

Refractory Choriocarcinoma: Complete Response With Oral Etoposide

CASE REPORT

A 33-year-old, married woman came to the hospital in 2015 with bleeding from the vagina and shortness of breath of 3 months' duration. Her obstetric history was as follows: the first pregnancy ended in a miscarriage, the second was a stillbirth, and the third was a molar pregnancy. She delivered a healthy girl after her fourth pregnancy 4 years ago. At presentation, her beta human chorionic gonadotropin (hCG) level was 450,000 mIU/mL, an ultrasound of the abdomen showed a 7 cm × 6 cm × 5 cm cystic mass in the endometrial cavity, a chest radiograph and a computed tomography scan of the chest showed multiple lung metastases, and magnetic resonance imaging of the brain showed hemorrhagic metastasis.

The patient was diagnosed with gestational trophoblastic tumor (GTT) and stage IV choriocarcinoma, with a WHO risk score of 20. A regimen of etoposide and cisplatin with etoposide, methotrexate, and dactinomycin (EMA-EP) was initiated, after which her hCG level declined in a logarithmic linear fashion, and the lung metastases resolved. However, after the seventh cycle of EMA-EP, her hCG level started rising. She was subsequently treated with combination chemotherapy comprising paclitaxel, ifosfamide, and cisplatin. Although the hCG level declined to a normal level after the second cycle, the patient developed life-threatening toxicity with grade IV neutropenic sepsis with liver and renal dysfunction. She refused further intravenous chemotherapy and was monitored without treatment. A month later, her hCG level was abnormal and a radiograph of her chest showed metastases.

The patient declined further intensive treatment, so she was prescribed oral etoposide 50 mg/day for 7 days every 3 to 4 weeks. After six cycles, she was in biochemical remission with a normal computed tomography scan of the chest and brain. She was treated with two more cycles of etoposide and she is currently well without any evidence of disease.

DISCUSSION

High-risk GTT is usually treated with combination chemotherapy.¹ However, approximately 20% of patients have a recurrence of disease after initial treatment. These patients are treated with second-line chemotherapy consisting of various combinations of drugs (eg, EMA-EP; vinblastine sulfate, ifosfamide, and cisplatin; paclitaxel, ifosfamide, and cisplatin; ifosfamide, carboplatin, and etoposide).^{2,3} The agents that have shown response in refractory GTT include ifosfamide,⁴ gemcitabine,⁵ and capecitabine.⁶ Ifosfamide alone or in combination (eg, combined etoposide, ifosfamide, and cisplatin) are active in patients with refractory disease.⁴ Gemcitabine plus cisplatin has shown activity in a patient who progressed after combination chemotherapy and EP-EMA.⁵ Capecitabine alone can produce complete and long-lasting remission in refractory GTT.⁶ If there is biochemical remission, then it could be consolidated with high-dose chemotherapy supported with peripheral blood stem cells.⁷

To the best of our knowledge, this is the first case of refractory GTT showing complete remission with oral etoposide without any significant toxicity. Etoposide, a topoisomerase II inhibitor, is a drug specific to cell-cycle phase and is active when given orally to maintain a cytotoxic trough level.⁸ It was not administered continuously in this patient because of previous toxicity; however, it could be considered to represent metronomic treatment. Metronomic chemotherapy has not been previously used in refractory choriocarcinoma. Systematic analysis has shown that metronomic chemotherapy is effective and safe in a broad range of tumors.⁹ The mechanism of action of metronomic chemotherapy is probably due to the effect on stromal components within a tumor. It had been thought that metronomic chemotherapy targeted angiogenesis,¹⁰ but recent data have shown that metronomic chemotherapy targets activated endothelial cells and decreases the chance of developing acquired drug resistance.¹¹

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In conclusion, oral etoposide is an active agent in the treatment of refractory choriocarcinoma. Further phase II studies are indicated.

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