a preventive therapy against abortion. On the other hand, there have also been numerous reports of cervical or vaginal CCAC appearing in young women with no history of intrauterine exposure to DES. As many as 31 cases of CCAC have been reported in Japan, a country where DES has never been prescribed to pregnant women. In the case report in this article, we have described a young woman with CCAC of the uterine cervix. We then examined whether the clinical findings and etiology differed between patients with and without histories of intrauterine DES exposure by analyzing and comparing the numerous clinical reports of CCAC of the uterine cervix in Japan and the Netherlands.

Case report An 18-year-old woman noted vaginal bleeding from March 1998, but did not seek medical attention. More than a year later, in May 1999, she visited a gynecologist because of the...
excretion of large clots from her vagina. A vaginal tumor was detected by pelvic magnetic resonance imaging (MRI) and the gynecologist referred her to our outpatient department on July 29, 1999. Vaginal examination and inspection showed a normal-sized uterus with a bleeding, tumor, approximately 6cm in size, protruding from the cervical os and filling the vagina. Findings on rectal examination were normal, with no invasion to the cardinal ligament or parametrium. Pelvic MRI showed a solid tumor, 8 × 4 × 6 cm in diameter. A solid mass appearing on the T2-weighted image (Fig. 1a, b) was suggestive of rhabdomyosarcoma, leiomyosarcoma, or malignant lymphoma. a Sagittal. b Transverse

Fig. 1a,b. Pelvic magnetic resonance imaging (MRI) showed a solid tumor, 8 × 4 × 6 cm in diameter. A solid mass appearing on the T2-weighted image was suggestive of rhabdomyosarcoma, leiomyosarcoma, or malignant lymphoma. a Sagittal. b Transverse

was initially performed to reduce the tumor size, in preparation for a radical abdominal hysterectomy. As NAC and intraarterial chemotherapy are not standard treatments for cervical cancer, we explained the risks and benefits of NAC and obtained the patient’s informed consent to receive the therapy. Initial intraarterial injections of 8 mg/m² of mitomycin, 270 mg/m² of etoposide, and 380 mg/m² of carboplatin were administered, on August 17, as NAC. As pelvic angiography had shown greater enhancement in the left uterine artery than in the right one (Fig. 2a, b), we decided to inject more of the anticancer drugs through the left uterine artery (2:1 ratio during the 40-min administration period). During the second 40-min intraarterial injections of the anticancer drugs on September 14, the drugs were injected exclusively through the left uterine artery, because the right uterine artery was undetectable by pelvic angiography. The tumor was slightly reduced in size after the NAC, but the cancer cells were histologically viable, without necrotic change. Concluding that the NAC had been ineffective, we performed a radical abdominal hysterectomy and pelvic lymphadenectomy, on October 12. As the woman was still young, the left ovary was left in place to avoid castration. There was a small accumulation of serous fluid in the peritoneal cavity, but no swelling of the pelvic lymph nodes.

Macroscopic findings showed a tumor, 6 cm in diameter, growing from the right side of the uterine cervix, with a fragile, necrotic surface (Fig. 3). There were no abnormalities in the ovaries or uterine corpus. Pathologically, the cancer cells had invaded the vaginal wall to a depth of 2.7 cm, but there was no invasion of the parametrium. The cell infiltration reached a position 2.7 cm from the surgical margin. The histological type was mixed pattern, with clear cells arranged into tubular, solid, and papillary structures, and no evident presence of hobnail cells (Fig. 4). The NAC did not appear to have benefited this patient, as the cancer cells were still viable, the cancerous tissue was free of necro-