Juvenile granulosa cell ovarian tumor: clinicopathological evaluation of ten patients

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Abstract

Objective: We aimed to analyze the clinical characteristics and management of ten patients who were diagnosed with juvenile granulosa cell ovarian tumor (JGCOT).

Material and Methods: The records of 10 patients diagnosed with JGCOT between April 1995 and January 2014 in the Gynecological Oncology Clinic of our institution were retrospectively evaluated.

Results: The median age of the patients was 21.5 years (range; 13-36). Nine patients had stage IA disease and one had stage IC disease according to the International Federation of Gynecology and Obstetrics (FIGO) criteria. Five patients underwent pelvic and para-aortic lymph node dissection. None of them had lymph node involvement. All but two patients underwent unilateral salpingo-oophorectomy. One of the other two patients had cystectomy and the other had total abdominal hysterectomy and bilateral salpingo-oophorectomy. Three patients had adjuvant therapy after surgery. Two of these patients took chemotherapy and the other took radiotherapy. Four of the five patients who desired pregnancy achieved five term pregnancies. The median follow-up time of the patients was 58 months (range; 3-113). No recurrence was observed in the follow up period.

Conclusion: JGCOT generally occurs during childhood. The primary management of JGCOT is through surgery. The role of adjuvant therapy is controversial. Because survival is long at early stages and most of the patients are young, fertility sparing surgery could be safely suggested to these patients. (J Turk Ger Gynecol Assoc 2015; 16: 32-4)

Keywords: Juvenile granulosa cell tumor, ovary, adjuvant therapy, fertility sparing surgery

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Introduction

Ovarian granulosa cell tumors are classified into two groups based on their clinico-pathological characteristics; juvenile and adult type. Juvenile granulosa cell ovarian tumor (JGCOT) was first described by Scully in 1977 (1). JGCOT comprises 5% of all granulosa cell neoplasms. Generally, it occurs in premenarchal girls or young women (2, 3). However, it is seen in a wide age range, in a 10 month old baby as well as in a 67 year old woman (3, 4). In contrast to adult granulosa cell tumor, JGCOT has a high mitotic index and more aggressive tumor growth via via this character (5). Microscopically it is seen as diffuse and regularly distributed neoplastic cells with a wide cytoplasm and pleomorphic hyperchromatic nucleus. Follicle formation, in various sizes and shapes, is important in JGCOT. Call-Exner bodies are infrequently seen in JGCOT in contrast to the adult type (3).

The most common finding on physical examination is a palpable mass (4). Generally, the prognosis is good. Surgical stage is the most important prognostic factor and the prognosis is much more aggressive in the advanced stage than in the adult type (5, 6). Although a standard adjuvant therapy for the advanced stage or recurrent disease is not well established because of the rarity of JGCOT, adjuvant chemotherapy is recommended in the advanced stage.

Material and Methods

The cases of ovarian granulosa cell tumors that were diagnosed between April 1995 and January 2014 in gynecologic oncology department were retrospectively reviewed. Among these patients, those with JGCOT were selected. Clinicopathological characteristics including age, symptoms, primary tumor location, stage, surgery and adjuvant therapy were collected from an electronic database and medical records. The pathological evaluation was made in our pathology department. The International Federation of Gynecology and Obstetrics (FIGO) 1988 classification was used for staging.

Results

During the study period, 143 patients were diagnosed with a granulosa cell tumor, and 10 (7%) of them with JGCOT. The

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Table 1. Characteristics of the patients

Patient no:	Age	Stage	Ascites (cc)	Tumor diameter (mm)	Surgery	Adjuvant therapy	Live birth after treatment	Follow-up (month)
1	26	1A	-	110	Cystectomy	-		23
2	36	1A	-	110	TAH+BSO+BPPLND+Om	-		76
3	22	1A	100	250	USO+BPPLND+Om	-		3
4	18	1A	5000	400	USO	-	1	113
5	25	1A	-	130	USO+BPPLND+Om	-	2	29
6	20	1A	50	180	USO+BPPLND+Om+App	-		63
7	17	1A	-	150	USO+Om	6×VAC		3
8	21	1C	-	120	USO+BPPLND+Om	4×BEP	1	67
9	13	1A	200	250	USO+Om+App	RT		53
10	24	1A	-	60	USO	-	1	79

TAH: total abdominal hysterectomy; BSO: bilateral salpingo-oophorectomy; USO: unilateral salpingo-oophorectomy; BPPLND: bilateral pelvic para-aortic lymph node dissection; Om: omentectomy; App: appendectomy; RT: radiotherapy; BEP: bleomycin, etoposide, cisplatin; VAC: vincristine, adriamycin, cyclophosphamide

