

Pure choriocarcinoma of the ovary: a case report

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Pure ovarian choriocarcinomas are extremely rare and aggressive tumors which are gestational or non-gestational in origin. Due to the rarity of the tumor, there is a lack of information on the clinicopathologic features, diagnosis, and treatment. We report a case of a pure ovarian choriocarcinoma, likely of non-gestational origin, treated by cytoreductive surgery in combination with post-operative chemotherapy. The patient was free of disease after a 12-month follow-up.

Keywords: Choriocarcinoma, Non-gestational, Ovary

INTRODUCTION

Pure ovarian choriocarcinomas are extremely rare malignancies which are of gestational or non-gestational in origin. The gestational type may arise from an ectopic ovarian pregnancy or present as a metastasis from a uterine or tubal choriocarcinoma, while the non-gestational type is a rare germ cell tumor with trophoblastic differentiation. The estimated incidence of gestational ovarian choriocarcinomas is 1 in 369 million pregnancies [1]. Non-gestational ovarian choriocarcinomas account $\leq 0.6\%$ of all ovarian neoplasms; the pure type is extremely uncommon [2]. Due to the rarity of pure ovarian choriocarcinomas, information on the clinicopathologic features, diagnosis, and therapeutic options is limited. Herein we present a case of a pure ovarian choriocarcinoma, likely of non-gestational origin, and discuss the diagnosis and treatment together with a brief review of the literature.

CASE REPORT

A 48-year-old woman was admitted to our department with a 6-month history of irregular vaginal bleeding and a 1-month history of a palpable abdominal mass. She had a normal vaginal delivery at 26 years of age and had no recent history of normal pregnancies, molar gestations, or abortions. The physical examination revealed abdominal tenderness and a fixed mass arising from the pelvis to 3 cm below the umbilicus. Ultrasound showed a 15-cm solid mass posterior to the uterus, and consistent with an ovarian tumor. The serum levels of tumor markers, with normal values in parentheses, were as follows: β -human chorionic gonadotropin (hCG), 7,664.3 mIU/mL (<5.0); CA-125, 217.3 U/mL (<35); CA19-9, 18.6 U/mL (<30); alpha fetoprotein (AFP), 1.9 ng/mL (<20); and carcinoembryonic antigen (CEA), 2.5 ng/mL (<5). There was no evidence of metastasis to other organs.

After written informed consent was obtained, an exploratory laparotomy was undertaken for a suspected ovarian tumor. Intra-operatively, a dark-red, soft, friable, 18×15×14 cm mass had replaced the right ovary, which was densely adherent to the colon, rectum, appendix, and posterior surface of the uterus. The left ovary and fallopian tube were normal in appearance. There was no ascites within the peritoneal cavity. Peritoneal washings were obtained for cytology. Cytoreductive

Received Mar. 21, 2010, Revised May 2, 2010, Accepted May 6, 2010

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surgery, including a sub-extensive total hysterectomy, bilateral salpingo-oophorectomy, pelvic lymphadenectomy, para-aortic lymph node sampling, omentectomy, appendectomy, and peritoneal biopsies was performed. Optimal debulking was achieved with no macroscopic residual tumor.

Microscopically, the tumor was confirmed to be a pure choriocarcinoma with widespread necrosis (Fig. 1). The appendiceal serosa and peritoneum were identified with tumor invasion. The uterus, left ovary, left fallopian tube, omentum and all of the extirpated lymph nodes were negative for malignancy. Immunohistochemically, the tumor was positive for β -hCG (Fig. 2A) and weakly positive for placental-like alkaline phosphatase (PLAP) (Fig. 2B). Eighty percent of the tumor cells were strongly positive for Ki-67.

Post-operatively, the patient was treated with bleomycin, etoposide, and cisplatin (BEP) chemotherapy (etoposide [100 mg/m² on days 1 and 2], cisplatin [20 mg/m² on days 1-5], and bleomycin [30 mg on day 2]) every 28 days. The serum β -hCG level decreased to 193.5 mIU/mL 1 week after surgery and was within the normal range after 3 cycles of chemotherapy (Fig. 3). The patient did well after surgery and tolerated 6 cycles of chemotherapy without problems and without evidence of disease after a 12-month follow-up.

