PURE PRIMARY NONGESTATIONAL CHORIOCARCINOMA OF THE Ovary: A CASE REPORT

Shu-Chin Chien, Lim-Woh Koh¹*, Song-Nan Chow

Department of Obstetrics and Gynecology, College of Medicine and National Taiwan University Hospital, Taipei, and
¹Department of Obstetrics and Gynecology, Show Chwan Memorial Hospital, Changhua, Taiwan.

SUMMARY

Objective: Pure primary ovarian choriocarcinomas are very rare, and the nongestational type is even more uncommon. No definitive treatment protocol for this disease has been established due to its rarity. We report the case of a 21-year-old female with a pure primary nongestational choriocarcinoma of the ovary and her response to multidrug chemotherapy after surgery.

Case Report: The patient received seven courses of postoperative chemotherapy with etoposide, methotrexate, actinomycin-D, cyclophosphamide and vincristine (EMA/CO) after suboptimal cytoreductive surgery. Serum levels of the tumor marker β-human chorionic gonadotropin (β-hCG) dramatically decreased, and no evidence of recurrence was detected. Unfortunately, the patient died of sepsis 7 months after diagnosis.

Conclusions: Pure primary nongestational choriocarcinoma is believed to have a poor prognosis. EMA/CO proved to be useful in decreasing serum β-hCG levels in our patient, but more clinical experience is required in the management of this aggressive malignancy. In addition, it is necessary to closely monitor the side effects of the chemotherapy.

Key Words: choriocarcinoma, nongestational, ovary

Introduction

Choriocarcinomas of the ovary are relatively uncommon but aggressive germ-cell tumors. Most choriocarcinomas are gestational in origin and arise primarily from the uterus or Fallopian tubes, with those found in the ovary mainly being metastases from these sites [1]. Thus, nongestational choriocarcinoma of the ovary (NGCO) is exceedingly rare. Pure NGCOs account for 0.6% or less of all ovarian neoplasms [2]. The average age of NGCO patients is usually less than 20 years, but a few cases have occurred in patients more than 20 years old [3]. Although an accurate diagnosis of nongestational choriocarcinoma based on conventional histopathologic investigations is virtually impossible if the patient is of reproductive age, the diagnosis can be helped if the NGCO occurs as a component of a mixed germ-cell tumor or if it occurs in a virginal female [4]. Here, we present a case of pure primary NGCO of International Federation of Gynecology and Obstetrics (FIGO) stage IIC. The patient received suboptimal cytoreductive surgery and postoperative chemotherapy. Clinical characteristics and outcomes of reported cases in the literature are briefly analyzed.

Case Report

A 21-year-old female presented with a 1-month history of intermittent postprandial vomiting and weight loss. She denied any sexual intercourse in the past. One huge, irregular abdominal mass situated 2 cm below
the umbilicus was noted. On examination, it was found to be non-mobile. Sonographic evaluation showed a huge hypechoic mass with central hypoechochogenicity measuring about 12 × 10 × 10 cm, along with ascites in the abdomen. The serum concentration of CA125 was 918.35 U/mL (normal, < 35 U/mL) and of β-human chorionic gonadotropin (β-HCG) was 1,787,052.3 mIU/mL (normal, < 5 mIU/mL). Both carcinoembryonic antigen and α-fetoprotein were within normal limits. Chest roentgenography revealed mild left pleural effusion. Cytology of the pleural effusion showed no malignant cells. Computed tomography of the abdomen and pelvis showed a left adnexal heterogeneous mass consistent with ovarian cancer. Colonoscopy revealed intact mucosa in the entire colon.

After colon preparation, the patient underwent exploratory laparotomy under the impression of ovarian cancer. During laparotomy, about 1 L of bloody ascites was found. A fragile left ovarian tumor, measuring about 15 × 15 × 10 cm, was found occupying the cul-de-sac with invasion of the colon, rectum and posterior uterine wall. The right Fallopian tube, omentum, stomach and liver surface were grossly free of tumor invasion. Suboptimal cytoreductive surgery including left salpingo-oophorectomy and tumor excision was performed due to severe pelvic adhesion and massive bleeding during the dissection. The remaining main tumor, more than 2 cm in size, was densely adherent to the colon, rectum and posterior surface of the uterus. Microscopically, sections of the left ovary revealed a picture of choriocarcinoma. The tumor cells forming a syncytial pattern were large, hyperchromatic and pleomorphic. Hemorrhage and necrosis were also seen. Cytology of the ascites was positive for malignant cells. The patient recovered smoothly after the operation.