median age of the patients was 21.5 years (range; 13–36). The presenting symptom was bloating in five patients, abdominal pain in four, and menometrorrhagia in one. CA-125 was found in five patients and its level was normal in four of them (<35 U/mL). In a patient whose CA-125 level was 74 U/mL, cyst rupture was noted. Nine of the patients had stage IA, and one had stage IC disease. The median tumor diameter was 140 mm (range; 60-400). The tumor was resected completely in all patients. The tumor was on the right side in five patients and on the left side in the other five. Ascites was found in four patients. In patients who had stage IC disease, the cyst had ruptured preoperatively, and cytology was negative. Five of the patients underwent pelvic and para-aortic lymph node dissection. The median removed lymph node count was 54 in patients who had lymphadenectomy (range; 7-94). None of the patients had lymph node involvement. One patient was treated with total abdominal hysterectomy and bilateral salpingo-oophorectomy in another center (patient no #2). The pathology slides of this patient were re-reviewed in our pathology department, and surgical staging was performed after the diagnosis was confirmed. One patient underwent cystectomy, and eight had unilateral salpingo-oophorectomy. Infracolic omentectomy was performed in six patients, partial omentectomy in one, and appendectomy in two. No tumor was found in the omentum in these patients. Frozen/section result was available in five patients. It was diagnostic for JGCOT in two of them. Sex-cord stromal tumor was diagnosed, but the histological subtype could not be specified in two of them and lymphoma was suspected in one. Three patients underwent adjuvant therapy, two had chemotherapy, and one had radiotherapy. The chemotherapy regimen was bleomycin, etoposide, cisplatin (BEP) for four cycles in one patient and vincristine, adriamycin, cyclophosphamide (VAC) for six cycles in another.

The median follow-up duration was 58 months (range; 3-113). Recurrence did not occur in any patient. Five pregnancies occurred in 4 of the 5 patients who desired childbearing, and all these pregnancies resulted in term birth. Only one patient could not achieve pregnancy despite desiring pregnancy. This patient had stage IA disease. One of the patients who achieved pregnancy and gave birth had stage IC disease and was treated with BEP chemotherapy for four cycles (patient no : 8) (Table 1).

Discussion

JGCOT is an ovarian tumor that occurs in premenarchal girls and young women, and the mean age at diagnosis is 13 years (4). Generally, case series in literature were reported from pediatrics. In our present study, which was presented from a gynecologic oncology clinic, the mean age was 22 years. Because it is frequently seen in premenarchal girls, puberty praecox, clitoral hypertrophy, and hair in pubic and axillary areas are frequent symptoms. The most common symptoms are abdominal pain and distension (4, 5). In our study, the main symptoms were bloating and abdominal pain.

Generally, JGCOT is diagnosed in stage IA as in our study. Its management depends on the age of the patient and dissemination of the disease. However, there is no standard protocol for adjuvant chemotherapy because of the rarity of the disease. Surgery is the primary standard initial treatment. A worse prognosis and early recurrence should be expected in the case of an advanced disease (5). Unilateral salpingo-oophorectomy is the treatment for children and women in the reproductive age with stage IA disease (7). Although there are no prospective, controlled, and randomized studies, fertility sparing surgery is recommended because the disease is commonly unilateral. In addition, wedge biopsy from the contralateral ovary and chemotherapy are not recommended (8). Because lymph node metastasis is rarely observed in patients with sex-cord stromal tumor, pelvic and para-aortic lymphadenectomy may not be included in the staging surgery of these patients. Five patients underwent pelvic and para-aortic lymph node dissection. None of the patients had lymph node involvement (9). In our series,

all cases had stage I disease, and no recurrence was noted in the follow-up period. Calaminus et al. (5) reported 2 recurrences out of 20 stage IA cases in their series. These two patients had a high mitotic activity, and one of them also underwent suboptimal surgery. Additionally in that study, 4 (50%) out of 8 stage IC patients had adjuvant chemotherapy, and the disease recurred in two of them. In our study, 9 out of 10 cases were in stage IA, and eight of them underwent fertility sparing surgery. No recurrences occurred in the 5-year median follow-up period. Four out of five patients who underwent fertility sparing surgery and who desired pregnancy got pregnant. Powel et al. (10) treated two patients who had stage III disease with fertility sparing surgery and adjuvant chemotherapy and they did not observe recurrence during the follow-up period. In contrast to adult-type, most of the recurrences occur in the first year after treatment (5, 8). Although in the largest series in literature it was reported that recurrence would not be expected after three years of treatment, late recurrence was reported (4, 11). For that reason, patients should be followed-up for a long period (11). It is thought that inhibin B is a reliable marker to detect recurrence during the follow-up period (11).

Surgical and adjuvant treatments in advanced stage or recurrent diseases are unclear. The combination of taxane and platinum can be an alternative treatment option (12). For residual or recurrent adult type granulosa cell tumors, radiotherapy is recommended (13). Hirakawa et al. (12) did not obtain any response with chemotherapy in a patient with recurrent JGCOT who had multiple abdominal masses. They observed a regression in the size of the tumors and clearance of the ascites with whole abdominal external beam radiotherapy. Palliative radiotherapy can be considered in these patients.

Although JGCOT occurs frequently during childhood, it is also seen in adults. Primary management of this disease is surgery. The benefit of adjuvant therapy is unclear. Because survival is long in the early stage and most of the patients are young, fertility sparing surgery can be safely chosen in these patients.

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