Survival and reproductive function after treatment of immature ovarian teratoma

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Summary

We conducted a clinical and pathologic review of nine patients with immature ovarian teratoma. The histologic grade of the tumor seemed to be a reliable indicator of prognosis. Low stage and low grade immature ovarian teratomas have an excellent prognosis. Platinum-based chemotherapy has been confirmed to be effective in the management of patients with ovarian germ cell tumors. Low grade pure ovarian immature teratoma is a potentially curable disease and a fertility-sparing surgical approach is possible.

Key words: Reproductive function; Immature ovarian teratoma.

Introduction

The pure immature teratoma accounts for fewer than 1.3% of all ovarian cancers, but it is the second most common germ-cell malignancy. This lesion represents 10-20% of all ovarian malignancies seen in women younger than 20 years of age and 30% of the deaths from ovarian cancer in this age group. About 50% of pure immature teratomas of the ovary occur in women between the ages of 10 and 20 years, and they rarely occur in postmenopausal women [1, 2]. Ovarian teratomas are neoplasms composed of three germ-cell layers. They may be classified as mature when all elements consist of mature adult tissue; or immature when varied amounts of immature tissues that resemble fetal tissue, often neuroectodermal, are present [3].

The prognosis for treatment of this tumor has improved recently. It is important to increase the cure rate while maintaining childbearing capacity. It has become essential to solve this problem through the proper combination of surgery and chemotherapy [1].

The aim of this study was to evaluate the outcome and reproductive function of nine young women treated for immature ovarian teratoma in our hospital since 1982.

Materials and Methods

We reviewed the tissue registry file at our hospital which disclosed nine cases of immature ovarian teratoma between 1982 and 1999. All tumors were graded according to the system proposed by Thrulbeck and Scully [4] and modified by Norris *et al.* [5]. Only pure immature teratomas were included in the analysis.

All patients underwent some form of surgical procedure at presentation. Initial work-up for all patients included a complete medical and obstetrics history, physical examinationed and complete blood count including renal and hepatic biochemical profile. Imaging studies included chest X-ray, computerized tomography scan and/or ultrasound of the abdomen and the pelvis. Tumors were staged according to the International Federation of Gynecology and Obstetrics (FIGO) classification [1].

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Second-look laparotomy was performed on all patients after completion of systemic treatment. Patients were followed-up with clinical and radiologic assessment.

Results

The ages of the nine patients ranged from 15 to 40 years (median age, 22.55 years) (Table 1). All patients were symptomatic at the time of initial examination and had the initial symptom of abdominal or pelvic pain. Some had abdominal fullness, dysuria and back pain, constipation, and an abdominal mass. Two women presented with menstrual irregularities.

Six presented with FIGO surgical stage I disease, three had pelvic metastases (stage II). Postoperative systemic chemotherapy was administered to seven women, including those with high-risk profile immature teratomas. The primary chemotherapeutic regimens included vincristine, actinomycin-d, and cyclophosphamide (VAC); or bleomycin, etopside and cisplatin (BEP).

Four patients were treated with a non-platinum-based chemotherapy regimen and three patients received platinum-based chemotherapy. After chemotherapy all patients underwent second-look laparotomy or laparoscopy. We observed recurrences in five of them.

Four women are alive without evidence of disease. Three of the nine patients had one pregnancy subsequent to chemotherapy and two had healthy children without any complications.

Pathologically the dimension of the teratomas ranged from 9 to 23 cm. The median tumor diameter was 15 cm. Typically, the immature teratomas were encapsulated and lobulated and contained both solid and cystic areas. The solid areas were firm and grayish-white, pink or tan. Cystic areas contained bloody fluid, gelatinous material, or sebaceous debris and hair. The external surfaces of the tumors were usually smooth and shiny.

Histologically, elements of all germ cell layers were represented. Gut epithelium, respiratory epithelium, squa-

mous epithelium, glial tissue, choroid plexus, bone and cartilage were common mature components. Immature tissues were usually neuroepithelial, including neurotubules and neuroepithelial rosettes. Occasionally, undifferentiated mesenchyme and immature cartilage were seen. The histologic grade distribution among them included grade I (n=4), grade II (n=3) and grade III (n=2).

Five patients had metastatic lesions. One was composed only of mature glial tissues - that is, gliomatosis peritonei and the others were composed of grade 2 and 3 immature ovarian teratoma (Table 1).

Discussion

Immature ovarian teratoma is a neoplasm of young women [6]. In our series, the median age was similar to that reported previously.

The histologic grade of immature ovarian teratoma is an important and reliable indicator of prognosis [3]. In a review of 150 cases from the literature, Gallion *et al.* [7] reported a 2-year survival of 81%, 51%, and 33% for patients with grades 1, 2 and 3 disease, respectively. In a series of 58 patients described by Norris *et al.* [5], survival was 82% in patients who had grade 1 tumors, 63% in those who had grade 2, and 30% in those with grade 3. In the study of Norris *et al.* [5], size and stage of the teratomas were correlated to survival and the grade of the primary tumor best determined the likelihood of metastatic spread while the grade of metastasis was correlated to outcome. Also, they observed progression of disease in 18% of patients with grade 1 disease, in 37% with grade 2, and in 70% of patients with grade 3 disease. Our findings support this trend in grade-related survival.