DISCUSSION

Pure ovarian choriocarcinomas are rare, but aggressive tu-

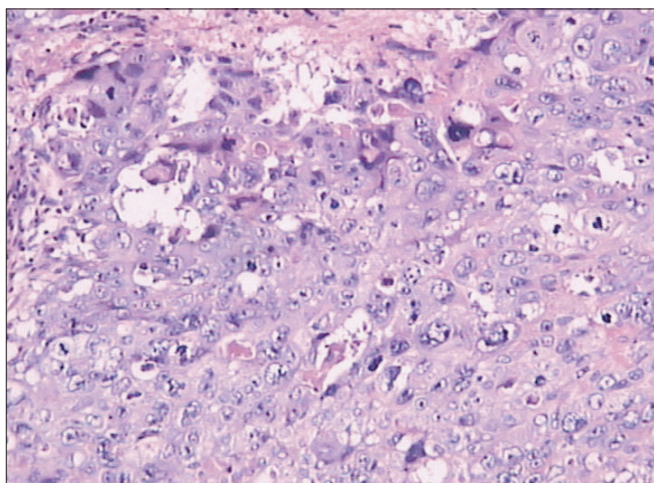


Fig. 1. Microscopic appearance of the tumor shows a pure choriocarcinoma with widespread necrosis (H&E, $\times 200$).

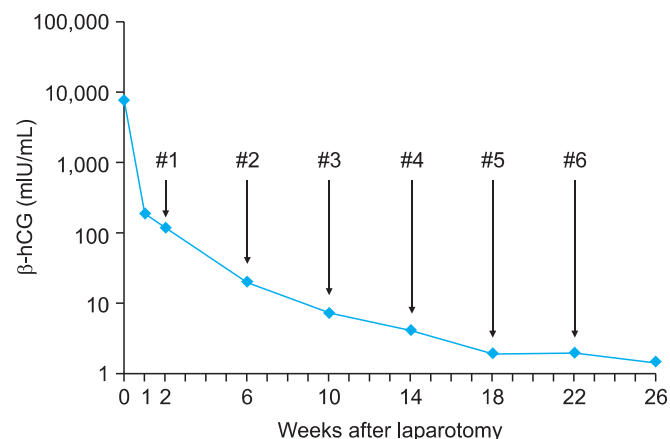


Fig. 3. Decrease in serum β -human chorionic gonadotropin (hCG) levels after surgery and combination chemotherapy with etoposide, cisplatin and bleomycin. *number indicates the cycle number of chemotherapy.

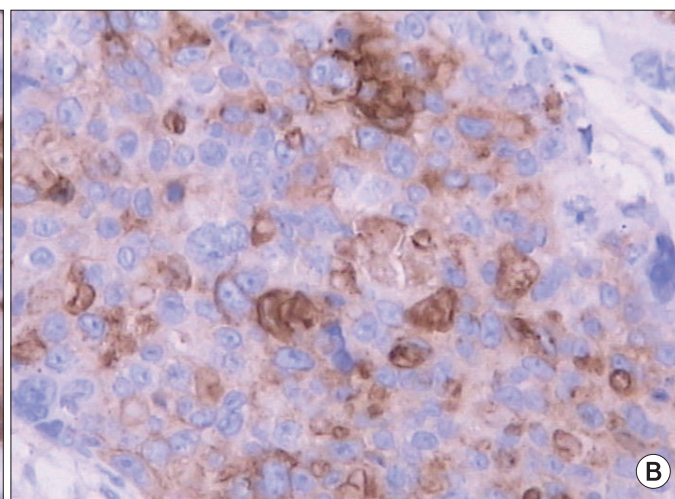
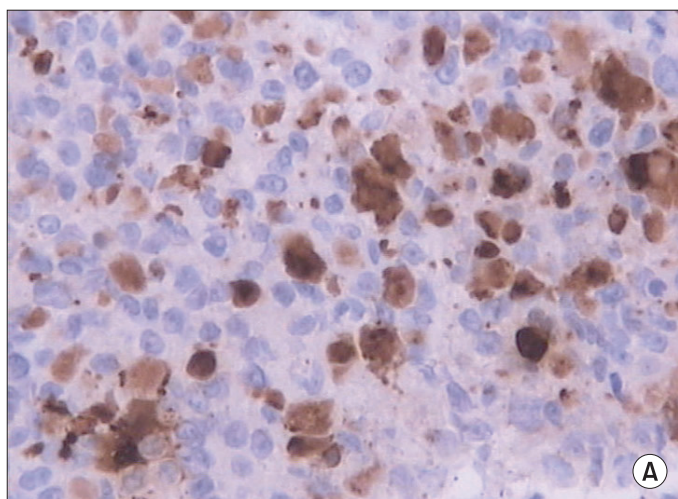


