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Small cell carcinoma of the endometrium mixed with endometriod adenocarcinoma: a case report

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Summary

Small cell neuroendocrine carcinoma of the female genital tract is very rare, with highly aggressiveness and poor clinical outcome. It can be mostly found in the cervix, followed by the ovaries. Endometrial small cell carcinoma (SCC) is extremely rare in perimenopausal or postmenopausal women. Here, the authors present a case of a 59-year-old postmenopausal woman, who had experienced vaginal bleeding and abdominal pain for a long time. After undergoing a hysteroscopy-guided biopsy which revealed small cell neuroendocrine carcinoma of the endometrium, she received a total abdominal hysterectomy with bilateral salpingo-oophorectomy, pelvic lymphadenectomy, and para-aortic lymphadenectomy. Her final FIGO Stage was IA. Recommendation from the tumor board was chemotherapy treatment after surgery, but this patient refused to take any measures. The patient experienced no indication of a tumor in the abdomen 14 months after the diagnosis. Endometrial small carcinoma is a very rare and aggressive cancer. The prognosis is unfavorable but timely surgical treatment and early pathological stage may improve the clinical outcome.

Key words: Small cell carcinoma; Endometrium; Endometrial cancer; Immunohistochemical staining.

Introduction

Small cell carcinoma (SCC) is a peculiar malignant tumor, possessing neuroendocrine function. The tumor is most commonly diagnosed in the lung. SCCs of female genital tract are rare, accounting for about 2% of all gynecologic malignant tumors [11]. They can be mostly found in the cervix, followed by the ovaries. Endometrial SCC is very rare, only accounted for 0.8% of endometrial cancers [1-3]. The tumor is highly aggressive and has poor prognosis. Patients are usually diagnosed at advanced stages of the cancer. Most of them die within 24 months after diagnosis. There is still no well-established consensus regarding treatment strategy. Following the standards of the treatment of endometrial carcinoma and the treatment of small cell lung cancer, most experts approve that surgery is of great importance, combined with treatment of radiation and chemotherapy. In this paper, the authors present a case of SCC of endometrium to discuss its clinical manifestation, pathological characteristics, treatment, and prognosis.

Case Report

This is a 59-year-old woman (gravida 0, para 0), who has been in menopause for 15 years. She was admitted in July 2016 for intermittent postmenopausal vaginal bleeding and abdominal pain for more than one month. The woman underwent a transvaginal ultrasound exam in the local hospital which revealed heterogeneous echoes from the uterus to the cervical canal. Her medical history was hypertension and coronary heart disease. She denied any breast or gynecologic cancers in her family

At the time of evaluation, the patient underwent vaginal examination with her gynecologist, which revealed that cervix atrophy, and bilateral adnexa appeared normal. Her thinprep cytology test (TCT) and laboratory tests including tumor markers are negative. MRI showed lesions at the bottom of uterus, the lower uterine segment. and the upper cervical canal segment.

After ensuring that the patient's physical condition could tolerate the surgery, an endometrial biopsy was performed. Pathological diagnosis showed small cell endometrial carcinoma, combined with immunohistochemistry. Syn, CgA, and Vimentin were positive. The positive rate of Ki67 was 80%.

On July 27, 2016, the patient received a total abdominal hysterectomy with bilateral salpingo-oophorectomy, pelvic lymphadenectomy, and para-aortic lymphadenectomy. During surgical exploration, atrophy uterus, normal tubes, and atrophic ovaries were encountered. There was no visible evidence of malignancy in upper abdomen, with smooth-appearing liver surface and diaphragm. The omentum was without abnormalities. Pelvic lymph nodes and peri-aortic lymph nodes appeared normal. Laparoscopy was not performed because of the atrophic cervix. The cervix almost disappeared, which posed difficulties for inserting the uterine manipulator.

A final pathology diagnosis revealed SCC of endometrium, with endometrial adenocarcinoma differentiation in focal sample (Figure 1). The size of tumor was 2×0.9 cm. Sections from cervix, both ovaries, and fallopian tubes were normal. All 24 lymph nodes were negative for metastasis. Immunohistochemistry analysis showed syn(+), CgA(+),ER(+++), PR(+++), and CK(+). The final pathological Stage was IA (Figures 2 and 3).

Postoperatively, the patient was recommended to receive chemotherapy. However, the patient and her family refused to adopt any measures. The authors were unable to discover the real reason why they refused chemotherapy. However to their delight,

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Figure 1. — A hematoxylin and eosin-stained section of the case. (×100).

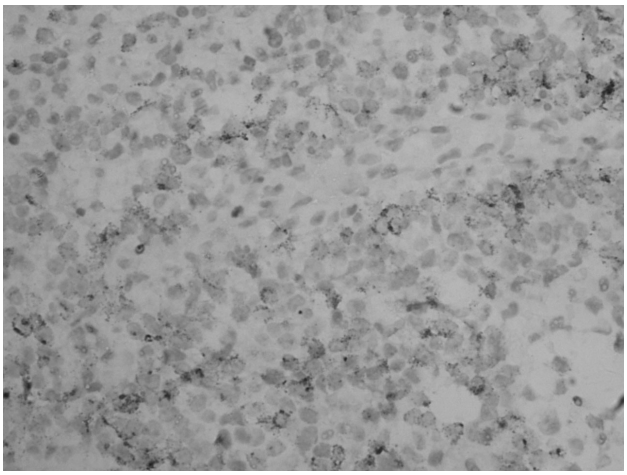

Figure 2. — Immunohistochemical staining of the case by anti-chromogranin A (CgA) antibody.The positive cell are distributed separately, focally. (×400)

