Med Oncol (2012) 29:2944–2948
DOI 10.1007/s12032-012-0194-z

ORIGINAL PAPER

Pure dysgerminoma of the ovary: a single institutional experience of 65 patients

Hamed AL Husaini · Hussein Soudy · Alaa El Din Darwish · Mohamed Ahmed · Amin Eltigani · Mustafa AL Mubarak · Amal Abu Sabaa · Wael Edesa · Taher AL-Tweigeri · Ismail A. Al-Badawi

Received: 4 February 2012 / Accepted: 16 February 2012 / Published online: 10 March 2012

Abstract Ovarian dysgerminomas are rare entity and account for only about 2% of all malignant ovarian neoplasm. The aim of this study was to evaluate the clinicopathologic characteristics, treatment, long-term survival, and fertility outcome of women diagnosed with ovarian dysgerminoma at our institution. Sixty-five women with histologically proven pure ovarian dysgerminoma were identified in this retrospective study. They were treated at King Faisal Specialist Hospital, Riyadh; Saudi Arabia between 1976 and 2010. The median age was 20 years. The most frequent symptoms at presentation were abdominal pain and abdominal/pelvic mass. Thirty-three patients (50.7%) presented with stage I, 2 (3.1%) had stage II, 22 (33.8%) had stage III, and 4 (6.2%) had stage IV (4 unknown stage). Unilateral oophorectomy was performed in 50 patients (76.9%) while bilateral oophorectomy ± hysterectomy was done in 12 patients (18.4%). Three patients had biopsy only. Forty patients (61.5%) received only chemotherapy, and 4 patients (6.2%) received radiotherapy alone. Recurrence was observed in 6 patients (9.2%). With median follow-up of 54 months, the 5-year disease-free survival (DFS) and overall survival (OS) were 88 and 95%, respectively. On univariate analysis, adjuvant chemotherapy was independent better prognostic factor for DFS (HR, 0.09; 95% CI, 0.01–0.84; $P = 0.034$). Of the 50 patients treated with fertility-sparing surgery, 16 patients (32%) achieved pregnancy with 14 live births. Patients with pure ovarian dysgerminoma have excellent long-term outcome. There is no difference at outcome between fertility-sparing and nonconservative surgeries. Adjuvant chemotherapy was associated with significant improvement in DFS. It is possible to maintain good reproductive function after conservative surgery followed by chemotherapy in our series.

Keywords Ovarian dysgerminoma · Chemotherapy · Surgery · Ovarian germ cell tumor

H. AL Husaini (✉) · H. Soudy · A. E. D. Darwish · M. Ahmed · A. Eltigani · M. AL Mubarak · A. A. Sabaa · W. Edesa · T. AL-Tweigeri
Department of Oncology, King Faisal Specialist Hospital, Riyadh, Saudi Arabia
e-mail: hhussaini@gmail.com

I. A. Al-Badawi
Department of Obstetrics and Gynecology, King Faisal Specialist Hospital, Riyadh, Saudi Arabia

Background

Ovarian dysgerminomas are rare and account for only about 2% of all malignant ovarian neoplasm [1]. They are female analogous to male seminoma and most commonly arise in adolescents and young women [2]. Seventy-five percent of women with dysgerminoma present with stage 1 at diagnosis and bilateral ovarian involvement occur in 10–15% [3, 4]. Lymph node metastasis found in 28% of patients with ovarian dysgerminoma and was an independent predictor of poor survival [5].

Stage 1A dysgerminomas are usually treated with fertility-preserving surgery without adjuvant chemotherapy or radiotherapy. Outcomes from postoperative surveillance for stage 1A are excellent with long-term cure are > 90% [6]. The recurrence rate for stage 1A is approximately 20%, which can be successfully salvaged by chemotherapy or radiation [7].

Ovarian dysgerminomas are extremely sensitive to radiation and chemotherapy. Therefore, patients with advanced disease still have good outcome with overall

5-year survival of over 90% [8, 9]. Women with stage 1B or higher ovarian dysgerminoma are usually treated with platinum-based chemotherapy. Bleomycin, etoposide, and cisplatin (BEP) are the most commonly used regimens due to superior efficacy and better tolerability [10, 11]. Recurrence usually occurs within 2 years of diagnosis.

