A case of neuroendocrine carcinoma developing from the broad ligament of the uterus

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Abstract

Neuroendocrine carcinoma (NEC), also called small cell carcinoma or large cell carcinoma, is a rare and aggressive tumor that develops mainly in the lung and intestine. More rarely, NEC develops in gynecologic organs, with poor prognoses. We experienced a case of NEC in the broad ligament of the uterus. The patient was a 74-year-old woman with symptoms of abdominal distension and constipation. Ultrasound sonography detected an abdominal tumor larger than 10 cm. She was then admitted to our hospital. She underwent surgery under the diagnosis of ovarian cancer, but the bilateral ovariectomy and bilateral ovariectomy were normal in appearance, and a tumor was developing instead from the broad ligament of the uterus. The patient then received a hysterectomy, salpingo-oophorectomy, and peritoneal membrane was stripped around the pelvic space. Despite our suggestion, she never accepted the adjuvant treatment. She discontinued her perioperative follow-up and was followed in another hospital. Generally, the prognosis of NEC is poor, and there is no established treatment for a tumor in a gynecologic lesion. However, we anticipate that the accumulation of experience treating such cases will eventually lead to a standard treatment for NEC.

Introduction

Neuroendocrine tumor (NET), which was first reported as small cell carcinoma, is a rare tumor arising from various neuroendocrine cells. NET can be classified as G1, G2, or neuroendocrine carcinoma (NEC) according to the pathological findings. Small cell carcinoma and large cell carcinoma are both types of NEC. The features of NEC are high N/C ratio, clear nucleus, condensation of chromatin, and over 20% of karyomytosis. And NEC cells have lower rates of differentiation and have higher proliferation.

When occurring in gynecologic organs, NEC is most likely to develop in the uterus and ovary, but these types of tumor are extremely rare. In the present case, we experienced NEC developing from the broad ligament of the uterus, the first such case to our knowledge. In this paper we describe peritoneal NEC.

Case Report

The patient was a 74-year-old woman, para 2, gravida 2. She consulted with a doctor at another hospital with the complaint of abdominal distension and constipation. A firm irregular mass larger than 10 cm was found in the intra-pelvis by ultrasound sonography, after which she was admitted to our hospital.

Computerized tomography (CT) and magnetic resonance imaging revealed a pelvic mass of over 10 cm and containing solid parts, leading to our suspicion of a malignant tumor. Small hemorrhagic ascites were also discovered. Moreover, the tumor was found to be adhering to the bilateral fallopian tubes, small intestine, and broad ligament of the uterus. The size and irregularity of the tumor made it unclear whether it also involved the bilateral ovaries CT found neither distant metastasis nor enlarged lymphadenopathy. In a blood examination, the CA125 value, a tumor marker of ovarian cancer, was elevated to 409 U/mL.

The patient underwent an operation as the primary treatment. The operative findings included normal uterus and bilateral ovaries. The tumor seemed to have developed from the broad ligament of the uterus (Figure 1). The tumor was diagnosed as a differentiated malignant Brenner tumor or large cell NEC by intraoperative pathological diagnosis. Therefore, we performed a total abdominal hysterectomy with bilateral salpingo-oophorectomy, subtotal omentectomy, and extensive pelvic and paraaortic lymphadenectomy, in accordance with the standard procedure for ovarian cancer. The histological findings included various sizes of cells with high N/C ratios, which were forming sheets (Figure 2). In addition, chromogranin A, neural cell adhesion molecule (NCAM), and synaptophysin were all positive in immunohistochemical staining (Figure 3). We finally reached a diagnosis of NEC arising from the broad ligament of the uterus (pT3cN1M0). And in this present case, there are no evidence of neither serous carcinomas nor mesothelial carcinomas, which are thought to be common peritoneal cancer, by histologic or immunophenotypic examination.

Postoperatively, we strongly recommended that our patient begin adjuvant chemotherapy. She sought out a second opinion, then consistently refused any kind of additional treatment. Fortunately, she has been alive without recurrence.

