Case Report
Middle East Journal of Cancer; July 2017; 8(3): 161-165

Small Cell Carcinoma of the Ovary: Report of a Case with Unusual and Aggressive Presentation

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Abstract

Small cell carcinoma of the ovary is an aggressive malignant tumor with no standard treatment. Despite surgery, chemotherapy and radiation, this tumor has a poor prognosis with rapid progression. The authors report a case of small cell carcinoma of the ovary in a 37-year-old woman who presented twice with an acute abdomen and unstable hemodynamics which led to two urgent laparatomies. The patient died two months after her diagnosis of small cell carcinoma of the ovary and one course of chemotherapy.

Keywords: Ovary, Small cell carcinoma

Introduction

Small cell carcinoma in neuroendocrine tumors is a less differentiated tumor associated with aggressive behavior.[1] Extra pulmonary small cell carcinoma is distinct from small cell lung carcinoma, but it mimics small cell lung carcinoma in response to treatment and survival patterns with unknown risk factors.[2]

Small cell carcinoma of the ovary (SCCO) is a rare, highly malignant tumor seen in young women. Despite different treatments, it is aggressive with rapid progression. Small cell carcinoma of the ovary has a poor prognosis and extremely high mortality rate.[3] Extrapulmonary small cell carcinoma is usually a fetal disease with a 5-year survival rate of 13%. The extent of disease at diagnosis represents the most sensitive predictor of survival.

This cancer has two different histologic types - similar to small cell carcinoma of the lungs and a large cell variant.[4] Paraneoplastic hypercalcemia is present in two-thirds of cases.[5]

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Received: December 6, 2016; Accepted: February 20, 2017

We report a case of rapid progress of SCCO with unusual presentation of acute abdomen and hemorrhagic shock during the first and second admissions.

Case report

A 37-year-old woman (gravida 13, para 6, abortion 7) presented to the Oncology-Gynecology Emergency Department on September 14, 2015 with complaints of abdominal pain, nausea, and vomiting one week prior to admission. Her symptoms became worse one day prior to admission and she had a history of fainting.

Physical exam revealed a blood pressure of 85/62, with a pulse of 120, temperature of 37.6 ◦C, respiratory rate of 24, and positive orthostatic changes. There was generalized abdominal and rebound tenderness. We palpated a large mass in the left lower abdominal quadrant. Vaginal examination was remarkable for an approximately 12 cm mass located in the pelvic cavity that deviated to the left side. The cul de sac was free of any palpable masses.

Bedside sonography showed the presence of a 14×9 cm heterogeneous solid cystic structure in the left side of the pelvic cavity that extended to the lower abdomen and a moderate amount of free fluid in the abdominal cavity. Laboratory workup showed the following: hemoglobin: 4.7 g/dl; WBC: 4600; platelets: 296,000; βhCG: negative; and normal levels for U/A, BUN, Cr, calcium, and other electrolytes.

The patient underwent an emergent explorative laparotomy after transfusion of 4 bags of packed cells. Midline laparotomy incision was done with these findings: 1000 cc of blood and a clot in the abdominopelvic cavity, with a grossly normal liver, spleen, bowel and omentum, uterus and right ovary surfaces. The left ovary had an 18×15 cm solid mass with an irregular border and a ruptured capsule with active bleeding. Abdominal fluid was aspirated, liver and diaphragm surface smear, and a partial omentectomy and left salpingo-oophorectomy were performed.

Histologic and immunohistochemical findings

The histologic sections showed diffuse infiltration of small highly malignant cells with prominent nucleoli and numerous mitoses, some of which showed epitheloid features (Figure 1). There were also a number of follicle-like structures (Figure 2). Immunohistochemistry results indicated immunoreactivity for cytokeratin, WT-1, EMA, CD99, vimentin, and chromogranin A (focal), but was negative for cytokeratin 7, cytokeratin 20, inhibin, CEA, leukocyte common antigen, estrogen and progesterone receptors, PLAP, S100, Myo D1, desmin, calretinin, c-Kit, and CD34 (Figure 3). Therefore, a diagnosis of SCCO was made.