Because of the rarity of these tumors, conducting randomized trial is difficult, and majority of data are derived from a few nonrandomized prospective trials and evaluation of retrospective series. Most of the case series include all type of ovarian germ cell tumors (OGCTs) making specific information on dysgerminomas difficult to obtain. Long-term outcome, prognostic factors of this population of patients, is of clinical importance. The aim of this study was to evaluate the clinicopathologic characteristics, treatment, long-term survival, and the fertility outcome of women diagnosed with ovarian dysgerminoma at our institution.

Materials and methods

The medical records of 65 women with histologically proven pure ovarian dysgerminoma were identified in this retrospective study. They were evaluated and treated between 1976 and 2010 at King Faisal Specialist Hospital, Riyadh; Saudi Arabia. The clinical data about patient demographic, clinical characteristics, type of surgery, postoperative treatment, fertility outcome, and long-term survival were collected. Patients were staged according to the International Federation of Gynecology and Obstetrics (FIGO) staging system. All pathology specimens were reviewed by expert pathologist in gynecologic oncology. Data about disease status at last follow-up and fertility outcome were updated by telephone interview in 12 patients.

Patient characteristics were summarized using descriptive statistics. Disease-free survival (DFS) was calculated from date of surgery to relapse of disease, death from any cause or last-follow-up data if the patient was alive without disease. Overall survival (OS) was calculated from date of diagnosis to last follow-up or the date of death. DFS and OS were calculated using the Kaplan–Meier curves. Statistical analysis has been done using SAS V9.2. Univariate analysis was constructed using proportional hazard regression model.

Result

Patient characteristics

The median follow-up period for survivors was 54 months (range, 0.3–428.4 months). The median age at the time of diagnosis was 20 years. The most frequent symptoms were abdominal pain (67.7%), abdominal/pelvic mass (56.9%), abdominal distension (21.5%), and amenorrhea (12.3%). Three women were diagnosed with dysgerminoma as accidental finding during pregnancy or at postpartum. Twenty-one (32.3%) patients had stage IA disease, 12 (18.5%) had stage IC disease, 2 (3%) had stage IIA/IIB disease, 4 (6.2%) had stage IIIA/IIIB disease, 18 (27.6%) had stage IIIC disease, and 4 (6.2%) had stage IV disease. The stage was unknown in 4 patients. The patient characteristics are summarized in Table 1.

Table 1 Patient characteristics

Characteristics	*N* (%)
Age (year)	
Median (range)	20 (15–65)
Stage	
IA	21 (32.3%)
IC	12 (18.5%)
IIA	1 (1.5%)
IIB	1 (1.5%)
IIIA	2 (3.1%)
IIIB	2 (3.1%)
IIIC	18 (27.6%)
IV	4 (6.2%)
Unknown	4 (6.2%)
Presenting symptoms	
Abdominal pain	44 (67.7%)
Abdominal/pelvic mass	37 (56.9%)
Abdominal distension	14 (21.5%)
Amenorrhea	8 (12.3%)
Asymptomatic	4 (6.2%)
Type of surgery	
Bilateral oopherectomy	4 (6.2%)
Bilateral oopherectomy and hysterectomy	8 (12.3%)
Unilateral oopherectomy	50 (76.9%)
Biopsy only	3 (4.6%)
Surgical outcome	
Optimal debulking	44 (67.7%)
Residual disease	18 (27.7%)
Unknown	3 (4.6%)
Lymph node metastasis	
Yes	19 (29.2%)
No	17 (26.2)
Unknown/not done	29 (44.6)
Postoperative therapy	
Chemotherapy	40 (61.5%)
Radiation therapy	4 (6.2%)
No adjuvant	21 (32.3%)

Most of the patients (76.9%) underwent unilateral oopherectomy, 4 (6.2%) patients underwent bilateral oopherectomy, 8 (12.3%) patients underwent bilateral oopherectomy and hysterectomy, and 3 (4.6%) patients with stage IV disease had only biopsy. Optimal surgical debulking was achieved in 44 (67.7%) patients in the entire group. The incidence of lymph node metastasis was 52.8% (19/36) in patients who underwent lymph node sampling or dissection.

