Malignant Ovarian Germ Cell Tumor in King Chulalongkorn Memorial Hospital

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Objectives: *To determine the frequency, characteristics, treatment and outcome of patients with malignant ovarian germ cell tumor (MOGCT) in King Chulalongkorn Memorial Hospital during the period January 1992 – December 2000.*

Study design: *Retrospective descriptive study*

Material and Method: *All patients with malignant ovarian germ cell tumor in King Chulalongkorn Memorial Hospital during the period January 1992 – December 2000 were analyzed by the characteristics of patients, treatment and outcome.*

Results: *Sixty-six patients with MOGCT were demonstrated in that period with a mean age of 22.6 years old. Most of the patients were nulliparous and premenopausal status. Primary surgery was done in all patients. Forty-two patients (63.6%) received conservative surgery. Eight patients received no adjuvant treatment after surgery due to stage IA dysgerminoma and immature teratoma stage I grade I. Fifty-six patients received chemotherapy for adjuvant treatment. VAC regimen was given in 27 cases (40.9%) and PVB regimen was given in 25 cases (37.9%). Salvage therapy in the patients with persistent and recurrent disease was treated in 9 patients, who received a platinum-base of regimen. Two-year survival was 88% with the median time to follow up 24 months. Overall five-year survival in the present study was 85%.*

Conclusion: *MOGCT in King Chulalongkorn Memorial Hospital had clinical characteristics similar to other studies in malignant ovarian germ cell tumor. Treatment by VAC regimen still has benefit in selected group.*

Keywords: *Malignant ovarian germ cell tumor, Survival*

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Malignant ovarian germ cell tumors (MOGCT) are much less common than epithelial ovarian neoplasm and account for less than 5% of all ovarian cancers[1].They typically occur in girls and young women, these type of tumors are highly malignant and grow rapidly growth. However, in this past two decades, the evolution of treatment in MOGCT by chemotherapy increased the survival time of patients. This also improves the quality of life and fertility function as well. The initial treatment approach includes conservative surgery in patients who desired to keep fertility function. Radiation was the treatment of choice in dysgerminoma for several decades until the evolution of combination chemotherapy[2]. At the present time, chemotherapy seems to be the major adjuvant treatment in most cases.

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The present study was focused on the characteristic of patients, clinical aspects of the disease, methods and outcomes of treatment in the patients with MOGCT at King Chulalongkorn Memorial Hospital. This descriptive study will provide the overview of situation of this disease.

Material and Method

King Chulalongkorn Memorial Hospital, run by the Thai Red Cross society, is one of the largest hospitals in Thailand and also provided the resources for medical students in the Faculty of Medicine, Chulalongkorn University. In the current period, King Chulalongkorn Memorial Hospital is the institute for specialty and subspecialty training. Furthermore, it is a tertiary hospital for cancer patients.

The present study analyzed every cases of MOGCT in the Department of Obstetrics and Gynecology, King Chulalongkorn Memorial Hospital from

January 1992 to December 2000. The medical records were retrieved from the database of gynecologic oncology unit. Data collection included the general characteristics of the patients, age, parity, and menopausal status. The patients were separated into one group whom were referred from other hospitals and patients who received primary treatment in King Chulalongkorn Memorial Hospital formed the other group. Other clinical data; presenting symptoms, gross description of the tumor, operative finding and stage of disease were recorded. Mode of primary treatment, adjuvant treatment and follow up data were also collected. During the period of the present study, most of the patients with early stage or completely surgical resection received VAC regimen (vincristine, actinomycin-D and cyclophosphamide) for adjuvant combination chemotherapy. VAC regimen was given by vincristine 1 mg/m^2 on the first day, actinomycin-D 300 microgram/m^2 and cyclophosphamide 150 mg/m^2 from day1 to day 5 every 3 weeks. In advanced stages or suboptimal cytoreductive surgery, the authors provided PVB regimen (vinblastine, bleomycin and cisplatin) for adjuvant treatment. PVB regimen was given by vinblastine 6 mg/m^2 on the first day, bleomycin 10 unit/m^2 on day 1 and day 5, cisplatin 20mg on day1 to day 5 every 3 weeks.

