Gynecologic Oncology Reports 18 (2016) 45–48

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

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

Case report

# Small cell ovarian carcinoma: Long term survival in juvenile case with poor prognostic features

Lauren Stewart, MD [a,*], Ruchi Garg, MD [b,*], Rochelle Garcia, MD [a,c], Elizabeth Swisher, MD [a]

[a] Department of Obstetrics and Gynecology, University of Washington Medical Center, Seattle, WA, USA
[b] Mid Atlantic Gynecology Oncology and Pelvic Surgery Associates, Annandale, VA, USA
[c] Department of Pathology, University of Washington Medical Center, Seattle, WA, USA

ARTICLE INFO

*Article history:*
Received 12 September 2016
Received in revised form 1 November 2016
Accepted 5 November 2016
Available online 9 November 2016

*Keywords:*
Small cell
Ovarian
Chemotherapy
Ovarian preservation

ABSTRACT

*Background:* Ovarian small cell carcinoma is a rare, aggressive neoplasm that occurs in young women and has a poor long-term prognosis. Treatment involves surgical resection and chemotherapy. The required radicality of surgery is uncertain, balancing cytoreduction with fertility preservation. Various chemotherapy regimens are utilized due to confusion regarding the neoplasm's lineage.

Case

We describe an adolescent with small cell carcinoma, hypercalcemic type, stage IA. Surgery included left salpingo-oopherectomy, left pelvic/paraaortic lymphadenectomy, omentectomy and peritoneal biopsies. She received four cycles of bleomycin, etoposide and cisplatin, similar to high-risk germ cell cancers. She has received no further therapy and is eleven years from diagnosis without evidence of disease.

*Conclusion:* This is the first long-term juvenile survivor managed with both fertility-sparing surgery and BEP (bleomycin, etoposide, cisplatin).



## 1. Introduction

Small cell carcinoma of the ovary (SCCO), hypercalcemic type, is an aggressive, rare neoplasm that tends to affect young women, with an average age at diagnosis of 23 years. Long-term prognosis is poor, with overall survival of one to two years in most cases (Young et al., 1994). Patients with early-stage disease confined to the ovary may experience longer survival (Young et al., 1994; Harrison et al., 2006; Distelmaier et al., 2006). There are a few case reports of patients with stage II or III disease surviving several years (Young et al., 1994; Harrison et al., 2006; Sholler et al., 2005; Christin et al., 2008; Kanwar et al., 2008; Tewari et al., 1997; Woopen et al., 2012; Pressey et al., 2013) and no cases of long-term survival in stage IV disease.

Treatment usually includes a combination of surgical resection and chemotherapy (Young et al., 1994; Harrison et al., 2006; Distelmaier et al., 2006; Senekjian et al., 1989; Peccatori et al., 1993; Sholler et al., 2005; Christin et al., 2008; Kanwar et al., 2008; Tewari et al., 1997; Woopen et al., 2012; Pressey et al., 2013). The extent of surgery required is uncertain due to the need to provide aggressive treatment while attempting to preserve fertility in these young patients (Woopen et al., 2012). Fertility-sparing surgery is debated, as many patients are young with unilateral ovarian involvement; however, recurrences in the contralateral ovary have been reported and are usually fatal. Due to the rarity of SCCO, there are no randomized controlled trials that identify optimal treatment. The majority of recommended treatment plans are derived from case reports and small case series. The only prospective trial to date treated 27 patients on a phase II trial consisting of radical surgical resection followed by four to six cycles of chemotherapy with cisplatin, adriamycin, etoposide, cyclophosphamide, and, in case of complete remission, additional high-dose chemotherapy with carboplatin, vepeside, cyclophosphamide (Pautier et al., 2007). This intensive regimen demonstrated a 49% 3-year overall survival rate, which was consistent with previously published reports with less intensive chemotherapy (Pautier et al., 2007).