Thorough surgical staging to confirm apparent stage I, grade I immature teratomas is crucial because it might

Table 1. — *Clinical, pathologic, and therapeutic profile of nine patients with immature ovarian teratoma.*

Case	Age	Chief complaint	Primary tumor grade	Primary tumor stage (FIGO)	Primary tumor size (cm)*	Treatment	Recurrent or metastatic lesions	Status
1	21	Pelvic mass, Abdominal pain	1	IA	12	LSO, partial omentectomy	Gliomasis peritonei	Alive and well at 69 mos, had an abortion at 63 mo.
2	40	Back pain, Abdominal pain, Pelvic mass, menstrual irregularities	2	IIC	17	TAH, BSO, omentectomy, excision of presacral mass initially; VAC	Grade 2 metastases at 14 mos.	Deat at 36 mo.
3	25	Pelvic mass, dysuria	2	IA	21	LSO, VAC	Grade 2 distant and intra-abdominal teratoma metastases at 10 mos.	Dead at 40 mo.
4	24	Pelvic mass, Abdominal pain	3	IIB	14	TAH, BSO, VAC	Widespread grade 3 intra-abdominal metastases at 10 mos.	Dead at 22 mo.
5	19	Pelvic mass, Abdominal pain	1	IA	15	BSO, omentectomy BEP	–	Alive and well at 76 mo.
6	22	Abdominal pain, menstrual irregularities	1	IA	9	LSO, VAC	–	Alive and well at 95 mos. had a child at 41 mo.
7	15	Abdominal mass and pain	3	IIA	23	TAH, BSO, BEP	–	Alive and well at 38 mo.
8	20	Abdominal pain	1	IA	10	RSO	–	Alive and well at 67 mo. had child at 50 mo.
9	17	Abdominal pain, constipation	2	IA	17	LSO, omentectomy, BEP	Grade 2 intra-abdominal metastases at 10 mos. Second operation TAH, RSO	Alive and well at 82 mo.

BSO = Bilateral salpingo-oophorectomy; FIGO = International Federation of Gynecology and LSO = Left salpingo-oophorectomy; RSO = Right salpingo-oophorectomy; TAH = Total abdominal hysterectomy; BSO = Bilateral salpingo-oophorectomy; VAC = Vincristine, actinomycin, cyclophosphamide; BEP = Bleomycin, etoposide, cisplatin.
* = The greatest dimension of the primary teratoma

identify women who can safely avoid postoperative chemotherapy. Higher-stage, higher-grade immature teratomas need postoperative systemic treatment [1].

Nielsen *et al.* [3] reported a favorable prognosis of patients with grade 0 metastatic growth in their series. Norris *et al.* [5] described six patients with ovarian teratoma and grade 0 metastatic lesions. In a report by Nogales *et al.*, [8] five patients had grade 0 metastatic lesions in association with primary tumors of grade 1 and 2. All five patients had a benign clinical course. Truong *et al.* [9] reported cases in which gliomatosis peritonei in a high-grade teratoma was associated with a better-than-expected prognosis. In our series, one patient had grade 0 metastatic growth, but she had excellent survival.

Combination chemotherapy, primarily the vincristine, actinomycine-D, and cyclophosphamide (VAC) regimen, became widely used as adjunctive management of ovarian germ cell malignancies [10]. Gershenson *et al.* [11] reviewed 41 patients with pure immature teratoma of the ovary. Twenty-one patients received combination VAC chemotherapy postoperatively, and 18 patients were cured. Slayton *et al.* [12] analyzed 76 patients treated with VAC chemotherapy postoperatively. Of 28 patients with grade 2 and 3 immature teratoma, five (18%) failed during or after treatment with VAC, including one of 20 patients with completely resected immature teratoma (recurrent disease) and four of eight patients with incompletely resected immature teratoma. Furthermore, in their analysis, unilateral salpingo-oophorectomy appeared to be just as effective as TAH/BSO in patients with stage I disease, thereby preserving fertility.

With the evolution of modern platinum-based chemotherapy for ovarian germ cell malignancies, most women will be able to retain their menstrual and reproductive potential after treatment. The efficacy of chemotherapy now allows conservative surgery (ie, unilateral salpingo-oophorectomy), with potential preservation of fertility. Modern treatment emphasizes shorter courses of chemotherapy and avoidance of prolonged exposure to alkylating agents, which characterized older treatment regimens and led to substantial ovarian toxicity. Women who retain one ovary might avoid sterility and premature ovarian failure, and the attendant risks of accelerated cardiovascular disease and osteoporosis [10]. In the series of Tewari *et al.* of 44 women treated with vinblastin, bleomycin, and cisplatin or bleomycin, etoposide, and cisplatin, only four patients did not go into remission [10]. Mitchell *et al.* [13] reported that platinum-based chemotherapy has been confirmed to be effective in the management of patients with dysgerminomatous and nondysgerminamatous ovarian germ cell tumors.

Cure without function loss should represent one of the highest goals for each physician and the ideal treatment for each patient. Effective chemotherapy and surgery make the survival of the majority of women with recurrence of germ cell tumors possible irrespective of conservative or radical surgery [14]. Gershenson [15] has reported that 33 of 44 women (83%) had regular menstrual cycles at follow-up after chemotherapy for ovarian germ cell tumors. Mitchell *et al.* [13] reported that, 24 of 26 women assessable for fertility subsequently recommenced regular menstrual function, and 11 patients had pregnancies. Ezzat *et al.* [16] described 44 women who retained their fertility after treatment for germ cell tumors, and they reported that no abnormality was observed in 16 pregnancies. In our study, the fertility of treated women with low grade and low stage immature teratoma support these results.

This study confirms that stage I and grade I immature teratoma have an excellent prognosis. Low grade pure ovarian immature teratoma is a potentially curable disease and a fertility-sparing surgical approach is possible.

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