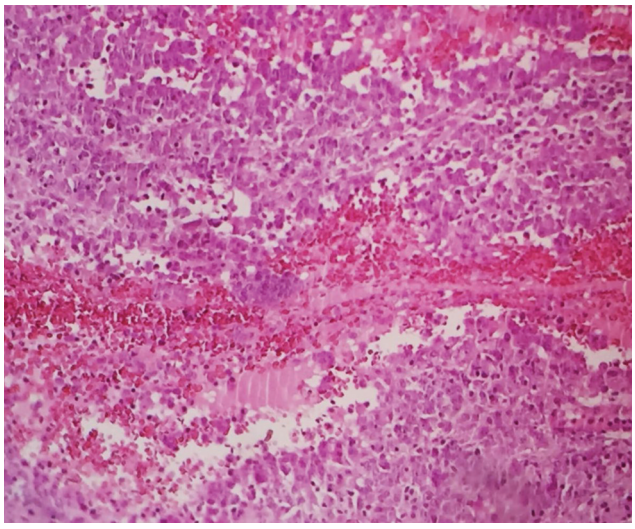

Figure 1. A section of the ovary tumor shows diffuse infiltration of malignant cells, some of which have epitheloid features. (H&E, 250×)

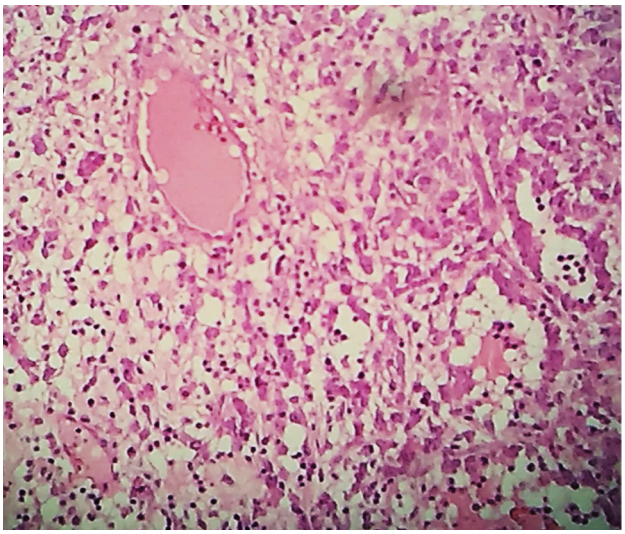

Figure 2. A number of follicle-like structures seen within the tumor. (H&E, 400×)

The patient did not return for a month, then she subsequently presented with severe abdominal pain and the same symptoms as the first presentation, a hemoglobin level of 7.2 g/dl. Sonography findings were severe free fluid in the abdominopelvic cavity and a 16×13cm lobulated mass in the left side of the pelvic cavity with multiple, round peritoneal nodules where the largest was 2 cm, which favored peritoneal seeding.

She underwent another urgent surgery and supracervical hysterectomy due to rectal involvement, a right salpingo-oophorectomy, 10 cm small bowel resection, and ileostomy was done.

The pathology report from the second operation showed a small cell carcinoma that involved one lymph node, the myometrium, left fallopian tube, and serosal surface of a segment of the ileum. The uterus, cervix, and endometrium were free of tumor.

The patient had normal calcium levels at both admissions.

The patient remained in the ICU for 20 days. She underwent one course of chemotherapy that consisted of carboplatin and etoposide as follows: (GFR+ 25) ×AUC and AUC=5 for three days for carboplatin and one dose of 100 mg/m^2 etoposide.

The patient was discharged without any complications. She returned to the hospital after 10 days with dyspnea and palpitations. We ruled out pulmonary emboli and began heparin. Abdominopelvic sonography results showed the liver had multiple hyperechoic lesions, the largest was 2×2 cm in the right lobe which was a possible metastatic lesion. A solid cystic structure (9×3 cm) was located in the anterolateral aspect of the right lobe of the liver and peritoneal thickening suggestive of peritoneal seeding was seen. She had severe ascites in her abdominopelvic cavity. She had a cardiopulmonary arrest and did not respond to resuscitation.

Discussion

Extrapulmonary small cell carcinomas are extremely rare and have been increasingly recognized as a distinct clinical pathologic entity. These carcinomas have an aggressive natural history characterized by early, widespread metastasis.[6]

There are two different variants of SCCO: one is similar to small cell carcinoma of the lung and a large cell component which is less common. Some have suggested an epithelial origin, whereas other suggest a germ cell origin.

