Pure dysgerminoma of the ovary: a review of 45 well staged cases

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Summary

Purpose: To evaluate the significance of meticulous surgical staging, and whether type of initial surgery or adjuvant therapy impacted on survival in cases of pure ovarian dysgerminoma.

Methods: Retrospective chart review of 45 patients treated for pure ovarian dysgerminoma at a single institute. Survival analysis with the Kaplan Meier and log rank test and the chi-square test for the comparison of categorical variables were used.

Results: Of the 45 patients subjected to a surgical staging procedure 30 (67%) had stage I disease, 2 (4%) had stage II, 9 (20%) had stage III, and 4 (9%) had stage IV pure ovarian dysgerminoma. Thirteen of these 45 patients were referred to have seemingly stage I disease. Restaging within 2 months proved stage IIIC disease in 3 (23%) of them. With a median follow-up of 61 months, the overall survival rate for ovarian dysgerminoma in this series was 84%. Significantly lower survival rates were found in patients with advanced stage (stage III-IV) ovarian dysgerminoma (53.9%), when compared with earlier stages (96.9%). Twenty-one patients with unilateral disease and fertility desire were treated with conservative surgery, 19 patients with nonconservative surgery, and in 5 suboptimal debulking could be carried out. As regards recurrence or survival rate, no significant difference was found between patients who were treated conservatively or nonconservatively, whether or not adjuvant chemotherapy or radiotherapy was given. Of the 21 patients treated with conservative surgery, 11 (52%) achieved one or more pregnancies.

Conclusion: After careful surgical staging and confirming unilateral disease, conservative surgery, followed if necessary by adjuvant chemotherapy, seems to be the ideal treatment in cases of pure ovarian dysgerminoma.

Key words: Surgical staging; Pure ovarian dysgerminoma; Adjuvant therapy.

Introduction

Dysgerminoma is the most common malignant germ cell tumor occurring in young females, and accounts for 2-5% of all ovarian malignancies [1]. Dysgerminoma has prominent features such as young age and early stage at presentation, nodal rather than transperitoneal dissemination [1-2], high sensitivity to adjuvant therapies and high survival rates [3-6]. Since adjuvant therapy has proved to be highly effective in ovarian dysgerminoma, it is very important to determine patients who do not require further therapy.

The purpose of this study was to evaluate the significance of meticulous surgical staging, and whether type of initial surgery or adjuvant therapy impacted on survival in cases of pure ovarian dysgerminoma.

Materials and Methods

Forty-five patients with ovarian dysgerminoma who were initially treated or consulted at Hacettepe University Hospital over a 25-year period were retrospectively reviewed. Follow-up information to the time of death or last tumor registry contact was available for all patients.

After a routine preoperative work-up all patients were subjected to a surgical staging procedure including peritoneal cytology, omentectomy, bilateral pelvic and paraaortic lymphadenectomy and multiple biopsies from suspicious areas. Of the patients, 21 underwent conservative surgery (unilateral salpingo-oophorectomy (USO) and wedge of the contralateral ovary), 19 were subjected to nonconservative surgery (total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH+BSO)), and in 5 suboptimal debulking (>1 cm residual disease) could be performed in addition to TAH+BSO.

The histological material were re-examined, and the diagnosis of pure ovarian dysgerminoma was confirmed. Four cases with mixed germ cell elements were excluded.

Survival analysis with the Kaplan Meier and log rank test, chi-square or Fisher's exact test for the comparison of categorical variables were used; $p<0.05$ was considered significant.

Results

The age distribution at the time of diagnosis ranged from 9-58 years. The mean and median age were 23.8 and 23 years, respectively. Thirty-seven out of 45 (82%) patients were younger than 30 years. Forty patients were postmenarcheal, 4 were premenarcheal including a 13-year-old girl with dysgerminoma in a gonadoblastoma, and only one was postmenopausal. Twenty were parous and 25 (56%) were nulliparous. The tumor was diagnosed during pregnancy in 2 and during puerperium in 3 cases.

The presenting symptoms were vague lower abdominal pain and swelling in 29 (64%) patients. Five patients (11%) presented with acute abdominal pain due to adnexal torsion or necrosis within the tumor.