Fig. 2. Supporting immunohistochemistry shows that the tumor is positive for β -human chorionic gonadotropin (A) and weakly positive for placental-like alkaline phosphatase (B) ($\times 200$).

mors that pose diagnostic and therapeutic challenges. The pre-operative diagnosis of pure ovarian choriocarcinomas is very difficult, especially for patients in the reproductive age due to the non-specific clinical symptoms which can mimic other more common diseases. In the presence of an adnexal mass with an increased serum β -hCG level and irregular vaginal bleeding, pure ovarian choriocarcinomas in the childbearing age can be easily mistaken for an ectopic pregnancy pre-operatively [3,4]. Some authors have reported the pre-operative diagnosis of pure ovarian choriocarcinomas based on fine needle aspiration cytology [5] or imaging and biologic findings [6]. Confirmation of the diagnosis still relies on the histopathologic findings. Indeed, the presence of malignant cytotrophoblasts and syncytiotrophoblasts, immunohistochemical staining with β -hCG, and placental

lactogen are diagnostic. There are no distinctive ultrastructural or immunohistochemical differences between gestational and non-gestational choriocarcinomas. Thus, to distinguish a gestational ovarian choriocarcinoma from a pure non-gestational ovarian choriocarcinoma based on conventional histopathologic studies is not currently possible in the reproductive age group. Molecular genetic analysis is a reliable method for identifying the genetic origin of pure ovarian choriocarcinomas [7-10]. However, since such techniques are always expensive and not generally available in all medical centers, the application is limited. For this very reason, we could not perform molecular genetic analysis on the tumor from our patient. In light of the long duration (22 years) from the antecedent pregnancy, the absence of intrauterine trophoblastic disease, and the relatively low β -hCG level, we

Table 1. Pure ovarian choriocarcinoma: summary of cases

Authors	Age	Gestational or non-gestational	β -hCG	Surgery	Chemotherapy	Outcome
Shin et al. [12], 1994	45	Non-gestational	132,005	TAH, BSO	MAC	1 yr NED
Byeun et al. [13], 1995	28	Non-gestational	13,378	RSO	EMA/CO	1 yr NED
Lorigan et al. [14], 1996	41	Gestational	151,500	TAH, BSO, omentectomy	BEP, IE	3 mo NED
Kim et al. [15], 1997	16	Non-gestational	565,000	TAH, BSO	MAC	Died during chemotherapy
Namba et al. [16], 2003	37	Gestational	990,000	RSO,	MAC	NED
Tsujioka et al. [7] 2003	19	Non-gestational	110,000	LSO, partial omentectomy, biopsy of right ovary	EMA/CO	NED
Chien et al. [17], 2004	21	Non-gestational	1,787,052.30	LSO, tumor excision	EMA/CO	Died of sepsis 7 mo after diagnosis
Balat et al. [3], 2004	24	Non-gestational	8,968 (when admitted) 45,701 (20 days after the first operation)	TAH, BSO, infracolic omentectomy, pelvic lymphadenectomy	BEP	Died of disease after the 1 st cycle of chemotherapy
Bazot et al. [6], 2004	38	Non-gestational	2,460,000	TAH, BSO	Yes, details NS	7 yr NED
Koo et al. [9], 2006	33	Non-gestational	185,000	AH, BSO, omentectomy, pelvic lymphadenectomy	MAC	NED
Gerson et al. [18], 2007	33	Gestational	564,000	TAH, RSO, LS, splenectomy	EMA/CO	1 yr NED
Yamamoto et al. [10], 2007	19	Non-gestational	206,949	LO	EMA/CO	12 mo NED
Mood et al. [19], 2009	31	Gestational	More than 1000	RSO	EMA/CE	7 yr NED
Mood et al. [19], 2009	32	Gestational	5,500	TAH, BSO, tumor debulking and infracolic omentectomy	BEP, EMA/CE	5 yr NED
Mishra and Crasta [20], 2008	25	Non-gestational	More than 1,000,000	TAH, BSO, omental biopsy	Yes, one cycle, details NS	Lost follow-up
Park et al. [21], 2009	55	Non-gestational	64,838	TAH, BSO, multiple biopsies	BEP	20 mo NED
Gon et al. [22], 2010	21	Non-gestational	279,000	RSO	NS	NS