Salvage therapy was also specified in the patients with resistant or recurrent disease. EP regimen was given by etoposide 100mg/m^2 and cisplatin 20 mg for 5 days in every 3weeks.

Finally, the authors followed the outcome of patients by median time to follow up and status of patients (alive, dead and lost to follow up). Descriptive statistics were used for analyzed data, Kaplan-Meier analysis was used to demonstrate pattern of survival. The study was approved by the ethical committee of the Medical Faculty.

Results

During the 9-year period, a total of 66 patients were diagnosed with malignant ovarian germ cell tumor. The mean age of these patients was 22.6 years mode (range 9-53 years). Most of the patients were nulliparous (44 patients). Chief complaints were abdominal mass in 34 cases (51.5%), abdominal pain 15 cases (22.7%), and abdominal discomfort 12 cases (18.2%). Almost half of the patients were referred cases (30 cases, 45.5%). The average duration of presenting symptoms was 3.8 months, and about one half of the patients experienced the symptoms for not more than 1 month (Table1).

Tumor characteristics

Regarding the tumor size, the average diameter was 16.3 cm. (range 4-30 cm.). In the operative findings, the average amount of ascites was 854 cc (range 0-11,000 cc). Tumors were found on the left side in 28 cases, right side 31 cases and bilateral in 3 cases (one dysgerminoma, one immature teratoma and one choriocacinoma). Conservative surgery was done in 42 patients (63.6 %) and radical surgery was done in 23 cases (34.8%). Residual tumor was recorded in completely resected 30 cases, optimal cytoreduction 24 cases and suboptimal surgery in 10 cases. Most of the patients were in the early stage (64.1%) (Table 2). The most common histology cell type was dysgerminoma 19 cases (29.2%), endodermal sinus tumor 18 cases (27.7%), and immature teratoma 18 cases (27.7%) respectively (Table3).

Treatment

Forty-two patients received primary treatment by conservative surgery (63.6%). Adjuvant chemotherapy was given in 56 cases. Two patients received radiation due to advanced stage dysgerminoma. Eight patients did not receive any adjuvant treatment due to

Table 1. Characteristics of the patients (N=66)

Age (mean) (Mode)	22.6 year (range 9-53) (40+)
Nulliparous	44 cases (66.7%)
Premenopause	65 cases (98.5%)
Referred case	30 cases (45.5%)

Table 2. Distribution by stage of tumor

Stage	Number of patients (N=64)
I	41 (64.1%)
II	7 (10.9%)
III	14 (21.9%)
IV	2 (3.1%)

Missing data 2 cases

Table 3. Distribution by tumor cell type

Histologic cell type	Number of patients (N=65)
Dysgerminoma	19 (29.2%)
Endodermal Sinus Tumor	18 (27.7%)
Immature teratoma	18 (27.7%)
Choriocarcinoma	4 (6.2%)
Mixed germ cell	6 (9.2%)

Mising data 1 case

stage I dysgerminoma and immature teratoma grade I. VAC regimen was given in 27 cases (40.9%). PVB regimen was given in 25 cases (37.9%) and 3 cases (4.5%) of cisplatin. Most of the patients received 6 courses (25 patients, 37.9%) and 4 courses (10 patients, 15.2%). Second line chemotherapy was given in 9 cases (13.7%), which were EP (etoposide and cisplatin) regimen (5 cases) and PVB regimen (4 cases).

Outcome of treatment

Median time to follow up was 24 months (range1-106 months). In the current period, 39 patients (59.1%) were still alive, 10 patients (15.1%) had died (7 from disease, one from HIV infection, one from leukopenic sepsis and one from suicide). Seventeen patients (25.8%) were lost to follow up. The overall two-year survival was 85% and 80% for 5-year survival (Fig. 1).