Of the 45 patients, 32 received initial surgery and staging at our institution, and 13 were referred cases who were subsequently subjected to a restaging procedure

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within two months. Of these 13 patients referred to have seemingly stage I dysgerminoma, 3 resulted (23%) in stage IIIC disease. Retroperitoneal surgical assessment documented lymphatic involvement in 27% (12/45) of the patients. Of these patients 7 (58%) had para-aortic, 3 (25%) had para-aortic and iliac and 2 (17%) had only iliac nodal involvement. Interestingly in 8 cases (18%) retroperitoneal nodal involvement was found to be the only extraovarian site of spread resulting in upstaging. In only one case (2.2%), abdominal peritoneal seeding was documented in the absence of nodal involvement.

In 8 patients (18%) bilateral ovarian involvement was encountered. Bilateral involvement was evident in 6 cases, but in 2 cases wedge resection of the contralateral, normal-appearing ovary proved occult involvement. All underwent nonconservative surgery (total abdominal hysterectomy and bilateral salpingo-oophorectomy) and complete staging.

The final staging of cases according to the International Federation of Gynecology and Obstetrics (FIGO) are listed in Table 1.

With a median follow-up of 61 months (2-312 months) the overall survival rate for the entire group was 84%.

Five-year survival rates in patients with stage I-II (n=32), and stage III-IV disease (n=13) were 96.9%, and 53.9%, respectively (Figure 1).

Twenty-one patients underwent conservative surgery and staging, 4 recurrences occurred in this group and 2 died of disease. Total abdominal hysterectomy and bilateral salpingo-oophorectomy with complete staging was performed in 19 patients, 3 recurrences occurred and one of them died. Stage distribution was comparable in the conservative and nonconservative surgery group; stage I patients constituting the majority of the cases in both groups (76%, 74%, respectively). There was 1 stage II, and 4 stage III diasease in each group. Neither recurrence nor survival rate was altered significantly by the type of initial surgery whether conservative or not (p=0.559, and p=0.538, respectively). Suboptimal debulking surgery could be carried out in 5 patients with advanced disease. Type of surgery performed in different stages and associated 5-year survival rates are listed in Table 2.

Of the 21 patients who underwent conservative surgery 4 received adjuvant radiotherapy, 5 received adjuvant chemotherapy and 12 did not receive any adjuvant therapy. None of the 4 patients who received radiation therapy resumed spontaneous menstrual function, whereas regular cycles were altered in only one patient who received surgery only and in none of the patients who received adjuvant chemotherapy. Statistically significant increased risk of ovarian failure was found in patients who were managed with adjuvant radiotherapy (p=0.001). Of the conservatively treated patients 11 (52%) achieved one or more pregnancies. Seventeen patients received an average of 4 courses of adjuvant chemotherapy. Eight received a combination of bleomycin, etoposide, and cisplatin (BEP), 6 received a combination of vincristine, actinomycine-D, and cyclophosphamide (VAC), and 4 received a combination of vinblastine, bleomycin, and cisplatin (VBP). Although not statistically significant, BEP therapy was associated with excellent survival (Figure 2). Of these 17 patients 14 survived (82%). No mortality was experienced in relation to chemotherapy.

Twelve patients received postoperative adjuvant radiotherapy. Of these patients 8 are alive (66.7%).

We observed slightly better survival rates in patients who were treated with adjuvant chemotherapy when compared with adjuvant radiotherapy, but no statistical significance was found (Table 3, Figure 3).

Eleven out of 45 patients (24%) experienced recurrence. Of these 11 patients, 7 (64%) had advanced stage disease. Four pelvic (only one originating from the conserved ovary), 1 retroperitoneal, 1 lung and 1 supraclavicular recurrence were diagnosed. In four cases progressive disease was observed. If these 4 cases, in which a complete response had never been achieved were excluded, 50% survival was achieved. Three of the recurrences were encountered in cases with stage I disease. Two of these recurrences occurred in patients who had been treated by surgery alone and one occurred in a patient who had been treated with surgery plus adjuvant radiotherapy. All these recurrences were salvaged by the help of secondary cytoreduction in combination with radiotherapy and chemotherapy.

