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Small cell ovarian carcinoma hypercalcemic type and endometrial adenocarcinoma in a 49-year-old patient: a very rare case

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Summary

Background: Small cell ovarian carcinoma hypercalcemic type (SCCOHT) is a rare ovarian malignancy with less than 400 cases worldwide. However, it affects mainly young women and has poor prognosis. The incidence of concurrent endometrial and ovarian cancer is as low as 10%, and has not been described, to our knowledge, with SCCOHT. *Case Report:* This is a rare case of a 49-year-old female who presented with abdominal pain, constipation, asymptomatic hypercalcemia, a large palpable abdominal mass, and was diagnosed with SCCOHT with concurrent Grade I endometrial adenocarcinoma endometroid type. *Conclusion:* This is an interesting case due to the concurrent endometrial cancer, the size of the tumor, and the age of the patient and aims to increase clinical suspicion around SCCOHT. The importance of the MDT should be highlighted, especially for this type of tumors which can be a diagnostic and treatment challenge.

Key words: Ovarian cancer; Small cell ovarian carcinoma; Endometrial cancer.

Introduction

Small cell ovarian carcinoma, hypercalcemic type (SCCOHT) is a rare ovarian malignancy with less than 400 cases worldwide and a five-year survival of approximately 10%. It affects mainly young women with a mean age of 23.4 years (youngest reported 14 months old, oldest 56 years) [1, 2]. Although the term 'small cell' is associated with lung cancer, and this is an ovarian malignancy, in essence, this tumor is genetically and histopathologically distinct, both from ovarian/fallopian and from lung cancer and is more close to rhabdoid malignancies. Its unique pathogenesis dictates the treatment plan and could lead to targeted treatment protocols and genetic counseling in the future.

Case Report

A 49-year-old female presented at the Emergency department of Patras University Hospital with progressively worsening abdominal pain and constipation and an asymptomatic hypercalcemia of 12 mg/dl (n.v 8.8-10.4). The patient was nulligravida, a non-smoker, and a social drinker. She had regular menstrual cycles since the age of 12 and was not on any medication. She had a body mass index of 24 kg/m^2, no significant family history, past medical or surgical history. On examination, bowel sounds were present, abdomen was soft non-tender with a palpable mass extend- ing from hypogastrium up to the umbilicus. Speculum and rectal examination were normal. Transvaginal ultrasound revealed a unilocular, hyperechogenic mass, 20×23 cm in size, with irregular margins, adjacent to the uterus. Yet, it was inconclusive regarding the origin and nature of the mass. The only remarkable laboratory findings were a C-reactive protein of 28 U/L (n.v <0.5), CA-125 of 250 U/ml, and LDH of 1,092 U/L. Pregnancy test was negative, and chest and abdominal X-rays were normal. The preoperative assessment included abdomen, brain, and chest CT, MRI of the abdomen and pelvis, sigmoidoscopy, intravenous pyelogram, cystoscopy, and pigtail ureteric catheter insertion. The imaging was negative for distal disease.

The patient underwent an exploratory laparotomy (Figure 1). Frozen section examination reported a high-grade undifferentiated carcinoma, raising the possibility of small cell carcinoma hypercalcemic type. Cytoreduction was only partially possible, due to extensive pelvic disease leading to frozen pelvis. The postoperative period was uneventful following an enhanced recovery program. Calcium levels normalized on day three. The patient was discharged on day seven and benefited from psychological support and a supportive family environment.

The histopathologic findings were those of high-grade carcinoma of small and focally large cells (Figure 2) expressing keratins (AE1/AE3), CD10, and EMA but negative for WT1, TTF-1, neuroendocrine, and several other immunohistochemical markers. The differential diagnosis included undifferentiated ovarian carcinoma, SCCOHT, small cell ovarian carcinoma pulmonary type and metastatic carcinoma. The presence of hypercalcemia along with the immunophenotype and the absence of a primary tumor elsewhere favored SCCOHT. Immunohistochemistry confirmed loss of SMARCA4 protein expression. Multiple omental tumor deposits were found and all biopsied lymph nodes were positive. There was a concurrent grade I endometrial adenocarcinoma endometroid type confined to the endometrium. The multidisciplinary team (MDT) decided on six cycles of carboplatin and etoposide, followed by further imaging.

