Efficacy and toxicity of vinblastine, cisplatin, cyclophosphamide, bleomycin, doxorubicin and etoposide (VPCBAE) in the management of patients with small cell carcinoma of the ovary-hypercalcemic type

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Background

- Small cell carcinoma of the ovary, hypercalcemic type (SCCOHT) is a rare and aggressive malignant tumor with a poor prognosis, primarily affecting young women.
- Most patients with SCCOHT are diagnosed at an advanced stage and usually progress despite treatment.
- Regardless of tumor stage, most patients relapse and die of disease within a short period.
- Prognosis greatly depends on tumor stage, with detection of the disease at an earlier stage having a more favorable prognosis.
- There is no consensus on the optimal treatment but it is hypothesized that multi-agent chemotherapy may extend survival.
- A regimen that includes vinblastine, cisplatin, cyclophosphamide, bleomycin, adriamycin and etoposide (VPCBAE) has been reported with a long term survival.

Objective

- To describe the response rates and associated toxicities of patients with SCCOHT treated with the VPCBAE chemotherapy regimen.

Methods

- We performed a retrospective study of 8 patients evaluated at MD Anderson Cancer Center (MDACC) between May 2004 and April 2014 with the diagnosis of SCCOHT treated with VPCBAE.
- Medical records were reviewed for demographic information, pathologic findings, treatment regimens and outcomes.
- Institutional review board (I.R.B) approval was obtained – Protocol PA 14-0342

Treatment

- Vinblastine (6mg/m2 intravenous (IV) over 30 minutes on Day 1)
- Cisplatin (90 mg/m2 IV over 4 hours on Day 1)
- Cyclophosphamide (1000mg/m2 IV over 60 minutes on Day 2)
- Bleomycin (15 units/m2 IV over 24 hours on Day 2),
- Doxorubicin (45 mg/m2 IV over 30 minutes on Day 3)
- Etoposide (200 mg/m2 IV over 2 hours on Day 3)
- Pegfilgrastim 6 mg administered following each cycle.

Results

- The median age at diagnosis was 28 years (range, 21-41).
- Five patients had stage I disease (63%), two had stage III disease (25%) and one had stage IV disease (12%) (Figure 1).
- Seven patients (88%) underwent unilateral salpingo-oophorectomy as initial surgery.
- Two patients had second look cytoreduction surgery post-chemotherapy, both with non evidence of disease.
- Five patients (63%) had an optimal tumor reduction with no visible residual disease, all stage I disease.
- All patients completed 6 chemotherapy cycles, and 7 (88%) had no evidence of disease after chemotherapy.
- Grade 3 to 4 toxicities included anemia, neutropenia, febrile neutropenia, thrombocytopenia and nausea (Table 1).
- There were 6 hospitalizations, 5 treatment delays, 1 dose reduction, and 1 drug discontinuation (bleomycin due to grade 2 pulmonary fibrosis).
- Red cell and/or platelet transfusions were administered in 5 patients (83%).
- There were no treatment related deaths.
- Two patients (25%) died of disease and 2 patients (25%) are alive with disease.
- 4 patients (50%), all stage I disease, are alive without evidence of disease with a median follow up of 37.5 months (range, 5-60 months).

FIGURE 1: STAGING

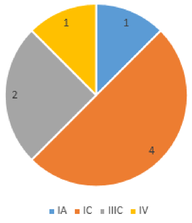

TABLE 1: GRADE 3/4 TOXICITY

TOXICITY	PERCENTAGE (%)
Anemia	83
Neutropenia	67
Febrile Neutropenia	33
Trombocytopenia	67
Nausea and vomiting	17

Conclusions

- The rarity of this disease has precluded the development of an established first-line chemotherapeutic regimen for this condition.
- To facilitate progression toward a more consistent standard of care for this rare gynecologic tumor, additional cases and case series should continue to be reported
- An accessible and frequently updated case registry may serve patients and their providers with the best hope in developing the most optimal treatment
- VPCBAE combination is effective in patients with SCCOHT and associated toxicities are tolerable

References

- Young RH, Oliva E, Scully RE. Small cell carcinoma of the ovary, hypercalcemic type. A clinicopathological analysis of 150 cases. Am J Surg Pathol. 1994 Nov;18(11):1102-16.
- Dickersin GR, Kline IW, Scully RE. Small cell carcinoma of the ovary with hypercalcemia: a report of eleven cases. Cancer. 1982;49:188–197.
- Senekjian, E.K., et al. Vinblastine, cisplatin, cyclophosphamide, bleomycin, doxorubicin, and etoposide in the treatment of small cell carcinoma of the ovary.Cancer 64 (6), 1183–1187 (1989).
- Tewari, K., et al. Advanced-stage small cell carcinoma of the ovary in pregnancy:long term survival after surgical debulking and multiagent chemotherapy. Gynecol Oncol. 66, 531–534 Feb (1997).
- Wallbillich JJ, Nick AM, Ramirez PT, et al. Vinblastine, cisplatin, cyclophosphamide, bleomycin, doxorubicin, and etoposide (VPCBAE) in the management of three patients with small-cell carcinoma of the ovary. Gynecol Oncol Case Rep. 2012 Feb 13;2(2):58-60.

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