Gynecologic Oncology Reports 24 (2018) 10–13

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gynor

Case report

Primary small cell ovarian cancer of pulmonary type: A case report

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ARTICLE INFO

Keywords:
Small cell ovarian cancer of pulmonary type
Small cell ovarian cancer of pulmonary type diagnosis
Small cell ovarian cancer of pulmonary type pathology
Small cell ovarian cancer of pulmonary type treatment

ABSTRACT

Background: Primary small cell ovarian cancer of pulmonary type (SCCOPT) is a rare aggressive ovarian tumour with an incidence of < 1%, usually occurring in perimenopausal or postmenopausal women and known to have a poor prognosis. Current treatment is platinum based but has not resulted in long term survival.
Case presentation: We report a case of a 77-year old Caucasian woman who presented initially with a one-week history of abdominal discomfort with raised inflammatory markers and Ca125 of 50 μ/ml. Calcium levels were normal. She underwent primary debulking surgery, and histology showed a tumour comprising areas of classical small-cell carcinoma morphology. 6 cycles of adjuvant chemotherapy with carboplatin was offered. Relapsed/progressive disease was noted after 3 months of chemotherapy and patient died 7 months after treatment completion.
Conclusions: SCCOPT is a rare aggressive malignancy with majority of the women having an overall survival of 2 years. There is no clear consensus for the diagnosis and optimal treatment.

1. Introduction

Primary ovarian neuroendocrine malignant neoplasms are extremely rare, accounting for < 2% of all ovarian cancers, and usually related to the large cell type (Reed et al., 2014). Primary small cell ovarian cancer was first described in 1979 (Reed et al., 2014). It is a highly aggressive tumour with an incidence rate of < 1% of all ovarian cancers and a poor outcome (Reed et al., 2014; Eichhorn et al., 1992). Two tumour variants are described; the small cell cancer of hypercalcemic type (SCCOHT) and the pulmonary type (SCCOPT) with SCCOHT occurring in younger women and SCCOPT in older women respectively (Reed et al., 2014; Atienza-Amores et al., 2014). They are not easily distinguished pre-operatively from common epithelial ovarian cancers and the differential diagnosis will include germ cell and granulosa/sex-cord tumors (Reed et al., 2014). To our knowledge, only 22 cases in total of SCCOPT have been described in the literature with majority of these arising in mature cystic teratomas (Eichhorn et al., 1992; Rubio et al., 2015; Ikota et al., 2012; Lim et al., 1998; Chang et al., 1992; Grandjean et al., 2007; Kurasaki et al., 2013; Mebis et al., 2004; Suzuki et al., 2007; Lo Re et al., 1994; Tsolakidis et al., 2012; Reckova et al., 2010). However, from these, only 8 cases are described as "pure" primary SCCOPT (Eichhorn et al., 1992; Kurasaki et al., 2013; Suzuki et al., 2007; Lo Re et al., 1994; Tsolakidis et al., 2012; Reckova et al., 2010) (Table 1).

We report a clinical case of unilateral primary SCCOPT presented in a 77-year old woman, the current treatment options and clinicopathological considerations.

2. Case presentation

A 77-year old woman presented to Accident and Emergency with 1-week history of low abdominal pain, intermittent difficulty initiating micturition and constipation. Clinical examination showed no ascites and a pelvic mass was found in the pelvis. Ultrasound of the pelvis demonstrated a 11.7 × 9.6 × 11.8 cm complex mass in the midline of the pelvis extending to the right adnexa (Fig. 1). Her blood results were satisfactory, except for a slight increase in inflammatory markers and Cancer Antigen (CA)-125 of 50 μ/ml, calculating the Risk of Malignancy Index (RMI) at 450 (Davies et al., 1993).

Hence, Computed tomography (CT) of chest, abdomen and pelvis was performed which revealed within the pelvic cavity a large 14 × 8.2 × 9.5 cm heterogeneous multi-septated mass with solid and cystic components originating from the right adnexa and mostly keeping with ovarian tumour (Fig. 1). There was no evidence of disease

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https://doi.org/10.1016/j.gore.2018.02.003
Received 6 January 2018; Received in revised form 6 February 2018; Accepted 7 February 2018
Available online 08 February 2018

Table 1
Case reports and clinopathological characteristics of primary ovarian small cell carcinoma of pulmonary type.

