

CASE REPORT

SMALL CELL CARCINOMA OF THE OVARY OF HYPERCALCEMIC TYPE: A RARE TUMOR

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ABSTRACT

Small Cell Carcinoma of the Ovary of Hypercalcemic Type (SCCOHT) is a rare entity. Very few cases have been reported to date. Most literature about SCCOHT is isolated clinico-pathological series and case reports. We report a case of SCCOHT in a 40 year old female with a pre-operative diagnosis of bilateral ovarian complex cysts. The patient underwent left ovarian cystectomy with right ovarian biopsy and histopathological examination revealed features of a poorly differentiated carcinoma with intervening extensive areas of necrosis (upto 80%). Tumor cells were positive for EMA, CK, CK7 (focally) CD10, synaptophysin and vimentin hence confirming the diagnosis of SCCOHT. Post surgery patient was started on Etoposide and cisplatin based adjuvant chemotherapy. In view of highly aggressive nature of this tumor, prompt diagnosis and imparting effective chemotherapy regimen to the patient is required.

Keywords: Small Cell Carcinoma, Ovary, Hypercalcemic Type, Immunohistochemistry, chemotherapy

INTRODUCTION

Small cell carcinoma of the Ovary is a rare malignancy. Approximately two thirds of patients with ovarian small cell carcinoma have hypercalcemia. In the literature only few cases of SCCOHT have been reported. SCCOHT usually occurs in young women. The median age is 24 years old. It is a highly aggressive tumor and usually presents at an advanced stage, hence associated with poor prognosis. We report a case of SCCOHT in a young female.

CASE REPORT

A 40-year-old female was evaluated for complaint of infertility. Ultrasound pelvis showed bilateral ovarian complex cysts. CT scan of the abdomen demonstrated an irregular thin walled cystic lesion in left adnexal region (4.4 x 3.6 cm) and another thick walled complex solid cystic lesion in right adnexal region (3.7 x 2.7 cm). Uterus was normal. There was no ascites or retroperitoneal lymphadenopathy. On these clinicoradiological findings patient was further evaluated. CA-125 value was 19.4U/ml. Left ovarian cystectomy with right ovarian biopsy with omentectomy was performed. On gross examination, outer surface of left ovarian mass (8.5x5x4 cm) was grey white in color, nodular with cystic, hemorrhagic & necrotic areas and on cut section, it was well encapsulated, solid grey white with areas of grayish pink colour filled with mucoid material, capsule thickness was 0.2cm. Biopsy from right ovarian cyst

(2x1x0.3cm) revealed smooth gray white outer surface with solid grey white areas on cut section. Microscopically left ovarian mass sections showed features of a poorly differentiated carcinoma with arrangement of cells in peritheliomatous pattern, cords and trabeculae and intervening extensive areas of necrosis (about 80% of area), brisk mitosis was also noted (Figure 1). On immunohistochemistry the tumor cells were positive for EMA, CK, CK7 (focally) (Figure 2a), CD10, synaptophysin (Figure 2b), vimentin while negative for chromogranin, WT1, PAX-8, sall-4. A diagnosis of small cell carcinoma- hypercalcemic type of left ovary was made based on the above findings. Biopsy from right ovary sections showed hemorrhagic corpus luteal cyst without any evidence of malignancy. Sections of omentum also free of tumor. PET scan was done which revealed solid cystic lesions in bilateral adnexal regions with metabolically active solid component. There were few sub centimeter size lymph nodes in left paraaortic, bilateral common iliac and bilateral external iliac regions with mild tracer uptake. She was started on Etoposide and Cisplatin based systemic chemotherapy.

DISCUSSION

The Small cell carcinoma of the Ovary of Hypercalcemic Type, first recognized by Dr Robert E Scully in the mid-1970s^[1]. Dickersin then described this tumor in his study in 1982^[2], that resulted in a wider appreciation of this exceedingly rare tumor.