Discussion and Conclusions

The sites of predilection for NEC are 60% in the intestine and 30% in the lung and bronchi. NEC in gynecologic organs, which is very rare is aggressive and progresses rapidly. It is said that the frequency of NEC is increasing; in 1973, the prevalence was 1.09 per 100,000 people, but reached 5.24 per 100,000 in 2004. Generally, patients with gynecologic NEC are younger than those with gynecologic neoplasms. Therefore, women with NEC sometimes face the possibility of infertility. Moreover, NEC is an aggressive neoplasm in spite of that lesion, and standard treatments for NEC have not been established. Since the prognosis is very poor for young women with NEC, there is a more important problem, in that young children may be left without a mother.

In the present case, the cancer developed from the broad ligament of the uterus. There is a consensus that the characteristics of a neoplasm developing from the peritoneal membrane are similar to those of epithelial ovarian cancer. Especially, high-grade serous cystadenocarcinoma of the ovary, fallopian tube, and peritoneum are treated. Therefore, we treated our patient the same as we would a patient with ovarian cancer.
cancer. According Gallegrao-Filoho et al., NEC of the ovary is diagnosed at a young age, and the diagnosis is poorer than those of other common epithelial types of ovarian cancers. Gallegrao-Filoho et al. reported that 80% of 47 patients with NEC were diagnosed at 20 to 39 years old. Interestingly, they also reported that the risk of recurrence of ovarian NEC was not associated with the clinical stage. Patients with ovarian NEC, stage I, had a recurrence rate of 28.6%. This rate is extremely high compared to that of common epithelial ovarian cancer. They reported that the median overall survival of patients with stage I NEC was 35.3 months, while that of stage IV NEC patients was only 3.3 months. Estel et al. reported that almost 50% of patients with stage I had survived for at least 5 years. This rate is extremely low compared with that of patients with common epithelial ovarian cancer.

We considered that the treatment for NEC developing from the peritoneum is the same as that for common epithelial ovarian cancer. If possible, primary debulking surgery and adjuvant chemotherapy should be performed at many hospitals. In many gynecologic NEC cases, the regimen of chemotherapy is some combination of taxol and carboplatin (TC) or etoposide and cisplatin/carboplatin (EC/P). This regimen originates in treatment for small cell carcinoma occurring in the lung, but there is no strong evidence to confirm this. In addition to combination chemotherapy with TC or EC/P, Estel et al. reported that VPCBAE (vinblastine, cisplatin, cyclophosphamide, bleomycin, doxorubicin, etoposide) were also effective against NEC. As is the case with common epithelial ovarian cancer, the effect of radiotherapy on gynecologic NEC is unclear. Abeler et al. treated ovarian NEC with radiation, but the effect of that radiotherapy was unclear.

We could not find any reports about NEC developing from peritoneal membranes. Probably this is the first report of NEC developing from the broad ligament of the uterus. As we have described previously, there are no established treatments for NEC occurring in gynecologic organs, including peritoneal NEC. In the present case, we performed primary debulking surgery (hysterectomy, bilateral salpingo-oophorectomies, subtotal omentectomy, and lymphadenectomy), in accordance with primary epithelial ovarian cancer. And we strongly encouraged our patient to undergo adjuvant chemotherapy, but she refused firmly. Now she was strictly followed in our hospital without any recurrence.

In summary, we experienced NEC occurring in the broad ligament of the

Figure 1. The tumor looks like ovarian cancer, but the ovaries and fallopian tubes look normal.

Figure 2. The tumor consists of diffuse sheets of various sizes of malignant cells with necrotic lesions (A). The tumor cells have scant cytoplasm, finely granular nuclear chromatin, and mitoses. Nucleoli are inconspicuous or absent (B).

Figure 3. Immunohistochemical staining was positive for synaptophysin (A), Chromogranin A (B), and NCAM (C).
uterus. We treated this patient in accord with the standard treatment for primary ovarian cancer. As reports accumulate, we hope that a standard treatment strategy will be established for NEC developing in each organ.

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