Case reports	Age (years)	FIGO stage	Origin and size (cm)	Treatment	Postoperative adjuvant treatment	Recurrence (months)	Overall survival (months)
Case 1: Eichhorn et al. (1992)	76	IIIB	ROV/NA LOV/NA	STAH, BSO	NA	NA	12
Case 2: Eichhorn et al. (1992)	64	IIIB	ROV/5.5 LOV/4.5	TAH, BSO, OMT, AP	Cisplatin and cyclophosphamide	8	NA
Case 3: Eichhorn et al. (1992)	49	IIIB	LOV/16	LSO, COL, LYM	Cisplatin, cyclophosphamide and doxorubicin	NA	13
Lo Re et al. (1994)	16	IIIA	LOV/9.5	TAH, BSO, OMT	Vinblastine, cisplatin, cyclophosphamide, bleomycin doxorubicin and etoposide	NA	13
Suzuki et al. (2007)	49	IC	LOV/15	TAH, BSO, OMT, LYM	Paclitaxel and carboplatin	NA	≥36
Reckova et al. (2010)	67	IV	ROV/6	TAH, BSO, OMT, AP	Carboplatin and etoposide	NA	24
Kurasaki et al. (2013)[a]	54	IIIA	NA	TAH, BSO, OMT	Paclitaxel and carboplatin	NA	NA
Tsolakidis et al. (2012)	55	IIIC	LOV/8	TAH, BSO, OMT, LYM	Carboplatin and etoposide	NA	≥21
Current case	77	II	ROV/15	TAH, BSO, OMT	Carboplatin	3	7

NA: Not available; ROV: Right ovary; LOV: left ovary; STAH: Subtotal abdominal hysterectomy; TAH: Total abdominal hysterectomy; BSO: Bilateral salpingoophorectomy; OMT: Omentectomy; LYM: Lymphadenectomy; AP: Appendicectomy.

[a] The patient was followed up for 22 months without recurrence.

