

Fertility Preservation with Treatment of Immature Teratoma of the Ovary

Chia-Hui Chen^{1,2}, Ming-Jie Yang^{1,2}, Ming-Huei Cheng^{1,2}, Ming-Shyen Yen^{1,2},
Chiung-Ru Lai^{2,3}, Peng-Hui Wang^{1,2*}

Departments of¹Obstetrics and Gynecology and³Pathology, Taipei Veterans General Hospital, and²National Yang-Ming University School of Medicine, Taipei, Taiwan, R.O.C.

Fertility preservation for a patient with advanced immature teratoma of the ovary is reported. The patient, a 29-year-old woman, delivered a healthy baby after having had ovarian immature teratoma, grade 3, uncertain stage, at 13 years of age. She was initially treated with unilateral salpingo-oophorectomy and a contralateral wedge resection for tumor invasion, followed by a 6-course cisplatin + vinblastine + bleomycin regimen, a second operation, and an additional 6-course etoposide and cisplatin regimen with complete remission. The patient delivered a healthy baby 16 years after the initial treatment. Based on this successful case, intensive fertility-preserving surgery followed by chemotherapy, even in advanced-stage immature teratomas of the ovary, may be effective in preserving the reproductive function of women with malignant immature teratomas of the ovary. [*J Chin Med Assoc* 2007;70(5):218–221]

Key Words: fertility-preserving surgery, immature teratoma, ovary

Introduction

Pure immature teratoma is the second most common germ cell malignancy of all ovarian cancers; it represents <1%.^{1–4} However, in women younger than 20 years, it amounts to 10–20% of all ovarian malignancies, and contributes 30% of the ovarian cancer mortalities in this age group.⁵ About 50% of pure immature teratomas of the ovary occur in women between the ages of 10 and 20 years; hence, treatment to preserve their future fertility should be considered because the majority of ovarian germ cell tumors (OGCT) are curable with the aid of conservative surgery and follow-up combination chemotherapy.^{6,7} The first report of a successful pregnancy following conservative surgery and chemotherapy for advanced-stage immature teratoma appeared in 1989.⁸ With further advanced development of chemotherapy and more understanding of the disease course of ovarian immature teratoma, fertility-preserving surgery followed by multiagent chemotherapy has become a choice in patients with immature teratoma of the ovary. The following case report describes a

woman with advanced immature teratoma of the ovary that had been treated with intensive conservative surgery and multiagent chemotherapy, who subsequently successfully delivered a baby.

Case Report

A 29-year-old woman, who had been diagnosed with and treated for ovarian tumor at 13 years of age, delivered a healthy baby. The initial treatment was unilateral salpingo-oophorectomy and wedge resection of the contralateral ovary. The final pathology showed ovarian immature teratoma, grade 3. The patient then received 6-course multiagent chemotherapy, including 3-day cisplatin 20 mg/m² + vinblastine 1.5 mg/m² + bleomycin 10 mg/m² (PVB), because of the presence of the immature teratoma, grade 3, uncertain stage (suspicious initial stage of at least International Federation of Gynecology and Obstetrics [FIGO] stage Ic) and incomplete staging surgery. Laparotomy was performed after the initial 6-course chemotherapy

*Correspondence to: Dr Peng-Hui Wang, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, R.O.C.
E-mail: phwang@vghtpe.gov.tw • Received: September 19, 2006 • Accepted: March 26, 2007

because imaging study showed residual tumors within the *cul-de-sac* and abdominal cavity. Tumor excision and complete staging surgery with fertility-preservation were performed. Pathology showed the residual tumor within the *cul-de-sac* to be an immature teratoma, grade 1, while the others, such as multiple sites of the random biopsies, were negative. Then, additional 6-course chemotherapy with a 3-day etoposide 100 mg/m² and cisplatin 20 mg/m² (EP) regimen was prescribed.

