A case of small cell carcinoma of the vagina

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Abstract

Primary small cell carcinoma of the vagina is quite rare, and a standard treatment has not been established yet. Herein, we report a case of an 81-year-old woman who was diagnosed with a vaginal tumor without continuity with the uterine cervix. Histopathological diagnosis indicated alveolar solid growth of nuclear chromatin-rich atypical cells with a high N/C ratio and a partially recognized rosette-like structure, suggesting a differentiated neuroendocrine system. Chromogranin A and synaptophysin were positive. Stage I vaginal small cell carcinoma localized to the vagina was diagnosed. The tumor disappeared by radiation monotherapy with external beam irradiation and endocavitary irradiation. The patient remains alive without any disease 1 year and 8 months after the treatment, suggesting the efficacy of radiotherapy in small cell carcinoma of the vagina.

Introduction

Although primary pulmonary small cell carcinoma is generally known, gynecologic small cell carcinoma is rare. Particularly, primary small cell carcinoma of the vagina is extremely rare, and a standard treatment has not been established. We present a case of small cell carcinoma of the vagina that was effectively treated using radiotherapy.

Case Report

The patient was an 81-year-old woman with 6 pregnancies, 1 childbirth, and menopause at the age of 56. Past medical history: at the age of 75, she developed hypertension and atrial fibrillation that were treated by a local physician with some medications. At the age of 79, the patient underwent cataract surgery. The patient repeatedly recognized menstruation-like genital hemorrhage 1 year before visiting a hospital. Speculum examination performed by the previous gynecologist detected a hemorrhagic tumor-like mass on the vaginal wall. Small cell carcinoma was diagnosed on histopathological examination, and the patient was referred to our department. Physical findings included a height of 150 cm and body weight of 53 kg. The blood pressure was 147/102 mmHg. Colposcopy detected a fragile, hemorrhagic tumor-like mass mainly on the posterior vaginal wall (Figure 1A). The mass did not have continuity with the uterine cervix. Transvaginal ultrasound suggested atrophy in the uterus, and there were no abnormal findings. A unilocular left ovarian cyst with the longest diameter of 40 mm was recognized. Cytodiagnosis of the vaginal tumor suggested relatively small atypical cells in conglomeration with a high N/C ratio or with bare nuclei that were densely stained with nuclear chromatin. Biopsy tissue diagnosis of the vaginal tumor indicated alveolar solid growth of nuclear chromatin-rich atypical cells with a high N/C ratio and a partially recognized rosette-like structure on the background of the necrotic tissue, suggesting a differentiated neuroendocrine system (Figure 2A). Immunostaining was positive for chromogranin A and synaptophysin (Figure 2B, C). According to the above, primary small cell carcinoma of the vagina was diagnosed.

MRI findings detected irregularity in the posterior vaginal wall (Figure 3A). PET-CT detected positive accumulation in the lesion in the superior vagina, which had been indicated by MRI (Figure 3B). No abnormal accumulation was recognized in any other organ including the lung fields (Figure 3C). Tumor markers were SCC 1.7 ng/mL, CA 19-9 3.5 U/mL, CA 125 5.6 U/mL, and NSE 13.4 ng/mL (normal value: 12.0 ng/mL or less).

Stage I vaginal small cell carcinoma was diagnosed. Considering the age and complication, radiotherapy was selected. Radiotherapy included whole pelvis irradiation with 45 Gy/25 fractions by Linac and high-dose-rate brachytherapy with 18 Gy/3 fractions. An adverse event due to radiotherapy was Grade 1 skin disorder alone. Colposcopy after radiotherapy detected only a trace-like elevation on the vaginal wall (Figure 1B). Cytological diagnosis of the same site was negative. On CT performed for evaluation after treatment, the lesion on the vaginal wall became ambiguous and no lymph node metastasis or metastasis in distant organs was recognized. The patient remains alive without any disease 1 year and 8 months after the treatment.