Discussion

The incidence of malignant ovarian germ cell tumor in King Chulalongkorn Memorial Hospital was 9.8% according to Trivijitsilp P et al[3]. This incidence was slightly higher compared to other studies[1,4]. Characteristic patients occurred in the young age group with short presenting symptoms. In the present report, the major clinical presentation was pelvic mass with rapid progress. About half of the patients experienced their symptoms for not more than 1 month. In the operative finding, tumor diameter was more than 10 cms, no different in both adnexae. In a previous report[5], most malignant germ cell tumors were unilateral. Bilateral ovarian involvement is rare, except in the case of pure dysgerminoma. Bilateral involvement also may occur in advanced disease in which there is metastasis from one ovary to the opposite and in cases of mixed germ cell tumors with a dysgerminoma component[6]. The present study found bilateral ovarian tumor in 3 cases (4.5%).

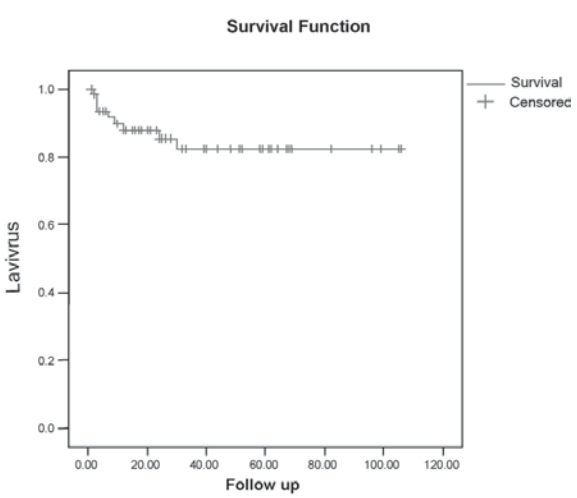

Fig. 1 Survival rate of MOGCT patients who were treated in Chulalongkorn Memorial Hospital

Dysgerminoma was the most common histology cell-type in the present data which was similar to others[7-8]. Endodermal sinus tumor and immature teratoma was the second most common. Most of the patients presented with stage I, this may be due to the rapid progression of tumors, thus, the early diagnosis was done. Because of unilateral and highly chemosensitive tumor[5,9], therefore, unilateral salpingo-oophorectomy with preservation of contralateral ovary and the uterus is appropriate surgical treatment for most patients with malignant germ cell. In the present study, more than 60% received conservative surgery for primary therapy. TAH with BSO were done due to the patients' age and some patients were referred after primary radical surgery.

For adjuvant therapy, women with pure dysgerminoma or pure immature teratoma were patients with stage IA and stage IA, grade I disease, respectively, may be treated with surgery alone[10,11]. In the institute, the authors also followed this management. Eight patients (12.1%) were defined in this group and didn't receive any adjuvant treatment. Before the chemotherapy era in the mid-1960s, the prognosis of most patients with non-dysgerminamatous tumors was dismal, virtually all patients with advanced stage disease died. Even in stage I disease, only 5-20% of patients survived after treatment with surgery alone [12-15]. In 1985, Slayton et al[16] reported long term survival of more than 70% in patients with completely resected MOGCT treated with combination VAC regimen. In the presented data, the authors used 6 courses of VAC regimen in 27 cases (40.9%) of completely resected tumors. VAC regimen has less toxicity compared to platinum combination chemotherapy. However, treatment with PVB regimen in subsequent clinical trials[17,18] showed superior response in patients with measurable or suboptimal disease. Twenty five patients (37.9%) in the present study received PVB due to incompletely resected tumor. Even the result of induction chemotherapy with BEP (bleomycin, etoposide and cisplatin) regimen was very impressive[19], long-term risk of secondary cancer after etoposide exposure should be of concern[11]. Dysgerminoma is very sensitive to radiation, but the patients will lose their ovarian function after radiation. In the current

period, radiation is rarely used due to the effectiveness of chemotherapy.

