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CASE REPORT

Carcinosarcoma of the uterine cervix with a clear cell adenocarcinoma component

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Abstract Carcinosarcoma of the uterine cervix is a rare neoplasm with only 40 reported cases, so there is no international consensus concerning its clinical characteristics, treatment, and prognosis. For the first time, we report a cervical carcinosarcoma with a clear cell adenocarcinoma component treated successfully by following guidelines for treating cervical carcinoma. The patient, a 47-year-old woman presenting with watery vaginal discharge, was diagnosed with uterine cervical carcinosarcoma. She underwent modified radical hysterectomy or type II hysterectomy with bilateral salpingo-oophorectomy and pelvic lymphadenectomy. The post-operative histopathologic stage was pT2b, pN0, M0 and pathological examination of the surgical specimens demonstrated carcinosarcoma with a clear cell adenocarcinoma component. She had no history of exposure to diethylstilbesterol in utero. We also performed a human papillomavirus detection and genotyping investigation and didn't find human papillomavirus in either the carcinomatous or the sarcomatous lesion. Post-operative concurrent cisplatin chemotherapy and whole pelvic irradiation plus brachytherapy were performed. The patient remained free of disease 5 years after her last treatment. Although the rarity of this tumor precludes the determination of an optimal therapy in the setting of a clinical trial, treatment according to the guidelines for high risk cervical carcinoma is likely a reasonable alternative.

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Introduction

Uterine carcinosarcomas (CS) are a relatively rare malignant neoplasm, which account for 4 % of all cancers of the uterus [1]. While most CS originates in the uterine corpus, they rarely occur in the cervix with approximately 40 cases being reported in the English literature [2–6]. None of these reports, however, describe a cervical CS with a clear cell adenocarcinoma component. The present report discusses the successful management of a single case of a cervical CS with a clear cell adenocarcinoma component.

Case report

A 47-year-old woman (gravida 1, para 1) was referred to our department complaining of watery vaginal discharge. She had no history of exposure to exogenous steroid hormones in utero. A pelvic examination revealed a friable cervical mass protruding into the vagina. The cervical mass measured about 4 × 5 × 5.5 cm on magnetic resonance imaging. Computed tomography and positron-emission tomography were performed and neither remote metastasis nor lymphadenopathy was detected. The tumor markers, cancer antigen (CA) 125, CA19-9, squamous cell carcinoma antigen (SCC) and carcinoembryonic antigen (CEA) were all within normal limits. A modified radical hysterectomy (RH) or type II hysterectomy with bilateral salpingo-oophorectomy (BSO) and pelvic lymphadenectomy (PLA) was performed for this patient. Induration was noted in the parametrium on both right and left sides, and left

parametrial involvement was confirmed through an intra-operative frozen section evaluation. Thus, we predicted broad parametrial invasion and opted to forego the planned RH in order to maximize extirpation and avoid injury to the pelvic splanchnic nerves. And we expected post-operative adjuvant therapy to effect a complete cure. The washing cytology was negative.

Gross examination of the surgical specimen showed a cervical mass without any abnormalities in either the endometrium or in the bilateral adnexae (Fig. 1). On examination with hematoxylin and eosin (HE) staining, the mass was composed of epithelial and non-epithelial lesions (Fig. 2). The epithelial cells had atypical nuclear figures and clear abundant cytoplasmic space showing solid, papillary, and glandular proliferation. Immunohistochemistry revealed strong positive reactions with cytokeratin AE1/AE3, cell adhesion molecule (CAM) 5.2, epithelial membrane antigen (EMA) and Cytokeratin (CK) 7. CK20, p63, CD 10 and CEA showed weak positive reactions. Vimentin, laminin and type 4 collagen were all negative. In addition to the immunohistochemistry study, positive staining with periodic acid-schiff stain (PAS) and negative staining after diastase digestion showed the presence of glycogen in the carcinoma cytoplasm. These findings indicated that the epithelial lesion was consistent with a clear cell adenocarcinoma. The non-epithelial lesion displayed spindle-shaped, poorly differentiated cells with atypical nuclear figures. Immunohistochemistry demonstrated a strong positive reaction to vimentin and a weak positive reaction to CD10 which was previously reported to be expressed in cervical stroma [7]. The negative staining with cytokeratin AE1/AE3, CAM5.2, EMA, CK7, α-smooth muscle-specific actin, S100 protein and desmin ruled out epithelial, muscular and nonnative differentiated origin. This lesion accounted for 20 % of the whole tumor and transitioned out of the carcinomatous lesion. These findings indicated that this lesion consisted of homologous sarcoma and may be derived from the carcinomatous lesion. Of the whole tumor cells, 80 % were positive for Ki-67. The final pathological diagnosis was a homologous CS with a clear cell adenocarcinoma component. The tumor invaded cervical stroma to a depth of 19 mm, as well as the vaginal wall. Vascular invasion and microscopic left parametrial involvement was noted. The surgical margins of the vagina and parametrium were free from tumor. The regional lymph nodes were all negative. The post-operative histopathologic stage was pT2b, pN0, M0. We also performed a human papillomavirus (HPV) detection and genotyping investigation using a DNA isolation kit and a PCR-based system. No HPV was found in either the carcinomatous or the sarcomatous lesion. All procedures have been approved by the Ethical Committee of Tohoku University School of Medicine, and the required informed consents were obtained.