Discussion

Although primary pulmonary small cell carcinoma is generally known, gynecologic small cell carcinoma is rarely reported. Regarding gynecologic small cell carcinoma, small cell carcinoma of the uterine cervix was first reported in 1972,[1] and several cases have been reported thereafter. Small cell carcinoma has been reported in the uterine cervix, endometrium, ovary, and vagina and is reported relatively frequently as cervical cancer. Primary vaginal malignant tumor is rare and accounts for 1 to 2% of gynecologic malignant tumors. Primary small cell carcinoma of the vagina is even rarer with only 20 cases reported so far.[2]

Small cell carcinoma of the vagina shows findings histologically similar to those of primary pulmonary small cell carcinoma. Nuclear chromatin-rich atypical cells with scanty cytoplasm and nucleus with an inconspicuous nucleolus demonstrate diffuse solid growth.[3] Neuroendocrine granules are occasionally recognized by the electron microscope.[4] Immunohistochemical staining was positive for CK20, cytokeratin (AE1/AE3, CAM5.2), NSE, chromogranin A, and synaptophysin.[4,5] Also in our case, small cell carcinoma was diagnosed on the basis of the following findings: alveolar growth of atypical cells with a high N/C ratio in the biopsy tissue of the vaginal tumor and immunostaining positive for chromogranin A and synaptophysin.

Even if histopathological diagnosis indicates small cell carcinoma, whole body screening is necessary because the most common primary sites are the lungs, as stated previously. In our case, whole body screening with PET-

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CT showed positive accumulation in the lesion in the vaginal wall alone, and abnormal accumulation was not detected in any other organ including the lungs. Accordingly, the primary site was identified as the vagina.

For small cell carcinoma of the vagina, a standard therapy has not been established till date because of the very small number of cases. According to the reports accumulated so far, surgical remedy, chemotherapy, radiotherapy, or a combination of these therapies is selected. For chemotherapy, a combination therapy of cisplatin + etoposide is mostly selected due to their efficacy in primary pulmonary small cell carcinoma. However, prognosis is poor, and most patients develop infiltration or metastasis at an early stage and die within 2 years. There are only few reports of long-term survival.[2] Considering the age and complication, the patient in our case was treated by radiation monotherapy because the tumor was localized to the vagina. After radiotherapy, the vaginal tumor contracted and was scarred, demonstrating the effectiveness of radiotherapy. The patient has been followed-up thereafter. Relatively long-term disease-free survival has been achieved, suggesting the effectiveness of radiotherapy in small cell carcinoma of the vagina.

Small cell carcinoma has neuroendocrine characteristics and may cause ectopic hormone production. In case of small cell carcinoma, Cushing's syndrome due to ectopic ACTH production is known. Cushing's syndrome is an endocrine abnormality where ACTH production from the tumor triggers hypercortisolemia that causes edema, muscle weakness, hypertension, and hyperglycemia, which further cause consciousness disturbance, electrolyte abnormality, and metabolic alkalosis. With or without the lungs as the primary site, it occurs in approximately 5% of all small cell carcinomas.[6] Cushing's syndrome was reported in two patients with small cell carcinoma of the vagina.[7,8] Both patients experienced symptoms caused by endocrine abnormality such as fatigability, muscle weakness, thirst, and disturbed consciousness during the follow-up period after initial treatment, underwent detailed examination, and were diagnosed with Cushing's syndrome. On detailed examination, metastatic and recurrent tumors were recognized, and acute exacerbation of the general condition followed, causing death. It is also suggested that ectopic ACTH production may be more likely to occur in metastatic lesions than in primary lesions. The patient in our case did not experience symptoms suggesting Cushing's syndrome during the follow-up period.

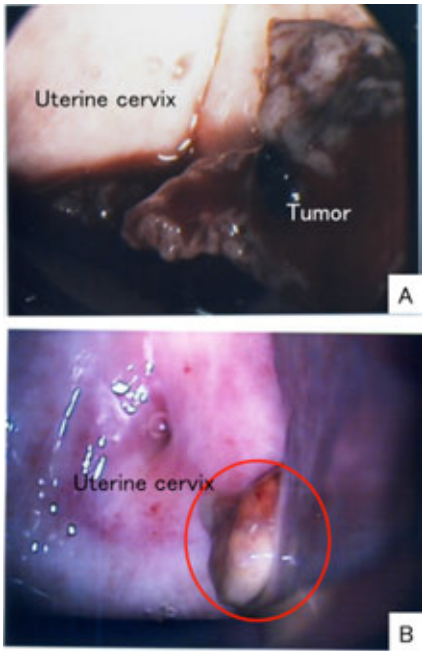

Figure 1. Macroscopic findings of the vaginal tumor. A) Before radiotherapy, a dark red, fragile, hemorrhagic mass without continuity with the uterine cervix was recognized on the vaginal wall. B) After radiotherapy, the tumor contracted markedly and was scarred (circled in red).