A total of 60% of cases are associated with paraneoplastic hypercalcemia and present with symptoms of abdominal pain, constipation, lethargy, weakness, and confusion. Clinical manifestation of hypercalcemia is rare.[5] This is a highly lethal ovarian malignancy in young women.[7]

Tendency to progression and recurrences are two main features of this malignancy and more than 50% of patients are diagnosed with stage III or higher.[8]

Different chemotherapy treatment options advocate for SCCO patients. Some adjuvant chemotherapy similar to protocols of epithelial cell carcinomas was obtained but they only improve

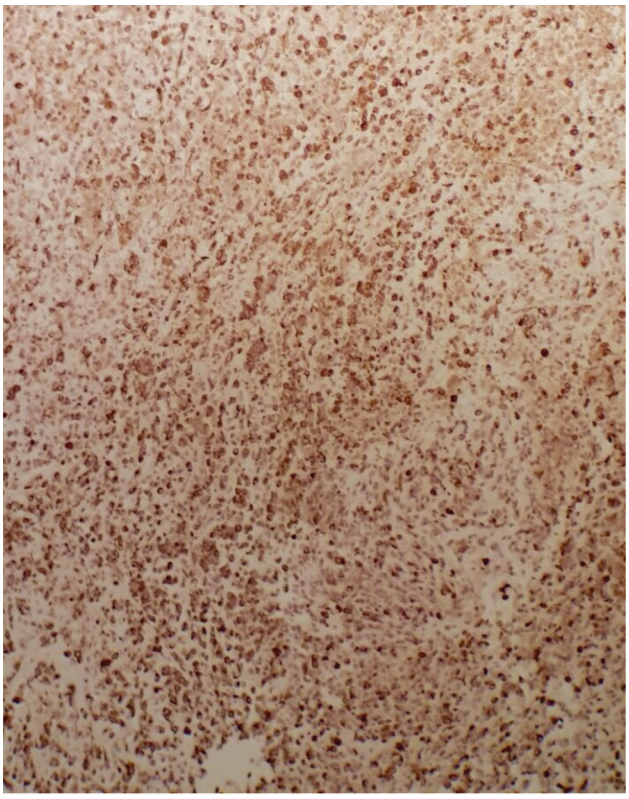

Figure 3. Cytokeratin immunostain of the tumor cells. (250×)

short-term response.[9,10]

Currently no standard treatment for SCCO can be recommended due to the rarity of this disease and lack of randomized controlled trials. Rapid disease progression does not allow patients to receive chemotherapy. Most clinical studies are small series or case reports where all have reported patients with rapid progression and poor prognosis, except one. Stewart et al. have described an adolescent with small cell carcinoma, hypercalcemic type, stage IA. The patient underwent a left salpingo-oophorectomy, left pelvic/para-aortic lymphadenectomy, omentectomy, and peritoneal biopsies. She received four cycles of bleomycin, etoposide, and cisplatin. The patient has received no further therapy and is 11 years from diagnosis without evidence of disease. This is the first long-term juvenile survivor managed with both fertility-sparing surgery and bleomycin, etoposide, and cisplatin (BEP) chemotherapy.[11]

The clinical diagnosis of SCCO should be strongly suspected in a young woman with hypercalcemia, a pelvic or abdominal mass, and absence of any parathyroid or bone disease. Although hypercalcemia on a paraneoplastic basis has been reported in association with other types of ovarian cancers, the patients diagnosed with SCCO and hypercalcemia are of a lower average age.

Agaimy et al. described 3 female cases that were 34, 34, and 37-years of age. Symptoms mainly included abdominal pain and presence of a mass. One patient was normocalcemic, and the other 2 had no preoperative serum calcium levels available. All patients underwent radical hysterectomy with salpingo-oophorectomy, lymphadenectomy, and variable multimodality therapies. Two developed abdominal recurrences/metastases and died of disease after 4 and 12 months. One patient was alive without disease 17 months after surgery and radiochemotherapy. Histologic examination showed undifferentiated neoplasms composed of diffuse sheets, nests and cords of non-cohesive monomorphic small blue/basaloid cells, and the second had large undifferentiated/rhabdoid cells with abundant cytoplasm admixed with minor small cell areas. One case contained rare isolated goblet cells, but lacked a true glandular component. All tumors expressed vimentin and variable levels of pancytokeratin and WT1. Nuclear SMARCB1 was intact in all cases. All tumors showed complete loss of SMARCA4.[12]

In conclusion, SMARCA4 immunohistochemistry represents a highly valuable emerging tool in identifying the SCCO hypercalcemic type in routine practice. Distinguishing this aggressive neoplasm from juvenile granulosa cell tumor and other undifferentiated ovarian cancers is mandatory to select appropriate chemotherapeutic regimens and will allow better characterization of this entity for which targeted molecular therapy has yet to be established.

Conflict of Interest

No conflict of interest is declared.

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