Table 1. — *Final assigned stage in 45 patients.*

Stage	No. patients
IA	23
IB	2
IC	5
II	2
IIIA	1
IIIC	8
IV	4
Total	45

Table 2. — *Type of surgery versus stage and 5-year survival rates.*

	Stage				
	IA N (%)	IB N (%)	IC N (%)	II-IV N (%)	Total N
Surgical staging + USO (Conservative surgery)	14 (100)		2 (100)	5 (60)	21
Surgical staging + TAH+BSO (Nonconservative surgery)	9 (100)	2 (100)	3 (100)	5 (80)	19
Suboptimal debulking				5 (20)	5
Total	23 (100)	2 (100)	5 (100)	15 (53.3%)	

N=number of cases
Numbers in parentheses are actuarial 5-year survival rates.

Table 3. — *Therapeutic modalities versus stage and recurrence-free survival.*

	Surgery only N (%)	Surgery + chemotherapy N (%)	Surgery + radiotherapy N (%)	Total N (%)	p
Stage I	16 (87.5)	9 (100)	5 (80)	30 (90)	0.403
Stage II			2 (50)	2 (50)	
Stage III-IV		8 (62.5)	5 (20)	13 (46)	0.179

N=number of cases
Numbers in parentheses are recurrence-free survival rates.

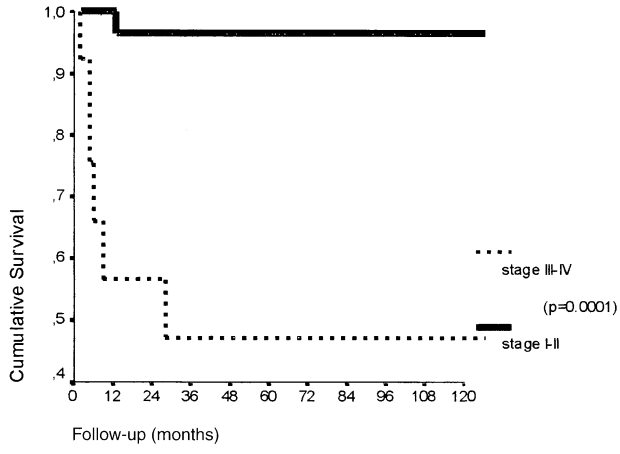

Figure 1. — Survival in stage I-II versus stage III-IV.

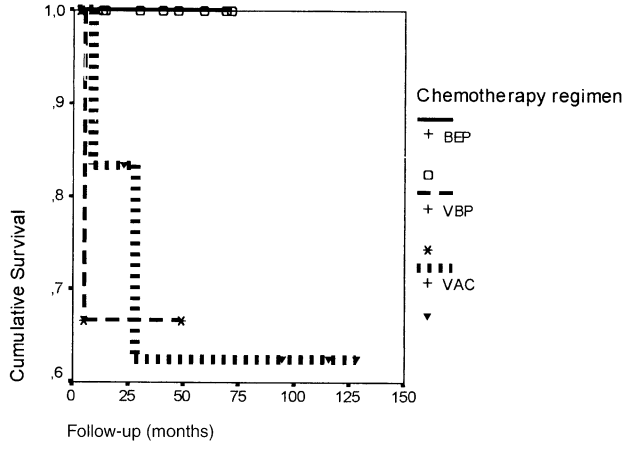

Figure 2. — Adjuvant chemotherapeutics and survival.

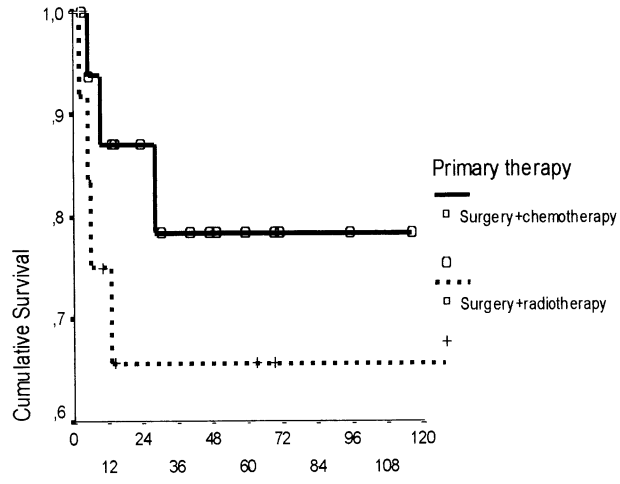

Figure 3. — Primary therapy and survival.