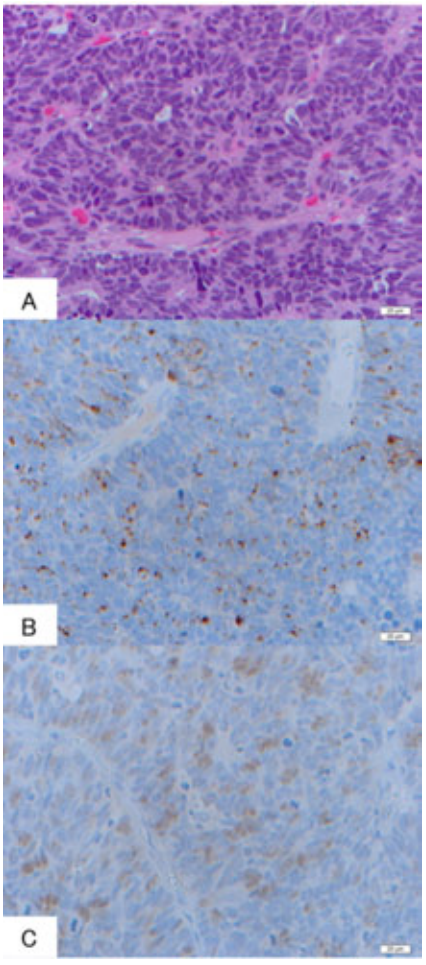

Figure 2. Histopathological findings of the vaginal tumor. A indicates alveolar solid growth of nuclear chromatin-rich atypical cells with a high N/C ratio, where a rosette-like structure was partially recognized. Immunostaining was positive for chromogranin A (B) and synaptophysin (C).

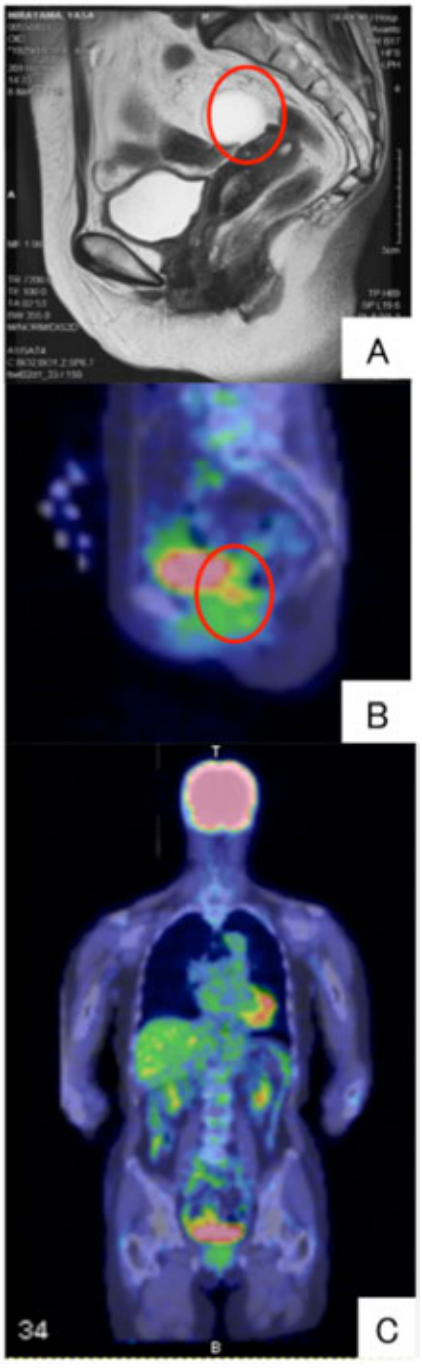

Figure 3. Imaging findings. A) MRI detected a tumor in the vaginal wall (circled). B) PET–CT. Positive accumulation of FDG was recognized in the site where MRI had detected the tumor (circled). C) No abnormal accumulation was recognized in any organ including the lung fields other than the vaginal wall.

Conclusions

Small cell carcinoma of the vagina is a rare disease with poor prognosis. The effectiveness of radiotherapy was shown in this case. If the expanse of small cell carcinoma of the vagina to other parts is denied by an imaging examination such as PET-CT, radiotherapy might be recommended. The follow-up of this disease is thought be enough as usual. However, Standard therapy has not been established for the disease, necessitating further accumulation of cases and discussions.

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