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Case report

Synchronous carcinosarcoma of the uterine cervix with adenoid basal carcinoma and cervical intraepithelial neoplasia III: A case report and literature review

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ABSTRACT

Carcinosarcoma and adenoid basal carcinoma (ABC) are both rare lesions in uterine cervix. There were only 5 cases of cervical carcinosarcoma combined with ABC and/without cervical intraepithelial neoplasia (CIN) reported in English literature. These limited studies showed that there was a strong association between HPV, carcinosarcoma, ABC and CIN, suggesting a common etiology for these lesions. Here, we present the case of a 65-year-old woman with cervical carcinosarcoma combined with ABC and CIN III. However, HPV-16, 18, 31 and 33 was negative in the cervical carcinosarcoma tissue by in situ hybridization detection. It indicated that there might be other subtype of HPV involved, or, HPV might play a role in some but not all cervical carcinosarcomas.

1. Introduction

Carcinosarcoma is uncommon malignancy in female reproductive system, composed of carcinomatous component and sarcomatous component [1]. It origins from the Müllerian ducts and the mesonephric duct remnants and is also called malignant müllerian mixed tumor [1]. Most of cases are related to human papillomavirus (HPV) infection, especially HPV 16. Adenoid basal carcinoma (ABC) is uncommon lesion in uterine cervix. Here, we present the case of an elderly woman with cervical carcinosarcoma combined with ABC and CIN III, without HPV 16, 18, 31, 33 infection.

2. Clinical summary

A 65-year-old gravida 4 para 4 female presented with irregular vagina bleeding for months. She was sexually inactive for years and no pap smears or human papillomavirus (HPV) testing record in the preceding years. Before menostasis at the age of 49, she had regular menstrual cycles of 30 days, with menarche at 14. No significant habit, past medical history and family cancer history was declared.

Pelvic ultrasound revealed a normal-sized uterus with a $3.0 \times 3.0 \times 3.0$ cm pedunculated polypoid mass in cervix. She had cervical mass resected under the colposcopy as out-patient. The mass was recorded having a 2.0 cm pedicle and the basis of pedicle was on the cervical canal. The laser electrocautery excision procedure was not performed. Pathologic diagnosis was malignant tumor and then the patient was proceeded to radical hysterectomy and pelvic lymph node dissection. Serum tumor markers, including α-fetoprotein, carcinoembryonic antigen, CA-125, CA-199, squamous cell carcinoma antigen and human epididymis protein 4, were within normal limits. Pelvic computed tomography (CT) scan demonstrated no positive finding with uterine corpus, cervix, vagina, adnexa, rectum, urinary bladder and pelvic lymph nodes. Pathology report indicated cervical ABC and CIN III without carcinosarcoma residue. The patient had an uneventful postoperative course and no adjuvant treatment was performed. The patient is still alive with no evidence of tumor for 26 months until this report submission.

3. Pathological findings

The cervical excised mass was reported as a grey non-capsulated nodule with 3.0 cm maximum diameter and a 2.0 cm pedicle. Microscopic examination revealed a mixed malignant epithelioid component and spindle component (Fig. 1A,D). The epithelioid

Abbreviations: ABC, adenoid basal carcinoma; CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus; CT, computed tomography.

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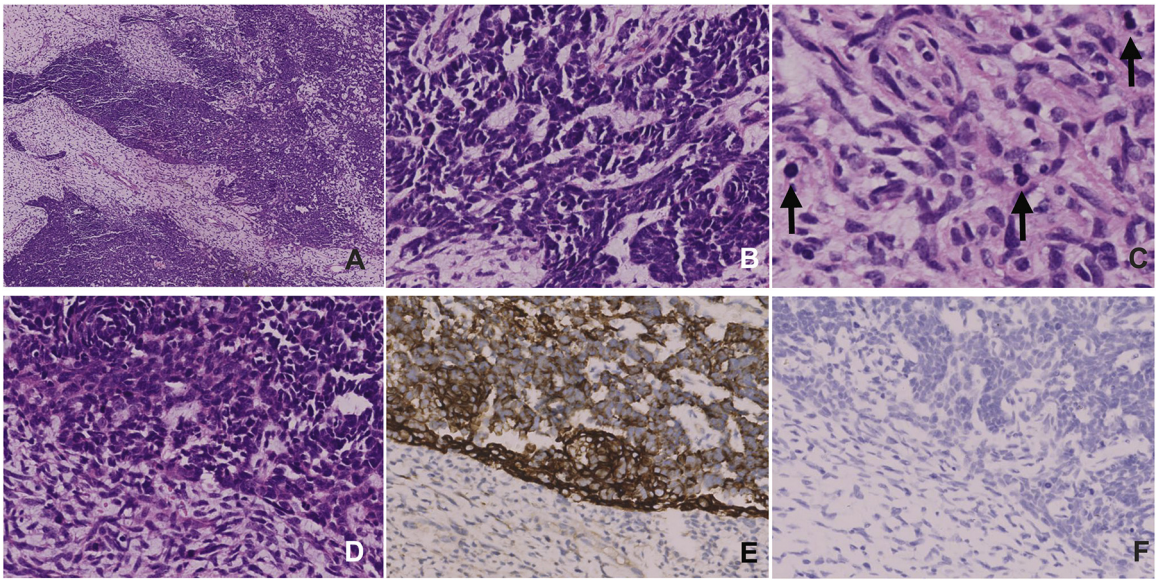