Menstruation occurred 1 year after complete therapy (at the age of 15 years). No menstruation disorder was recorded during the follow-up. The patient married at the age of 26 and underwent 3 cycles of clomiphene for ovarian induction due to 2-year subfertility but in vain. However, she became pregnant spontaneously without the assistance of a reproductive technique and delivered a healthy baby at the age of 29 years.

Discussion

Immature teratomas are solid tumors containing immature or embryonic tissues and account for approximately 20% of all malignant OGCT.¹⁻³ Immature neuroepithelium is the predominant immature tissue found and can be used for tumor grading, such as grades 1, 2 and 3, when immature neuroepithelium occupies 0 or 1, ≤ 3 , or ≥ 4 low-power fields (40 \times) per section, respectively.¹

The prognosis of immature teratomas is governed by grade and stage.^{9,10} For example, cases of grade 1 in stage I might have up to a 94% survival rate, whereas cases of grade 2 or 3 in stage I might drop to an 82% chance of survival.⁹ Grade also contributes to the recurrence rate, with higher grades having a higher recurrence rate.¹⁰

Treatment is dependent on the age of the patient and the specific tumor type. Although surgery is the most common form of treatment for immature teratoma, extensively destructive surgery, including total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, lymph node sampling and appendectomy is seldom considered for immature teratoma, except for those patients who have completed their fertility. Therefore, fertility-preserving surgery is the treatment of choice for younger women, because postoperative adjuvant chemotherapy has dramatically improved the prognosis of immature teratoma. In the present case, we further confirmed this concept.

Four controversial issues brought to our attention in this case should be mentioned: (1) the best

combination chemotherapy regimen for malignant OGCT; (2) the role of second-look operation or secondary operation for malignant OGCT; (3) the consideration of ovarian function and future fertility in cancer patients; and (4) the safety of chemotherapy.

One of the great triumphs in the field of gynecologic oncology has been the attainment of cure in the vast majority of young patients with malignant OGCT.¹¹ Smith and Rutledge¹² had begun using the combination of vincristine, dactinomycin, and cyclophosphamide (VAC), with cure rates therefore unimaginable. The demise of the VAC regimen as standard therapy, however, was essentially sealed by the introduction of PVB,¹³ and subsequent reports that revealed that VAC was very active for patients with stage I disease, but rather ineffective for those with advanced-stage tumors.¹⁴ Culine et al¹⁵ added etoposide to VPB and showed promising results in malignant OGCT; however, toxicity was very high. Because equal efficacy and less toxicity favored the combination of bleomycin, etoposide and cisplatin (BEP) as standard treatment for malignant OGCT in the 1990s, subsequent reports further confirmed the BEP regimen as first-line therapy for OGCT.¹⁶⁻¹⁹ To further decrease the toxicity of the BEP regimen, the following modifications were reported in the literature, including carboplatin used as a replacement for cisplatin in the BEP regimen and a 3-day modification protocol for the BEP regimen.^{20,21} Taken together, a postoperative 3-cycle or 4-cycle 3-day BEP (standard-dose cisplatin) regimen should be administered in patients with ovarian immature teratoma after fertility-preserving surgery.^{22,23}

Is there a place for second-look operation in OGCT? In our case, due to the initial incomplete surgery, the uncertain stage, teratoma component and of most importance, the visible "residual" tumor in the imaging study, all of which fulfilled the suggested criteria for second-look operation in OGCT in the literature,^{24,25} laparotomy might have been a better choice. The following conditions, including an incompletely resected tumor that contains a teratoma,²⁴ or persistent radiologic abnormalities along with normal serum tumor markers at the end of chemotherapy,²⁵ could lead to a consideration of second-look laparotomy or re-exploratory laparotomy.

Since patients with OGCT are young, what is the effect of chemotherapy on ovarian function or future fertility? A recent review addressed various views to expand possibilities for fertility preservation in cancer patients,²⁶ including (1) the number of women who become infertile after cancer treatment is unknown; (2) infertility can affect patients with any cancer treated with radiation therapy or chemotherapy, but the greatest

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