Under the impression of a pure primary NGCO of FIGO stage IIC, combination chemotherapy with EMA/CO (300 mg/m² methotrexate on day 1, 100 mg/m² etoposide and 0.5 mg/m² actinomycin-D on days 1–2, and 600 mg/m² cyclophosphamide and 1 mg/m² vincristine on day 8) was scheduled. Response to chemotherapy was reflected in the patient’s decreasing serum levels of β-HCG (Figure). Seven courses of chemotherapy were administered at irregular intervals due to poor compliance by the patient. However, left flank pain developed 1 week after the seventh course of chemotherapy and ultrasound revealed left hydronephrosis. Intravenous pyelography showed stenosis over the lower portion of the left ureter. Subsequently, a left double-J catheter was smoothly inserted by a urologist, and prophylactic antibiotics were prescribed after the procedure. Unfortunately, 5 days later, high fever and unconsciousness were noted. Empirc antibiotics were immediately prescribed for septic shock after infectious workup. Despite the aggressive treatment, she died the next day.

**Figure.** Decrease in β-human chorionic gonadotropin (β-HCG) levels after cytoreductive surgery and combination chemotherapy (C/T) with etoposide, methotrexate, actinomycin-D, cyclophosphamide and vincristine.
Discussion

Pure primary choriocarcinomas of the ovary are usually of gestational origin [5]. No distinctive ultrastructural or immunohistochemical differences have been reported between those of gestational and nongestational origin [2]. However, ascertainment of the origin of the tumor is important in selecting the most appropriate treatment regimen and offering an accurate prognosis [6]. Confirmation of the gestational type relies on detectable products of conception, while an NGCO is suggested by a history of virginity or inability to conceive [7]. Diagnosis of an NGCO is also favored by the presence of a choriocarcinoma admixed with other neoplastic germ-cell elements. However, human leukocyte antigen typing for paternal antigens and genetic analysis are by far the most reliable tools in differentiating between gestational and nongestational choriocarcinomas [1,4].

It is widely recognized that trophoblastic tumors respond well to chemotherapy. Multiple-drug regimens are proposed due to the possible occurrence of cross-resistance due to sequential introduction of drugs. EMA/CO to treat high-risk patients with gestational trophoblastic diseases was initially introduced by Bagshawe [8], and overall survival rates of more than 80% have been reported [9]. Two cases of advanced pure primary NGCOs treated with adjuvant EMA/CO chemotherapy have been reported [1,6]. They were both Japanese women who presented with a painful abdominal mass and multiple lung metastases. The diagnosis of pure NGCO was confirmed in both by DNA polymorphism analysis. The EMA/CO regimen consisted of 200 mg/m² etoposide, 300 mg/m² methotrexate, 1.0 mg actinomycin-D, 600 mg/m² cyclophosphamide and 1.0 mg/m² vincristine, but the interval was not available. Serum levels of β-HCG were elevated, given as 1,800 ng/mL in a 45-year-old woman (normal, < 0.2 ng/mL) and 110,000 IU/L in a 19-year-old virginal female (normal, < 5 IU/L). The first woman died of respiratory failure due to disease progression after four courses of chemotherapy following suboptimal cytoreductive surgery; no decrease in the β-HCG level was found. The second woman survived after multiple courses of chemotherapy following cytoreductive surgery, and the serum level of β-HCG returned to normal. Our patient showed dramatically decreased serum levels of β-HCG after surgery and chemotherapy but still died of septic shock. Hematologic toxicity, the main problem with this regimen, often requires dose reductions and treatment delays [10]. Successful treatment usually hinges on shortened intervals of chemotherapy, which overcome drug resistance. In addition, we need to pay more attention to preventing all kinds of infectious diseases during administration of the chemotherapy.

NGCO of the ovary is generally believed to have a poor outcome [11], and several authors base the clinical prognosis on surgical staging of the disease [4,12]. Long-term survival, unrelated to the size of the residual tumors, can be achieved after combination chemotherapy [3]. In spite of a clinical response to the chemotherapy in our case, it is still important to pay special attention to the hematologic toxicity of the EMA/CO regimen. Although the addition of granulocyte colony-stimulating factor to each cycle of this regimen may benefit patients by achieving a proper dose intensity without adverse effects [10], we need to emphasize the prevention of all infections as much as is possible during the course of chemotherapy. So far, the effectiveness of EMA/CO in treating this aggressive carcinoma has not been well documented, highlighting the need for greater clinical experience in this area.

References