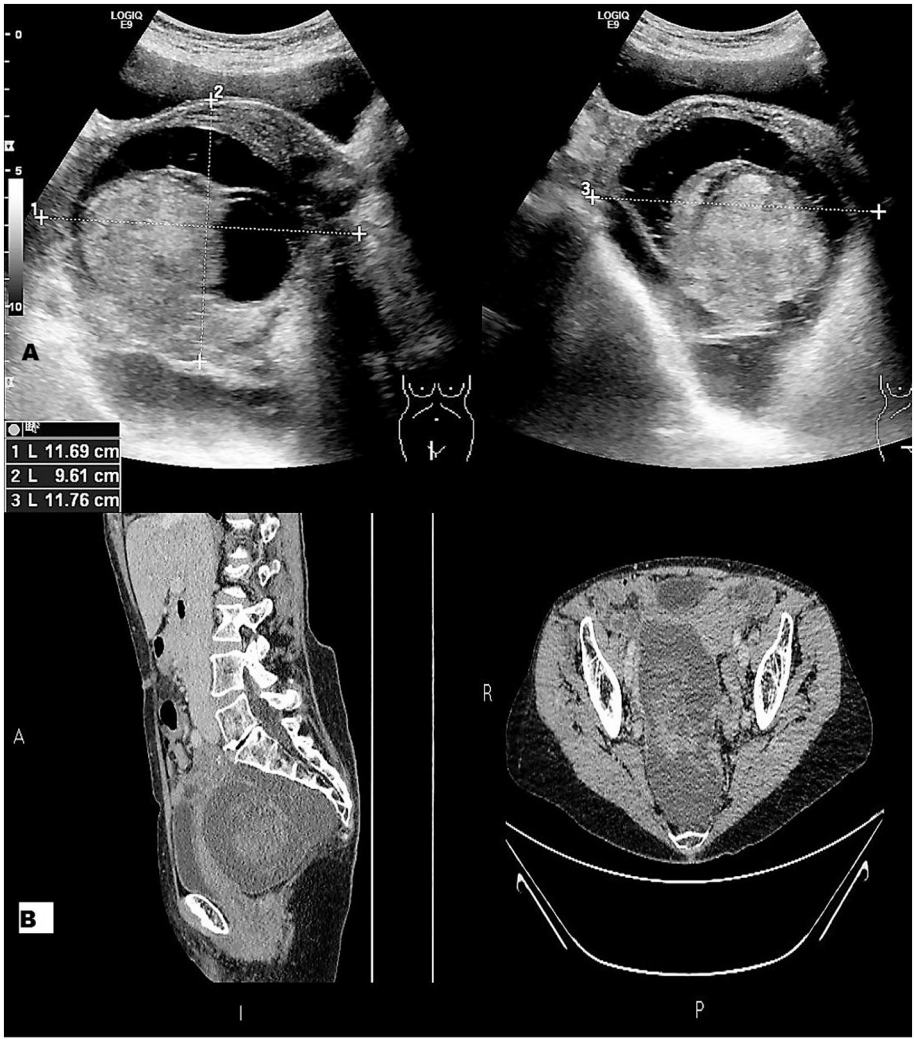

Fig. 1. Imaging findings: (A) Ultrasound of the pelvis demonstrating a 11.7 × 9.6 × 11.8 cm complex mass in the midline of the pelvis extending to the right adnexa (B) Abdominal CT scan demonstrating a 14 × 8.2 × 9.5 cm heterogeneous multi-septated mass with solid and cystic components originating from the right adnexa.

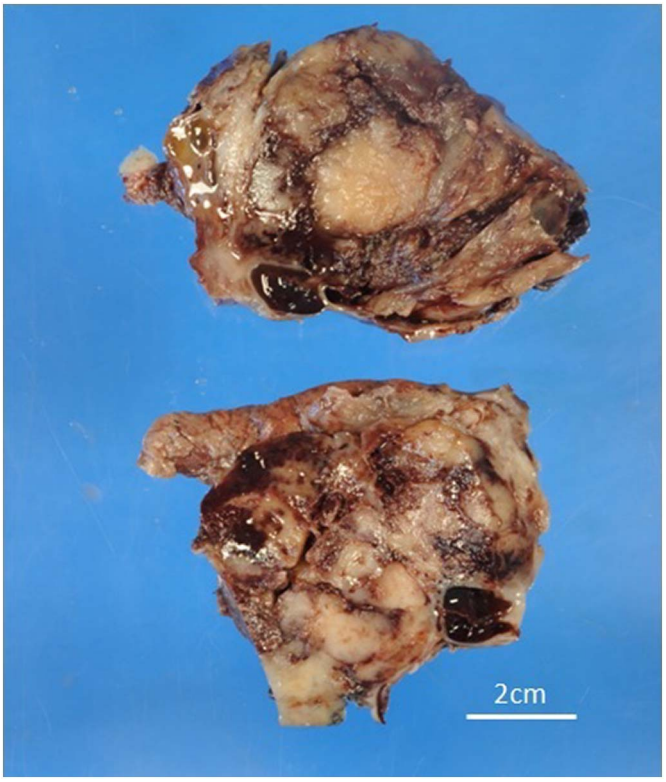

Fig. 2. Macroscopic pathology.

outside the pelvis with a radiological staging of FIGO stage I and no evidence of pelvic nor para-aortic lymphadenopathy. The mass was causing extrinsic compression of the sigmoid colon and the bladder accounting for her symptoms.

After Multi-Disciplinary Team (MDT) discussion, decision was made for laparotomy and upfront debulking surgery for suspected ovarian cancer surgery in a gynaecologic oncology center. At laparotomy, a 15 cm hemorrhagic pelvic mass with mostly solid, friable and necrotic areas arising from the right ovary was found. It was adherent to the uterus, bladder, sigmoid, and right pelvic side wall. A thorough assessment of upper abdomen and pelvis showed no evidence of peritoneal/upper abdominal disease/lymphadenopathy. Total abdominal hysterectomy, bilateral salpingo-ophorectomy, total omentectomy and washings was performed, achieving no residual disease and complete debulking. Intraoperative blood loss was 650 ml. Postoperative period was uneventful apart from a short spell of ileus which resolved with conservative management. Patient was discharged home in a week.