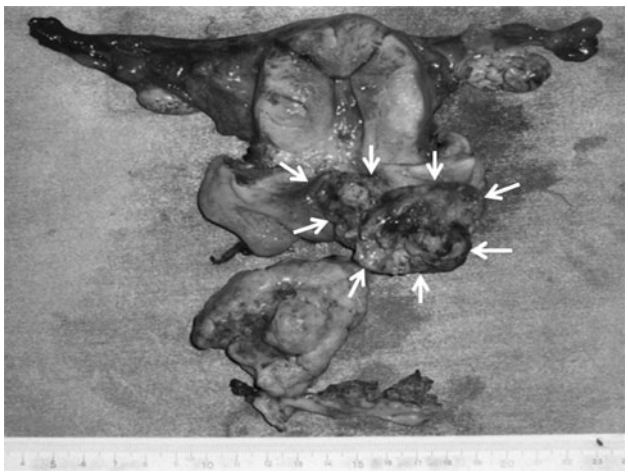

Fig. 1 Gross appearance of the resected specimen. The tumor arising from the uterine cervix is highly necrotic and invades the vaginal wall (*white arrows*)

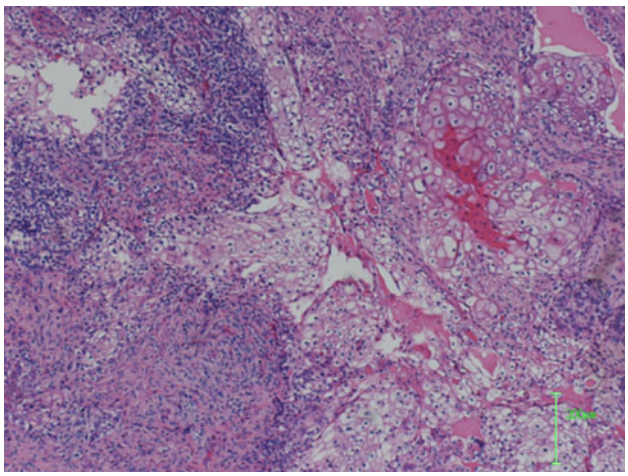

Fig. 2 Microscopic findings of a cervical CS. Sarcomatous lesion is on the left and the carcinomatous lesion is on the right (H&E stain, original magnification ×40)

She had six courses of postoperative chemotherapy planned, consisting of 40 mg/m^2 of cisplatin weekly, but received only three courses because of the side effects. In addition, she received 50 Gy of whole pelvic irradiation and 10 Gy of brachytherapy. The patient was doing well and was without any evidence of recurrence or metastasis 5 years after treatment.

Discussion

To our best knowledge, 40 reported cases of cervical CS, including the present case, have been reported in English literature [2–6]. The age of patients varied widely from 23 to 93 years old (average 62.4) and 75 % (30/40) of the patients were >50 years old. They had various treatments

inconsistently because of their rarity. With regard to the CS epithelial components, various histological subtypes have been observed; however, there are no reports yet describing a clear cell adenocarcinoma associated with a cervical CS. This may reflect the differences in prevalence and pathogenesis among the various histologic subtypes of carcinoma. Clear cell adenocarcinoma of the cervix accounts for only 4–9 % of all cervical adenocarcinomas [8]. The association of cervical clear cell adenocarcinoma with in utero exposure to diethylstilbesterol (DES) is well established; however, a recent review has shown that at least 29 % of patients develop this disease without antecedent DES exposure [9]. The present case also doesn't have a past history of DES exposure. The contribution of HPV infection to clear cell adenocarcinoma of the cervix is controversial at present, in contrast with squamous cell or mucinous cervical carcinomas [10]. In the present case, no HPV was found in both the carcinomatous and the sarcomatous lesions.

There is increasing clinical and pathological support for the idea that CS are carcinomas which have undergone sarcomatoid or metaplastic change rather than being a subtype of uterine sarcomas [11]. Considering the National Comprehensive Cancer Network (NCCN) guidelines 2011 which also deal with uterine CS as a poorly differentiated endometrial carcinoma with regard to the treatment, it may be reasonable to treat cervical CS in the same manner as cervical carcinomas. For this present case, our therapeutic management had a good prognosis by deeming it as equitable to cervical carcinoma stage IIB, considering the large tumor size, deep stromal invasion, vascular space invasion and parametrial involvement, which were high-risk factors for cervical carcinoma. This showed the possibility of treating cervical CS similarly to cervical carcinomas while also achieving a good prognosis. However, more cases are needed to clearly ascribe which proper treatment will be standardly indicated for cervical CS.

In summary, a rare case of carcinosarcoma of the cervix, composed of clear cell adenocarcinoma and sarcoma, is presented. Given the rarity of cervical carcinosarcoma, optimization of its treatment will be best accomplished through the accumulation of a series of cases with unified treatment strategies.

Conflict of interest The authors declare that they have no conflict of interest.

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