Fig. 1. Pathological findings of cervical carcinosarcoma. Cervical polypoid mass was excised and diagnosed microscopically as carcinosarcoma (A), composed of epithelioid (B, D upper) and spindle sarcomatous area (C arrows: mitotic figures, D bottom). AE1/AE3 immunohistochemical staining showed positive in epithelioid component (E upper) and negative in sarcomatous component (E bottom). HPV-16, 18, 31 and 33 were negative neither in epithelial (F upper) nor sarcomatous area (F bottom). (ABCD: H.E staining; E: immunohistochemical staining, DAB staining; F: in situ hybridization, DAB staining.).

component was poor-differentiated nonkeratinizing squamous cell carcinoma with small nucleus and scant cytoplasm (Fig. 1B,D). Immunohistochemical staining showed AE1/AE3 positive (Fig. 1E). P63 and CK5/6, which indicated squamous differentiation, were both focally positive. The sarcomatous component had the appearance of nonspecific sarcoma, composed of pleomorphous spindle cells with active mitotic figures (Fig. 1C,D). It was AE1/AE3, P63 and CK5/6 negative (Fig. 1E). Pathologic diagnosis was malignant müllerian mixed tumor. HPV-16, 18, 31 and 33 were not detected by in situ hybridization, either in the epithelial component or in the sarcomatous component (Fig. 1F).

One month later, the patient was proceeded to total abdominal hysterectomy and bilateral salpingo-oophorectomy and pelvic lymph node dissection. Macroscopically, uterine corpus was atrophic with normal size bilateral adnexa. The cervix was soft with rough surface, and no grossly detectable mass. Microscopically, the lesion was composed of cervical CIN III and ABC, without carcinosarcoma residue (Fig. 2A). The epithelium demonstrated ulceration and multiple sites of CIN III with glands involvement (Fig. 2C). The ABC was located superficially with infiltrating depth of 0.3 cm. Although CIN III and ABC were very close, no collision or transition between them was detected. The focus of ABC was composed of small nests and cords with a rounded or lobulated appearance and palisading pattern at the periphery of some nests (Fig. 2B). Some of nests had central lumen but no intraluminal hyaline material was noted. The tumor cells were small and uniform, resembling basal cell carcinoma of the skin, with scant cytoplasm, oval nuclei, inconspicuous nucleoli, and very low mitotic activity. Neither the cervical CIN III nor ABC was positive for HPV-16, 18, 31 and 33 detected by in situ hybridization. We did not find carcinosarcoma residue in the whole cervix tissue.

4. Discussion

Carcinosarcoma is uncommon malignancy in female reproductive system, composed of carcinomatous component and sarcomatous component [1]. Uterus corpus is the most common location of carcinosarcoma, however, it can be also located in uterine cervix, ovary, fallopian tube, vagina, Douglas pouch or even peritoneum [2]. Cervical carcinosarcoma is rare. Including this case, fewer than 70 cases of cervical carcinosarcoma have been reported in the English literature [1].

In the present case, cervical carcinosarcoma coexisted with cervical ABC and CIN III. There were only 5 reported cases with coexistence of cervical carcinosarcoma and ABC, and all of these cases were associated with CIN III or invasive squamous cell carcinoma (Table 1) [3–5]. To our knowledge, this is the sixth case in the English language literature. In these reported cases, they shared similar features, such as happening in elderly women, polypiod mass, and defined in pelvic cavity [3–5]. The coexistence with these there tumors indicate the possibility of sharing the same etiology. In the reported cases mentioned previously, besides in ABC and CIN III or cervical squamous cell carcinoma, HPV was also detected positive in carcinosarcoma, including carcinomatous component and sarcomatous component, especially HPV 16 [4,5]. Meanwhile, ABC is high-risk HPV-related tumor [6], as same as CIN III and cervical squamous cell carcinoma. These indicate HPV may be involved in the etiology of carcinosarcoma, as well as in ABC and CIN.

Until now, the pathogenesis of carcinosarcoma is still a subject of controversy. Two theories are currently widely accepted, including "combination" theory and "metaplastic carcinoma" theory. The "combination" theory postulated that most carcinosarcomas of the uterus were monoclonal and sharing a common "stem cell" origin [7]. The "metaplastic carcinoma" theory is popular in these years. It also favors a common cell of origin and postulates the sarcomatous component evolves from the carcinomatous component by a metaplastic process or dedifferentiation [8]. In the previous studies, HPV especially HPV 16 was detected positive in cervical carcinosarcoma, including carcinomatous component and sarcomatous component [5,9]. Since HPV is not involved in the etiology of true sarcoma, the result that HPV was detected in both carcinomatous component and sarcomatous component lends support to the "metaplastic" theory. In the present case, cervical carcinosarcoma coexisted with ABC and CIN, which were high-risk HPV-related tumors, suggesting HPV involvement, and also supporting the "metaplastic carcinoma" theory.

However, in the present case, HPV-16, 18, 31 and 33 were negative either in the epithelial component or in the sarcomatous