Various chemotherapy regimens have been proposed, in part due to uncertainty over what cell lineage SCCOs arise from (or differentiate towards); it is not certain whether the neoplastic cells in SCCO derive from ovarian epithelium, sex-cord stromal cells or germ cells (Young et al., 1994; Ulbright et al., 1987). Based on their histology, a number of neoplasms can be confused with SCCO including granulosa cell tumors, dysgerminomas, primitive neuroectodermal tumors, melanoma, lymphomas, round cell sarcomas, and small cell desmoplastic tumors (Distelmaier et al., 2006; McCluggage et al., 2004). Some of these may be excluded based on immunohistochemistry (IHC) protein expression profiles. However, IHC does not clearly distinguish between the possibilities of epithelial and stromal differentiation.

* Corresponding author at: University of Washington Medical Center, Department of Obstetrics and Gynecology, 1959 NE Pacific Street, Box 356460, Seattle, WA 98195, USA
*E-mail address:* stewart4@uw.edu (L. Stewart).

http://dx.doi.org/10.1016/j.gore.2016.11.002

Poor prognostic factors for SCCO include early age of onset, large tumor size, and elevated serum calcium (Young et al., 1994). We describe our experience with an adolescent patient diagnosed with early stage disease with multiple poor prognostic features who has done well with both conservative surgery and less intensive adjuvant chemotherapy.

## 2. Case report

In October 2004, a healthy 14-year-old girl presented to the emergency department complaining of abdominal pain following a sexual assault. Her past medical and surgical history was remarkable for drug and alcohol use. Physical exam revealed a large, firm, immobile mass extending from the pubic symphysis to the umbilicus. Pelvic ultrasound demonstrated a 16 × 10 × 17 cm mass and ascites (Fig. 1). Laboratory analyses showed beta HCG <3 mIU/mL, mildly elevated LDH at 202 U/L, CEA 1.1 ng/dL, AFP < 5 ng/mL, inhibin A < 10 pg/mL, inhibin B 25 pg/mL and CA-125 81 U/mL. Her calcium was mildly elevated at 10.9 mg/dL and ionized calcium was also high at 1.53 mmol/L. She was anemic with a hemoglobin of 9.8 g/dl. She underwent exploratory laparotomy. The left ovarian mass (17 × 15 × 12 cm, 1042 g) was removed and frozen section was reported as malignant neoplasm, possible granulosa cell tumor, favor small cell carcinoma. Complete surgical staging was performed including left pelvic and para-aortic lymph node dissection, infracolic omentectomy and peritoneal biopsies. There was no evidence of disease outside of the left ovary and the right ovary appeared normal. Final pathology returned as SCCO, hypercalcemic type, stage IA. By histologic examination, the neoplasm consisted of sheets of cells with small to moderate-sized, irregular nuclei and scant cytoplasm (Fig. 1). The cellular proliferation index was high, with numerous mitotic figures per high-powered-field, apoptotic cell debris and areas of geographic necrosis. Rare follicle formation was present. By IHC the neoplastic cells were negative for CD45, chromogranin, and inhibin and positive for vimentin and cytokeratin AE1/AE3 (Fig. 1).

The patient was treated with four cycles of BEP (bleomycin 30 U day 1, etoposide 100 mg/m$^2$ days 1–5, and cisplatin 20 mg/m$^2$ days 1–5, every 4 weeks) from November 2004 to February 2005. After completing chemotherapy, she was followed with serum ionized calcium, pelvic exam (PE), and transvaginal ultrasound (TVUS) of the retained ovary every three months, and CT scan of the chest, abdomen, and pelvis every six months for two years and then with decreased frequency. Her ionized calcium was normal immediately following chemotherapy, but upon recheck 3 months later it was slightly elevated. PE, TVUS, and CT scan were normal at that time. FDG-PET scan showed a focus with SUV 3.3 in the region of the right external iliac lymph nodes and in the upper abdomen posterior to the liver. These findings were concerning for disease recurrence. The patient was taken to the