Discussion

The young age distribution of patients with dysgerminoma in our series is in accordance with the literature [1, 7-9]. Appropriate surgical staging proved that the majority of the cases (67%) had stage I disease. This figure was slightly lower than previous reports indicating that 75% of cases were confined to one ovary [1, 10-11]. This difference may be explained by the uniform staging procedure employed in our series resulting in upstaging.

The incidence of bilaterality in our series was 18%, similar to the series of Kurman and Norris [12]. Wedge resection proved contralateral synchronous occult involvement in 8.7% of the patients with a normal appearing contralateral ovary. This emphasizes the importance of sampling the ovary tended to be preserved. Most of the recurrences in the remaining ovary reported to present within 2 years after initial surgery [11]. This suggests the possible presence of undiagnosed synchronous disease in those cases. In our series, routine biopsy of the conserved ovary at the time of initial surgery precluded synchronous involvement and resulted in a low recurrence rate.

DePalo *et al.* [2] suggested lymphography to assess retroperitoneal involvement in cases of ovarian dysgerminoma, and reported 31.6% positive results in their series. In the presented series, systematic lymphadenectomy documented lymphatic involvement in 27% of the patients, and resulted in upstaging in 18% of them. To date this was the only series to present the results of a uniform surgical staging including systematic lymphadenectomy in cases of pure ovarian dysgerminoma. The most exciting finding was the dramatic response of cases with retroperitoneal disease to adjuvant chemotherapy and radiotherapy. In the absence of peritoneal or parenchymal metastasis, a 75% survival rate was achieved in accordance with the series reported by DePalo *et al.* [2].

Systematic lymphadenectomy increased both the detection of retroperitoneal disease and employment of adjuvant therapies which promoted survival.

In the series 93% 5-year recurrence-free survival and 100% 5-year total survival rates were observed for stage IA disease regardless of the type of surgery performed and regardless of the adjuvant therapy whether or not used. Similar excellent survival rates have been reported in previous well staged series [1-2, 8, 11].

The overall survival rate of 84% in our series was similar to the recent series of Casey *et al.* reporting 88% survival in cases of pure ovarian dysgerminoma [13]. The overall recurrence rate was 24%. Pelvic recurrences were predominant as previously reported [3, 14] but unlike Casey *et al.* [13] no relationship between recurrence and conservative surgery was documented. Former reported high recurrence rates up to 52% may be due to the inclusion of mixed tumors in those series [15-16].

Although pure dysgerminomas are known to be markedly radiosensitive, radiotherapy has certain limitations such as detrimental effects on ovarian function leading to ovarian failure which in our series was found to be significant. Radiotherapy has also limited efficacy in intraperitoneal disease [2, 17].

The use of chemotherapeutics gained momentum due to the handicaps of radiotherapy. The combination of vincristine, actinomycin-D, and cyclophosphamide (VAC) were used. Slayton reported that the combination of vinblastine, bleomycin, and cisplatin (BVP) was more effective [18]. Recently the toxicity of this regimen was lowered while maintaining equal efficacy by replacing vinblastine with etoposide (BEP) [19]. In the presented series slightly improved results were obtained by the BEP regimen when compared with the previous combinations, and the overall survival following adjuvant chemotherapy was 82% without compromising ovarian function.

Conclusion

In cases of pure ovarian dysgerminoma, meticulous surgical staging results in significant upstaging, and determines a group of patients who will substantially benefit from adjuvant therapies. If future fertility is an issue, conservative surgery with adequate staging should be followed and if necessary combination chemotherapy should be the recommended first-line treatment.

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