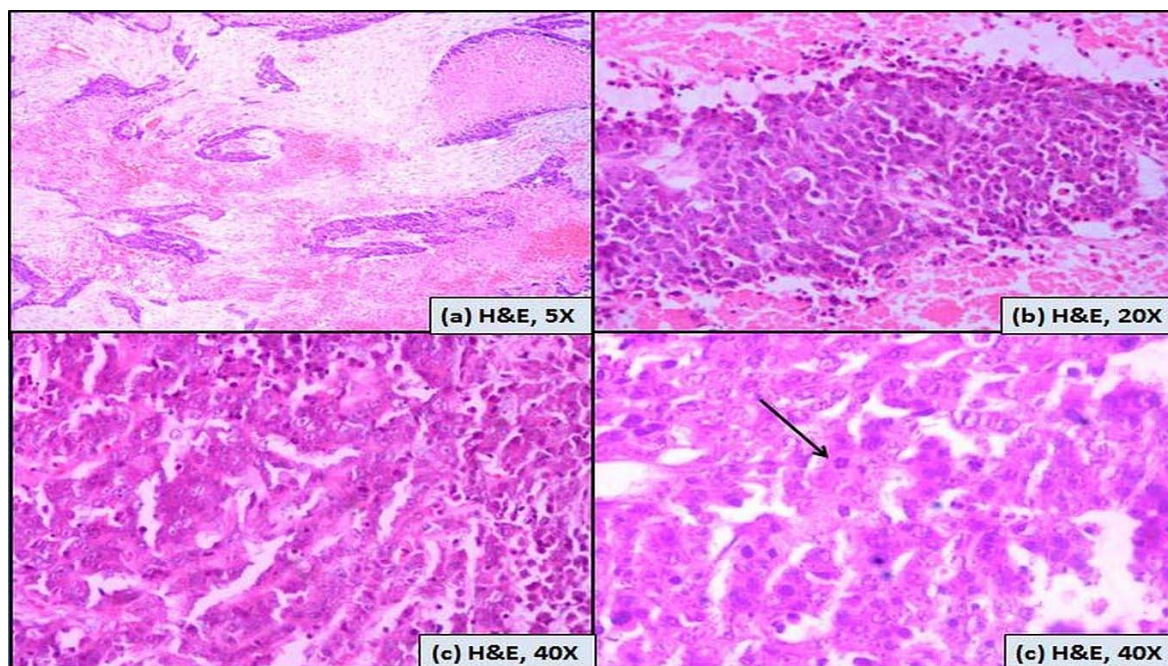


Figure 1 (a) H&E 5x: section shows perivascular tumor with surrounding extensive areas of necrosis and hemorrhage. (b) H&E 20x: showing diffuse sheet of tumor cells. (c) H&E 40x: section shows tumor cells with fine granular chromatin, conspicuous nucleoli, moderate cytoplasm with significant mitosis (arrow).

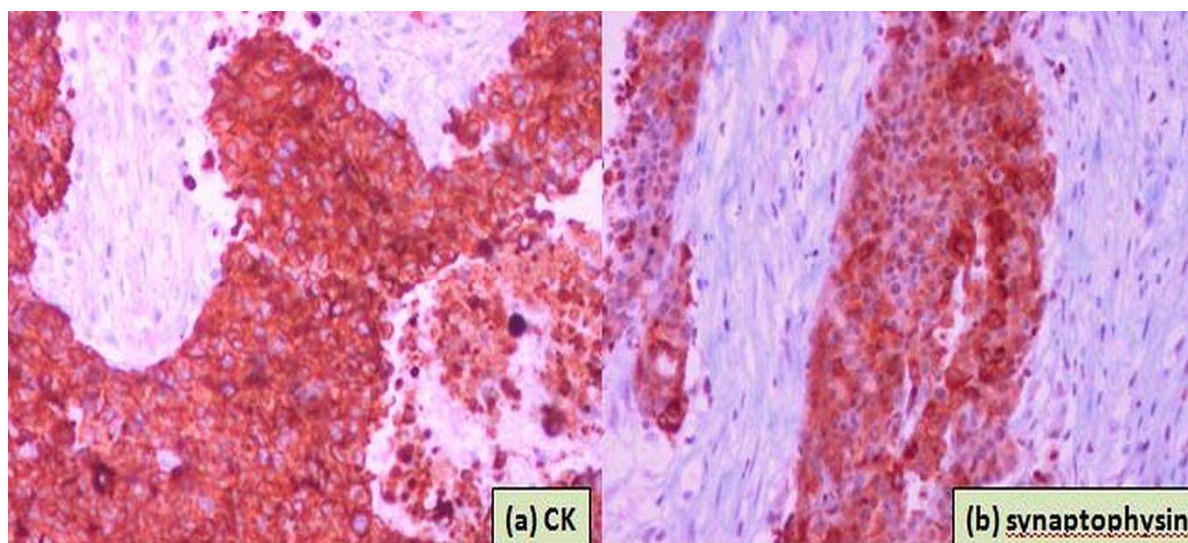


Figure 2 (a) Ck: tumor cells are positive for pan-cytokeratin. (b) synaptophysin: tumor cells are positive for synaptophysin.