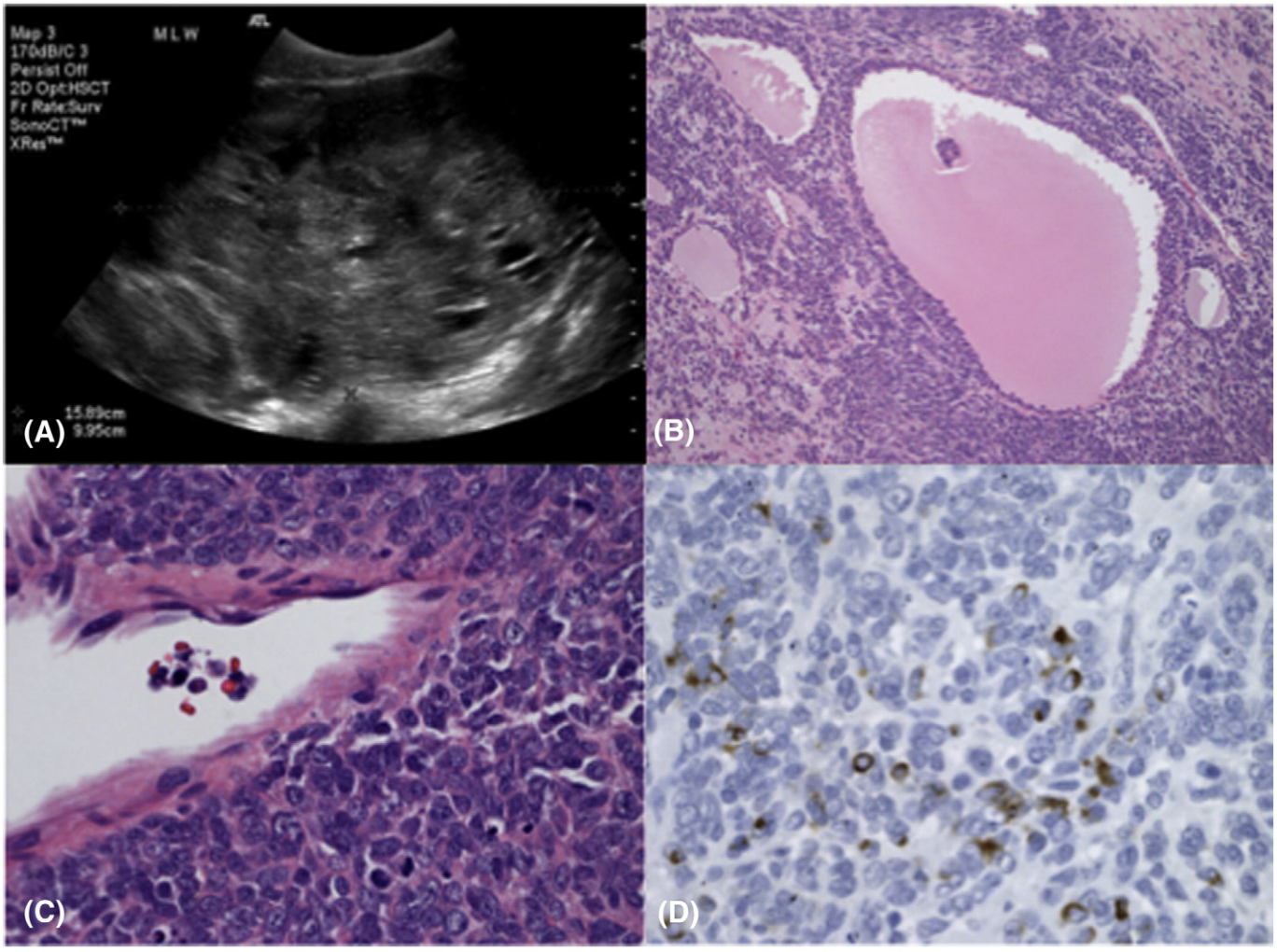


**Fig. 1.** Selected radiologic and histologic images. A) Transvaginal ultrasound demonstrating the cystic/solid nature of the large mass. B) H&E 100×. Sheets of neoplastic cells form follicles with pink eosinophilic secretions. C) H&E 600×. The neoplasm is composed of small to moderate sized cells with hyperchromatic nuclei and scant cytoplasm. Mitotic figures and apoptotic debris are easily visible. D) Immunohistochemical detection of cytokeratins (brown stain) using AE1/AE3 600×. Cytokeratin expression is common but often scanty in SCCOs as is seen in this case.