hCG, human chorionic gonadotropin; TAH, total abdominal hysterectomy; R, right; L, left; B, bilateral; S, salpingectomy; O, oophorectomy; MAC, methotrexate, actinomycin-D, cyclophosphamide; EMA/CO, etoposide, methotrexate, actinomycin-D, cyclophosphamide, vincristine; BEP, bleomycin, etoposide, cisplatin; IE, ifosfamide, etoposide; EMA/CE, etoposide, methotrexate, actinomycin-D, cisplatin, etoposide; NED, no evidence of disease; NS, not stated.

suggest that our patient had a pure non-gestational ovarian choriocarcinoma.

We have reviewed the previously reported cases of pure ovarian choriocarcinoma and summarized the details of these cases including β -hCG level, operation procedures, chemotherapy and outcome. Since Goswami et al. [11] made a detailed summary and analysis about 30 cases of pure non-gestational choriocarcinoma in 2001, we only present cases not mentioned by Goswami et al. [11] or reported after Goswami's study in our article (Table 1). According to the previous reports, it seems that pure ovarian choriocarcinoma responds well to the combination of surgical ablation and post-operative chemotherapy. To date, no definitive treatment modality has been established for pure ovarian choriocarcinomas due to the low incidence. Thus, pure ovarian choriocarcinomas are generally treated by the same protocols used for ovarian germ-cell tumors and gestational trophoblastic disease. In the current case, the treatment included cytoreductive surgery followed by post-operative chemotherapy. Optimal cytoreductive surgery was indispensable in our patient, as demonstrated by the dramatic decline in the serum β -hCG level post-operatively. There is no consensus on the optimal chemotherapy following surgery. Non-gestational ovarian choriocarcinoma has been found to have a worse prognosis and requires more aggressive chemotherapy compared with gestational ovarian choriocarcinoma. Gestational choriocarcinoma usually responds well to methotrexate-based chemotherapy; however, non-gestational choriocarcinoma may be resistant to this therapy [11]. Because non-gestational choriocarcinoma is considered as a germ cell tumor differentiating to trophoblastic components, a germ cell tumor treatment protocol may be effective [3,21]. BEP chemotherapy is the current regimen for germ cell tumors of the ovary [23]. Thus, our patient underwent BEP chemotherapy for a presumed primary pure non-gestational choriocarcinoma. The patient had a good response to the BEP regimen with a satisfactory decrease in the serum β -hCG level. There was no evidence of recurrence or metastasis after a 12-month follow-up. Our case provides evidence that cytoreductive surgery in combination with post-operative chemotherapy may be an effective therapeutic strategy for pure ovarian choriocarcinomas. Considering that pure ovarian choriocarcinoma is aggressive with a high risk of metastasis, close follow-up with serum β -hCG and imaging examinations is essential.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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