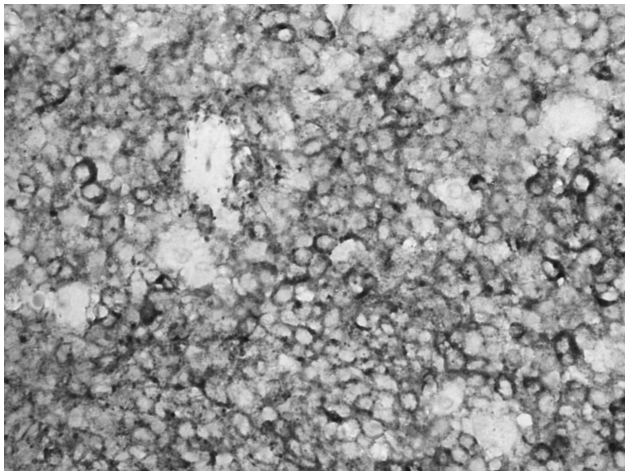

Figure 3. — Immunohistochemical staining of the case by anti-synaptophysin (Syn) antibody. Many tumor cells are positively stained for Syn (×400).

the patient had no indication of recrudesce 14 months after diagnosis.

Discussion

SCC is a neuroendocrine tumor, which arise from the neuroendocrine cells in lymph nodes, endocrine glands, skin, and the general endocrine system. SCC is usually found in the lung (95%) [3, 4]. However, tumors that originates from female genital tract are rare [1], where it shows most commonly in the cervix [1-3]. Endometrial SCC only accounts for 0.8% of endometrial cancers. This uncommon cancer is particularly aggressive and has a poor outcome. The mean age is over 60 (range 23–87) years [4].

Clinical presentations are as follows: postmenopausal bleeding, lower abdominal mass, chronic abdominal pain, and menorrhagia [1]. Attention should be paid to the fact that many patients may have para-neoplastic signs such as Cushing's syndrome [4, 5]. This endocrine disorder symptom is due to the hormone or serum immunity antibody that originates from tumor cells. The major symptom was postmenopausal vaginal bleeding in the present case. Nor paraneoplastic signs or other particular presentation was encountered. The disease is highly aggressive. Compared to other kinds of endometrial carcinoma, it is easier to metastasize to pelvic lymph nodes, peri-aortic lymph nodes, and to distant organs. Many patients have distant metastasis already when they are diagnosed. There is no special vaginal examination and routine test before surgery. Some patients may have tumor markers positive, such as CA-125, CA-199. In the present case, all tumor markers were normal. Transvaginal ultrasound and MRI usually describe a cervical mass, with a high possibility of malignancy. It is worth noting that MRI has an advantage over ultrasound or CT, which cannot only judge the infiltration degree of tumor, but identify other types of endometrial malignancy.

SCC final diagnosis should be based on pathologic examination and immunohistochemical staining. The gross examination shows pale, brittle, fish-like specimen mass, which is often accompanied by large areas of hemorrhage and necrosis. Also, the boundary between tumor and muscular layer is not clear. Furthermore, if the carcinoma is a mixed tumor, we may find papilla in the section of the tumor. Macroscopic examination of surgical specimen shows a malignant tumor composed of all small cells, or a mixed compound based small cells. The most common mixed compound of SCC of the endometrium includes adenocarcinoma component, carcinosarcoma, and adenosquamous carcinoma [4, 6, 7]. It has been revealed that the prognosis of mixed compound of SCC is determined by the small cell component, since the metastases are often connected with the small cell component [8]. In the present

case, the final pathology diagnosis showed SCC, with endometrial adenocarcinoma differentiation in focal sample. In addition, the case met the characteristic as mentioned before. Immunoreactivity studies are proposed positive for chromogranin A, synaptophysin, p53, p16. and CD56 in SCC [9-11]. It can be seen from the present case that synaptophysin was positive, which identifies neuroendocrine cells and the central nervous system in synaptic transmission.

As mentioned above, the diagnosis of endometrial SCC relies on biopsy and immunohistochemical results: (1) tumor comprises small cells, with or without the other tumor ingredients, such as adenocarcinoma, (2) immunohistochemical examination must have at least one kind of positive nervous endocrine markers, and (3) a clear evidence for primary endometrial cancer is essential in order to exclude all other parts of SCC invasion or metastasis.

Although there is no consensus regarding the appropriate treatment guideline of endometrial SCC, it is recommended that multimodal strategies are of great value, including radical surgery, chemotherapy, and radiotherapy. The extent of surgery includes total uterectomy, bilateral salpingo-oophorectomy, and pelvic/para-aortic lymphadenectomy [4, 12, 13], which consult other kinds of endometrial cancer. Resembling the chemotherapy of SCC of lung, chemical therapy is based on cisplatin and etoposide. Other combinations generally indicated include docetaxel + cisplatin, paclitaxel + carboplatin, cisplatin + irinotecan [4, 14].

The prognosis of endometrial SCC is usually less optimistic. What is noteworthy is that the prognosis is still poor, although the patient is in her early stage. It is proposed that timely surgery and adjuvant therapy may confer a better clinical outcome. The patient in the present case had no indication of relapse since she underwent surgery. Notwithstanding that the follow up time is somewhat short, the authors estimate that the early stage and timely surgery may play a part in determining her prognosis.

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