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Case Report

Radiotherapy for recurrent small cell carcinoma of the ovary: A case report and review of the literature

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Introduction

Small cell carcinoma of the ovary, hypercalcemic type (SCCOHT) is a highly aggressive tumor that is generally fatal when it spreads beyond the ovary. Although stage IA disease is associated with a better prognosis, approximately 67% of patients recur regardless of treatment type (Young et al., 1994). Once recurrent disease develops, the tumors tend to be poorly responsive to chemotherapy and effective treatments have not been described (Young et al., 1994; Pautier et al., 2007; Scully, 1993). However, there are a few reports of rare patients who have survived after multi-modality treatment that included surgery, chemotherapy and radiation therapy for recurrent disease (Young et al., 1994; Cannon et al., 1975; Dickersin et al., 1982; Benrubi et al., 1993; Harrison et al., 2006; Niimi et al., 2006; Isonishi et al., 2008; Christin et al., 2008). Furthermore, previous reports have suggested that radiotherapy in the adjuvant setting has activity in the primary as well as recurrent SCCOHT (Young et al., 1994; Pautier et al., 2007; Scully, 1993; Cannon et al., 1975; Dickersin et al., 1982). In this report, we describe the case of a 35-year-old woman with stage IA SCCOHT with a sustained complete response following surgery and radiotherapy for recurrent disease. In addition, we review the available literature describing treatment for recurrent SCCOHT.

Case report

The patient initially presented at age 35 years with pelvic pain and abdominal distention. A contrast-enhanced computed tomography (CT) scan revealed a large right ovarian mass extending to the level of the umbilicus. Her CA125 level was 35 U/mL. She did not desire fertility preservation and underwent surgery including a total abdominal hysterectomy with bilateral salpingo-oophorectomy and a partial omentectomy. Final pathology revealed SCCOHT of the right ovary. The left ovary, bilateral fallopian tubes, uterus and omentum were all negative for disease. She received four cycles of adjuvant chemotherapy with cisplatin (75 mg/m^2 on day 1) and etoposide (100 mg/m^2 on days 1, 2 and 3) administered every three weeks. She tolerated the chemotherapy without major toxicities. After completion of chemotherapy, imaging showed no evidence of disease. She was followed on a three-month interval with pelvic exam, CT scan of the abdomen and pelvis, chest radiograph, and CA125 level. Twenty months after completing primary treatment, she developed recurrent disease with an isolated

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8.2 cm para-aortic mass noted on CT scan. She underwent surgery including complete resection of the mass, as well as sampling of surrounding left para-aortic lymph nodes and a biopsy of the remaining omentum. Pathology confirmed recurrent SCCOHT in the para-aortic mass. The remaining para-aortic lymph nodes and omentum were negative.

The patient received postoperative radiotherapy to the para-aortic lymph nodes from T12/L1 to L4/L5, with an initial dose of 45 Gy using a 4-field technique with 18 MV photons. The fields were then reduced to cover only the operative bed as demarcated by clips placed at the time of surgery. This region was treated for an additional 5.4 Gy to a total dose of 50.4 Gy in 28 fractions. Treatment was delivered over a total of 36 days. No chemotherapy was given. The treatment was tolerated well with the only symptom being mild nausea controlled with antiemetics. Imaging at the completion of therapy showed no evidence of disease. The patient has been followed with regular CT scans, chest radiographs and CA125 levels, and remains without evidence of disease fifteen years following the completion of radiotherapy for recurrent disease.

Discussion

SCCOHT is an aggressive disease and most patients develop progressive or recurrent disease despite treatment. No standard approach has been recommended for the treatment of recurrent disease, although multi-modality treatments including surgery, chemotherapy and radiotherapy have been described. Although adjuvant thoracic radiotherapy has been demonstrated to improve survival in conjunction with chemotherapy in limited stage, small-cell lung carcinoma (Van Meerbeeck et al., 2011), the role of radiotherapy in the treatment of primary or recurrent SCCOHT is unclear.

Table 1
Long-term survivors following treatment for recurrent small cell carcinoma of the ovary, hypercalcemic type (SCCOHT).