DISCUSSION

The Small cell carcinoma of the Ovary of Hypercalcemic Type, first recognized by Dr Robert E Scully in the mid-1970s^[1]. Dickersin then described this tumor in his study in 1982^[2], that resulted in a wider appreciation of this exceedingly rare tumor. The histogenesis of SCCOHT and the mechanism of the development of the hypercalcemia are unknown. SCCOHT appears to be a unique clinical entity that it behaves very aggres-

sively, typically affects young women, unilateral in 99% of cases and exhibits paraneoplastic hypercalcemia in approximately 62% of patients. Average age of diagnosis is 24 years old^[3]. Some studies have documented serologically the presence of parathyroid hormone (PTH)-related protein (PTHrp), but the ectopic production of PTH is rarely reported^[4].

The presenting symptoms and images of SCCOHT are non-specific and similar to other ovarian tumors. At

least half of them have spread beyond the ovary at the time of laparotomy. Many women diagnosed with this tumor are diagnosed at an early stage but the aggressive behavior leads to a strikingly poor prognosis^[5]. Most women die within a year of diagnosis.

The differential diagnosis of SCCOHT includes other high grade neoplasms including malignant melanoma, lymphoma, sex cord-stromal tumors, germ cell tumors, primitive neuroectodermal tumors and various sarcomas (Ewing, rhabdomyosarcoma), and rhabdoid tumors^[6, 7].

Grossly, SCCOHT are large (mean diameter, 15 cm), predominantly solid, cream-colored mass resembling an ovarian lymphoma or dysgerminoma. Rupture is present in at least 20% of the tumors. Areas of necrosis, hemorrhage, and cystic degeneration are common.

Microscopically, the tumor is composed of diffuse sheets of small, closely packed, round to occasionally spindle-shaped cells with scanty cytoplasm and nuclei containing single nucleoli. Mitotic figures are common. The tumor also grows as small islands, cords and trabeculae. Follicle-like structures lined by tumor cells are present in approximately 80% of cases. These spaces typically contain eosinophilic, but occasionally basophilic fluid. In approximately 40% of tumors, a variable proportion of large cells have abundant eosinophilic cytoplasm, which may have a globular, hyaline quality, and large nuclei that have prominent nucleoli.

To better address the diagnosis, an immunohistochemical analysis is necessary. Immunohistochemical markers are used to confirm the epithelial nature of the tumors. 90% of tumors are immunoreactive for one or more cytokeratins, most consistently for CAM5.2 and CK7; staining for EMA is present in 30% of the tumors^[2, 8]. Over half the tumors are immunoreactive for vimentin and neuron-specific enolase, and a sizable minority stain for chromogranin A. Immunoreactivity for p53 was documented in 80% of tumors in one study, supporting the presence of p53 mutations in these tumors^[9].

Optimal management of patients of SCCOHT is not well defined. There are reports in the literature showing benefit and response to platinum-based chemotherapy and radiotherapy, the majority of patients have relapsed despite aggressive multi-modality treatment. Harrison et al. presented a review of management of 17 cases in a GCIG study, with poor results noted^[5].

The preferred treatment for SCCOHT is surgical resection followed by chemotherapy and radiotherapy treatment. The role of radiotherapy is not clear, but it may be advocated in locally advanced disease. Postoperative

chemotherapy for SCCOHT is usually used and can improve the prognosis^[10, 11]. The benefit and impact of chemotherapy were difficult to interpret as a variety of regimens were used. The most commonly used chemotherapy is platinum-based combination chemotherapy.

CONCLUSION

Small cell cancer of Ovary, hypercalcemic type is a rare, aggressive tumor with very poor prognosis. Immunohistochemical staining of epithelial markers (cytokeratin, EMA), CD10, synaptophysin and vimentin plays a great role in confirming the diagnosis. Multimodality treatment including surgery, combination chemotherapy and radiotherapy is recommended for SCCOHT.

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