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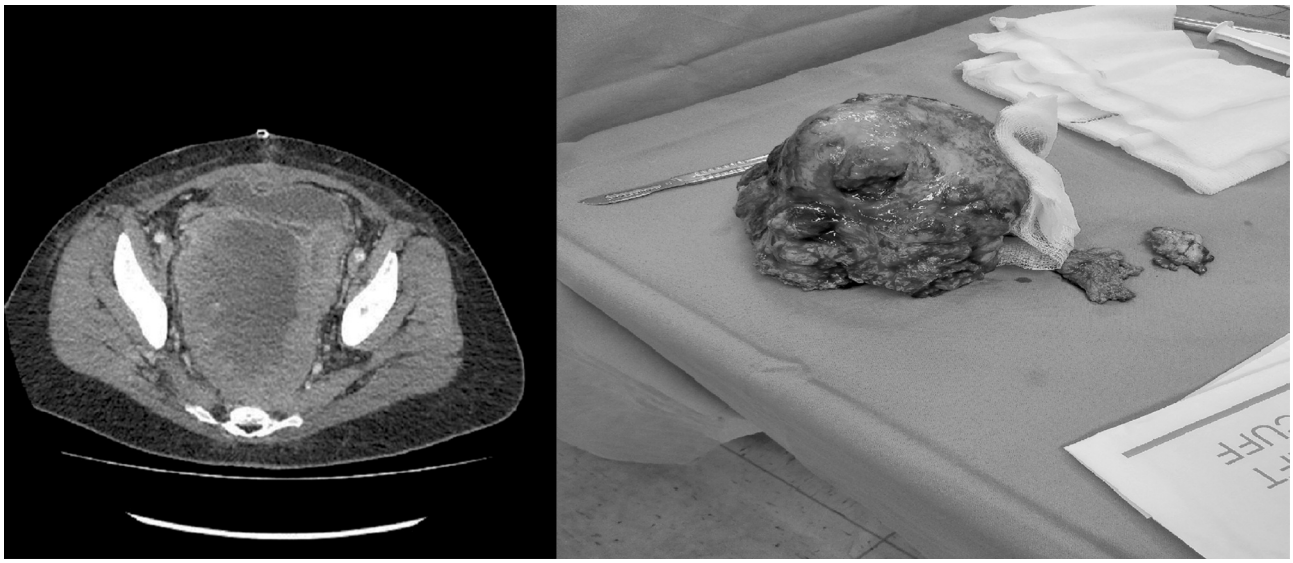

Figure 1. — MRI image and surgical specimen.

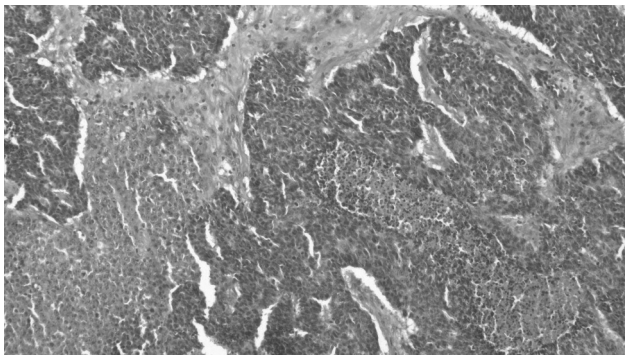

Figure 2. — Hematoxylin & Eosin section (×10 magnification) of the tumor, depicting a nested growth with central necrosis and prominent apoptosis. The spindled small cell element and the minor large cell element with nucleolar prominence are juxtaposed.

One month post-surgery CA-125 normalized. At four-month follow up, the patient was alive with disease (minimal response to treatment on imaging) and had a good quality of life.

Discussion

The incidence of concurrent endometrial and ovarian cancer is as low as 10%, and has not been described, to the present authors' knowledge, with SCCOHT, which makes this case even more interesting [3]. In addition, this is one of the largest tumours reported (maximum diameter 24 cm).

This malignancy is poorly discussed in the literature with mostly case reports or case series, the largest by Young *et al.* (1994) [4] with 150 cases and Callegaro-Filho *et al.* (2016) [5] with 47. The present patient was 49-years-old, diagnosed at Stage III as half of their patients. Two-thirds have hypercalcemia, and as in this case, this could be one of the few initial manifestations of the disease, therefore it should be noted that even asymptomatic hypercalcemia should be thoroughly investigated. Although most commonly the tumour seems to affect the right ovary, in the present case it originated from the left.

Callegaro-Filho *et al.* propodec that multi-agent chemotherapy could benefit these patients, therefore this patient started within the following 30 days from diagnosis (mean range in the literature being 40 days). Most studies agree on surgical management followed by adjuvant chemotherapy. The proposed protocols are vinblastine, cisplatin, cyclo-phosphamide, bleomycin, doxorubicin, and etoposide (VPCBAE), bleomycine, etoposide, platin (BEP), also used for small cell lung cancer, and those for malignant rhabdoid tumours. Radiotherapy was not considered an option for the present case due to the stage at diagnosis, however it may be of benefit at the initial stages [6].

The discovery of SMARCA 4 mutations in the pathogenesis of SCCOHT which can also be found in the germline [7] will possibly lead to targeted treatments and indicate that this could be a hereditary disease, while these patients are also possibly susceptible to rhabdoid malignancies [8]. CA-125 and calcium levels can be used during the follow up.

Conclusion

The authors presented this case in order to increase clinical suspicion of SCCOHT which affects young women and is often diagnosed late with a poor prognosis. This is an interesting case due to the concurrent endometrial cancer, the size of the tumor, and the age of the patient. The importance of the MDT should be highlighted, especially for this type of

tumors which can be a both a diagnostic and a treatment challenge.

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