Ten patients died in the present report, 7 died with disease, but 3 died from other causes. Five years survival in the present study was 80%, which was similar to other reports[18,19]. Patients with persistent and recurrent disease, there is little information concerning salvage therapy in these patients. Patients who did not respond to non-platinum regimen subsequently received PVB or etoposide-containing regimens for salvage therapy. The institute used EP regimen for salvage therapy in patients with platinum resistane which appeared to have no long term benefit. Currently, high dose chemotherapy with stem cell rescue may be the solution in this group.

In conclusion, MOGCT in King Chulalongkorn Memorial Hospital had clinical characteristics similar to other studies. Treatment by VAC regimen still has benefit in selective group. The new chemotherapy regimen of treatment should be applied in platinum resistant patients.

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มะเร็งรังไข่ชนิด Germ cell tumor ในโรงพยาบาลจุฬาลงกรณ์

เรืองศักดิ์ เลิศขจรสุข, วิชัย เติมรุ่งเรืองเลิศ, อภิชัย วสุรัตน์, ตุลย์ สิทธิสมวงศ์, พงษ์เกษม วรเศรษฐสิน, ดำรง ตรีสุโกศล

วัตถุประสงค์: *เพื่อศึกษาหาอุบัติการณ์, ลักษณะทางคลินิก, การรักษา ตลอดจนผลการรักษาของผู้ป่วยในกลุ่มมะเร็งรังไข่ชนิด Germ cell tumor ในโรงพยาบาลจุฬาลงกรณ์ ช่วงระหว่าง ปี พ.ศ.2535-2543*

ลักษณะการศึกษา: *เป็นการศึกษาแบบย้อนหลัง*

วัสดุและวิธีการ: *เก็บข้อมูลจากผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็นมะเร็งรังไข่ชนิด Germ cell tumor ในโรงพยาบาลจุฬาลงกรณ์ ช่วงระหว่างปี พ.ศ.2535-2543 และนำข้อมูลมาวิเคราะห์*

ผลการศึกษา: *มีผู้ป่วยที่ได้รับการวินิจฉัยเป็นมะเร็งรังไข่ชนิด Germ cell tumor ทั้งหมด 66 ราย ในช่วงเวลาที่ทำการศึกษา อายุเฉลี่ยของผู้ป่วย 22.6 ปี พิสัย 9-53 ปี ผู้ป่วยส่วนใหญ่ยังไม่เคยมีบุตรและอยู่ในช่วงวัยเจริญพันธุ์ ผู้ป่วยทุกรายได้รับการผ่าตัดเป็นการรักษาปฐมภูมิ ผู้ป่วย 42 ราย (63.6%) ได้รับการผ่าตัดแบบ conservative ผู้ป่วย 8 ราย ไม่ได้รับการรักษาเพิ่มเติมหลังการผ่าตัด เนื่องจากวินิจฉัยเป็น dysgerminoma ระยะ 1A และ immature teratoma ระยะ 1 grade 1 ผู้ป่วย 56 ราย ได้รับเคมีบำบัดเป็นการรักษาเพิ่มเติม เคมีบำบัดสูตร VAC ให้ในผู้ป่วย 27 ราย (40.9%) และเคมีบำบัดสูตร PVB ให้ในผู้ป่วย 25 ราย (37.9%) การรักษาในกลุ่มผู้ป่วยที่ดื้อยาหลังให้เคมีบำบัดมี 9 ราย ซึ่งได้รับเคมีบำบัด platinum-based อัตราการอยู่รอดที่ 2 ปี เป็น 85% และอัตราการอยู่รอดที่ 5 ปี เท่ากับ 80% ค่ามัธยฐานของระยะเวลาในการตรวจติดตามเท่ากับ 24 เดือน*

สรุป: *มะเร็งรังไข่ชนิด Germ cell tumor ในโรงพยาบาลจุฬาลงกรณ์ มีลักษณะทางคลินิกใกล้เคียงกับมะเร็งรังไข่ชนิดนี้ในการศึกษาอื่น ๆ และการรักษาโดยให้เคมีบำบัดสูตร VAC ยังได้ประโยชน์ในคนไข้บางกลุ่ม*