The final pathologic report was discussed at MDT. Histology demonstrated a solid hemorrhagic malignant tumour (Fig. 2) comprising areas of classical small-cell carcinoma morphology, showing cells with scant cytoplasm, stippled chromatin and nuclear moulding. However, other areas of the tumour were comprised of spindled cells and epithelioid cells with more abundant cytoplasm. Immunohistochemistry showed that the lesion was positive with the neuroendocrine markers CD56 and PGP 9.5, and showed dot-like positivity with the cytokeratin EMA, including in the spindled and epithelioid components. A final diagnosis of Primary SCCOPT was made and histologically staged as FIGO stage IC3 but clinical stage II due to the dense adhesions between the tumour and pelvic structures. A decision for adjuvant chemotherapy was made at MDT with 6 cycles of Carboplatin and Etoposide and follow up for the next 5 years (3 monthly for the first 3 years and 6 monthly for the next 2 years) as per the hospital ovarian cancer protocol. Etoposide was omitted from the chemotherapeutic regime in view of performance status.

3 months following treatment, patient had abdominal discomfort which triggered a CT scan that confirmed a pelvic relapse. Relapse/progression of disease soon after treatment indicated a poor prognosis of survival. Palliative radiotherapy was unlikely to prolong overall survival and second line chemotherapy with cyclophosphamide, doxorubicin and vincristine (VAC) was discussed but declined by the patient. The patient died 7 months after treatment completion.

3. Discussion

SCCOPT is an extremely rare and aggressive ovarian malignancy (Reed et al., 2014; Rubio et al., 2015). Patients are being aged between 28 and 85 years but most often occurs in perimenopausal and postmenopausal women with a median age of 59 years (Eichhorn et al., 1992). Usually it is not seen with hypercalcaemia, and 45% of patients will have a unilateral involvement (Eichhorn et al., 1992). Tumors size range from 4.5 to 26 cm (mean 13.5 cm) and are mostly solid, with a variable minor cystic component (Eichhorn et al., 1992).

Surgical treatment is analogous to that of epithelial ovarian cancers as there are usually no features to differentiate SCCOPT form epithelial ovarian neoplasms. Thereafter, the usual method of clinical examination, measurement of tumour markers, radiological imaging/staging, and review at MDT is required (Reed et al., 2014). Patients who are found to be suitable for primary debulking surgery should be referred to gynecological oncology center and this should be offered as the treatment of choice (Reed et al., 2014).

There is no clear consensus for the optimal regime for postoperative chemotherapy because of the small number of patients and unavailability of follow-up data (Eichhorn et al., 1992). In general, adjuvant chemotherapy with carboplatin and etoposide combination will be offered, which is the commonly used combination chemotherapy used to treat small cell lung cancer and extrapulmonary uterine and cervical gynecological small cell cancers (Reed et al., 2014; Eichhorn et al., 1992). However, there is no supportive evidence that chemotherapeutic agents are shown to be effective with SCCOPT (Suzuki et al., 2007).

Patients diagnosed with SCCOPT usually have a very poor survival, generally dying rapidly within 2 years (Reed et al., 2014; Eichhorn et al., 1992). In the case series by Eichhorn et al., 5 of 7 patients after long-term follow-up died at 1–13 months (mean 8 months), 1 died after an unknown interval, and 1 was alive at 7.5 years. 2 other patients had recurrent or residual disease at 6 and 8 months (Eichhorn et al., 1992). In the published case reports; it is interesting to note that the overall survival did not differ between stage 1 and stage 4 indicating its aggressive nature regardless of the staging. Moreover, the older age of SCCOPT patients and poor performance status may also limit treatment choices as opposed to SCCOHT, where some successes are occurring with aggressive and quite toxic multi-drug regimens.

4. Conclusions

SCCOPT is an aggressive malignancy with majority of the patients dying within 2 years after diagnosis. However, it is interesting to highlight that the two of the longest survivals seem to be with carboplatin and paclitaxel (Suzuki et al. 36 months and Kurasaki et al. followed up the patient for 22 months without recurrence noted). To date, all treatments so far reported in the literature have been platinum -based. Upfront surgery should be offered and performed in a gynaecologic oncology center. Histologically and immunohistologically, the tumour cells share features similar to those of pulmonary small cell carcinoma. To our knowledge, only 8 cases in the literature are described as ‘pure’ primary SCCOPT. Given the extreme rarity of this ovarian carcinoma, more multicenter registries are needed with data collection in order to understand its behavior and enhance current or identify new treatment options. Thus, each and every case of SCCOPT if reported and published in literature could help the gynecological oncology society to make appropriate decisions.

Author's statement

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Funding

None.

Declaration of interests

The authors have no conflicts of interest to declare.

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