Study author, year	FIGO stage	Age at diagnosis (years)	Primary surgery	Primary adjuvant treatment	Recurrence interval (months)	Recurrence site	Treatment for recurrence	Outcome
Cannon et al. (1975), Young et al. (1994)	IA	23	RSO	None	12	Pelvis	Surgery: resection of the right broad ligament. Radiotherapy: pelvis Chemotherapy: chlorambucil	NED at 10 years
Dickersin et al. (1982)	IA	26	RSO	Radiotherapy	2	Para-aortic LN and omentum	Surgery: TH, LSO and retroperitoneal LN dissection	NED at 9 months
Young et al. (1994)	IA	19	RSO	Chemotherapy: cisplatin, velban, bleomycin	4 18	Pelvis Anterior abdominal wall	Surgery: TH and LSO Chemotherapy: doxorubicin, cyclophosphamide, etoposide Radiotherapy: pelvis Surgery: resection of mass Chemotherapy: doxorubicin, cyclophosphamide, etoposide	NED at 45 months
Young et al. (1994)	IA	10	LSO	Chemotherapy: cisplatin, velban	5	Para-aortic LN	Chemotherapy: cisplatin, velban, doxorubicin, vinblastine, etoposide	NED at 4 years, 5 months
(Young et al. (1994), Benrubi et al. (1993))	IIB	16	RSO	Chemotherapy: cyclophosphamide, doxorubicin, cisplatin, vincristine, etoposide Surgery: TH, LSO, omentectomy, appendectomy, para-aortic and pelvic LN dissection	6	NR	Surgery: TH, LSO, omentectomy, para-aortic LN dissection. Radiotherapy: whole abdomen	NED at 7 years
Harrison et al. (2006)	IC	28	USO, omentectomy	Chemotherapy: cisplatin, etoposide and carboplatin, paclitaxel	9	NR	Surgery: USO and omentectomy.	NED at 16 months
Niimi et al. (2006), Isonishi et al. (2008)	IIC	24	LSO, omentectomy	Chemotherapy: cisplatin, etoposide, docetaxel	8	Uterus	Surgery: TH and pelvic lymphadenectomy. Chemotherapy: docetaxel	NED at 4 years
Christin et al. (2008)	IIIC	12	LSO and para-aortic LN dissection	Chemotherapy: doxorubicin, etoposide, cisplatin, cyclophosphamide, carboplatin Surgery: RSO, omentectomy, pelvic and para-aortic LN dissection	2	Pelvis	Surgery: resection of parietal nodule and TH. Chemotherapy: carboplatin and ifosfamide followed by high-dose chemotherapy (carboplatin, etoposide, melphalan) with autologous bone marrow transplantation	NED at >14 years
Christin et al. (2008)	IIC	13	LSO and omentectomy	Chemotherapy: bleomycin, etoposide, cisplatin, ifosfamide Surgery: TAH, RSO, omentectomy, pelvic and para-aortic LN dissection	0	Para-aortic LN	Chemotherapy: ifosfamide and etoposide, followed by high-dose chemotherapy (carboplatin, etoposide, melphalan) with autologous bone marrow transplantation.	NED at >10 years.
Callegaro-Filho (2014)	IA	35	TH, BSO, and omentectomy	Chemotherapy: cisplatin, etoposide	20	Para-aortic LN	Surgery: para-aortic LN dissection and biopsy of the omentum. Radiotherapy: para-aortic LN	NED at 15 years

TH: total hysterectomy; BSO: bilateral salpingo-oophorectomy; LSO: left salpingo-oophorectomy; RSO: right salpingo-oophorectomy; LN: Lymph node; NED: no evidence of disease.

In 1994, Young et al. (1994) described a large series of 150 cases of SCCOHT, with 75 patients (50%) having stage I disease. Fourteen of the forty two patients (33%) with stage IA disease for whom follow-up information was available remained without evidence of disease an average of 5.7 years following surgery (range 1–13 years). The remaining 28 patients (67%) with stage IA disease developed recurrent disease, with the majority dying of their disease. Five of the 14 patients with stage IA disease received adjuvant radiotherapy, and four (80%) are long-term survivors, suggesting that radiotherapy may have a role in the adjuvant therapy of this tumor. A previous study by Dickersin et al. (1982) described 11 patients with stage I/II SCOOHT. All patients were treated with surgery; four patients received adjuvant chemotherapy, four patients received adjuvant radiotherapy, and three patients received no adjuvant treatment. Two patients experienced durable responses with radiotherapy alone after initial surgery. Another series by Harrison et al. (2006) reported on 17 cases of SCCOHT. All patients underwent surgery and adjuvant platinum-based chemotherapy. Seven patients received adjuvant radiotherapy, and five (71%) are long-term survivors. Three of the four patients with stage I disease who did not receive radiotherapy developed recurrent disease. The results of these reports suggest that radiotherapy may play an important role in the primary treatment of SCCOHT.

Additional reports also provide evidence for radiotherapy in the treatment of recurrent SCCOHT. Young et al. (1994) and Cannon et al. (1975) described a patient with stage IA disease who developed a pelvic recurrence 12 months following a right salpingo-oophorectomy without adjuvant treatment. She underwent secondary tumor reductive surgery, pelvic radiotherapy and chemotherapy and remained without evidence of disease 10 years after completing therapy for recurrent disease. Furthermore, the series by Young et al. (1994) described two patients treated with chemotherapy and radiotherapy for recurrent disease that were alive at 3.8 and 7 years after completing treatment.

Given the rarity of SCCOHT, the available literature consists of small case series and single patient case reports. A review of the literature was therefore performed to evaluate patients who had a sustained complete response following treatment for recurrent SCCOHT, similar to the one presented in this report. Including the patient described in our report, 10 patients were identified meeting these criteria (Table 1). The median age at diagnosis was 21 years (range 10–35 years). Six patients had stage I disease (60%), three had stage II disease (30%) and one had stage III disease (10%). Nine patients (90%) underwent initial unilateral salpingo-oophorectomy. Eight patients (80%) initially underwent adjuvant chemotherapy, one (10%) underwent radiotherapy alone, and one (10%) did not receive any adjuvant treatment. All patients developed recurrent disease in the pelvis and/or abdomen. Surgery for recurrent disease was performed in eight patients, with two patients receiving no other adjuvant treatment for recurrence. Two patients had surgery followed by radiotherapy, two had surgery followed by chemotherapy, including one patient treated with high dose chemotherapy followed by autologous bone marrow transplantation; and two had surgery followed by radiotherapy and chemotherapy. Two patients did not undergo surgery and received chemotherapy alone, including one patient treated with high dose chemotherapy followed by autologous bone marrow transplantation. All patients had complete response after recurrent disease and were alive and without evidence of disease at time of publication.

Conclusion

We describe the case of a patient with SCCOHT with long-term survival despite recurrent disease. Rare cases have been reported in the literature suggesting that some patients with recurrent disease may respond to salvage surgery, chemotherapy, radiotherapy or a combination of these modalities.

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