Forty patients (61.5%) received chemotherapy alone, 4 (6.2%) received radiotherapy only, and 21 (32.3%) did not receive postoperative therapy. Of the 40 patients who received chemotherapy, 3 had stage IA, 9 had stage IC, 2 had stage IIA/IIB, 3 had stage IIIA/IIIB, 18 had stage IIIC, 4 had stage IV disease, and one had unknown stage. All chemotherapy regimens were platinum based, and the most common regimen was bleomycin, etoposide and cisplatin (BEP) given in 30 (75%) patients. Other regimens were etoposide/cisplatin (EP) in 5 patients, cisplatin/cychlophosphamide in 1 patient, vinblastin, bleomycin, cisplatin (PVB) in 2 patients, cisplatin/Adriomycin in 1 patient, and bleomycin/Carboplatin/etoposide in the last patient. The median number of chemotherapy cycles was 4. Four patients received radiation therapy between the years 1977 and 1991 (2 whole abdominal radiation, 1 pelvic and paraortic radiation, 1 unknown type).

Out of the 65 patients, recurrence occurred in 6 patients (9.2%) and was encountered within 9 months of the primary diagnosis (see Table 2). Five out of six recurrences developed in patients who did not received adjuvant chemotherapy. The sixth recurrence occurred in stage IIIC patient who received adjuvant BEP chemotherapy. Two out of 18 (11%) patients with stage IA not receiving chemotherapy recurred. Recurrence developed in 2 out of 4 (50%) patients received postoperative radiation therapy alone. The site of relapse was Pelvic mass and retroperitoneal lymph nodes in 3 patients, contralateral ovary in 2 patients and liver and lung metastasis in 1 patient. Three patients with recurrence were treated with BEP chemotherapy, two were treated with surgical resection followed by chemotherapy (1 EP, 1 vinblastin/ifosfamide/cisplatin [VIP]), and one was treated with whole abdominal radiation. All patients with recurrence were successfully salvaged and become free of disease on last follow-up with median of 5.5 years (range, 1–9 years).

The five-year DFS and OS were 88% (95% confidence interval (CI), 78.2–97.8%) and 95.2% (95% CI, 89.3–100%), respectively (Fig. 1). On univariate analysis, patients who received adjuvant chemotherapy had significant improvement in DFS as compared to patient who did not receive chemotherapy (HR, 0.09; 95% CI, 0.01–0.84; $P = 0.034$). There was no significant difference at outcome found between patients who underwent fertility-sparing surgery or nonconservative surgery (hysterectomy and/or bilateral oopherectomy). Optimal debulking and no lymph node metastasis improved DFS but that were not statistically significant (HR, 0.47; $P = 0.4$ and HR, 0.51; $P = 0.58$, respectively).

Of the 50 patients treated with fertility-sparing surgery, 16 (32%) patients achieved pregnancy resulted in 14 live

Table 2 Characteristics of patients with recurrence

Patient	Age at diagnosis	Type of surgery	Stage at diagnosis	Adjuvant therapy	Site of relapse	Time to relapse (mo)	Salvage therapy	Outcome
1	36	USO	IA	None	Contralateral ovary	7	Tumor resection + EP X4	NED at age 40
2	20	USO	IC	None	Pelvic, peritoneum, retroperitoneal, spleen	9	BEP X5	NED at age 23
3	17	BSO + omentectomy	Unknown	WART	Lung, liver	5	BEPX6	NED at age 24
4	41	TAH + BSO + LNS/D	IIIB	Radiation unspecified	Pelvic, paraaortic lymph node, abdominal mass	7	BEPX4	NED at age 43
5	16	USO + omentectomy	IA	None	Pelvic, retroperitoneal	6	WART	NED at age 51
6	14	USO + omentectomy + LNS/D	IIIC	BEP X3	Contralateral ovary	5	Wedge resection + VIP X4	NED at age 35

USO unilateral salpingo-oopherectomy, *BSO* bilateral salpingo-oopherectomy, *TAH* total abdominal hysterectomy, *LNS/D* lymph node sampling/dissection, *BEP* bleomycin, etoposide, and cisplatin, *VIP* vinblastin, ifosfamide, and cisplatin, *WART* whole abdominal radiation therapy

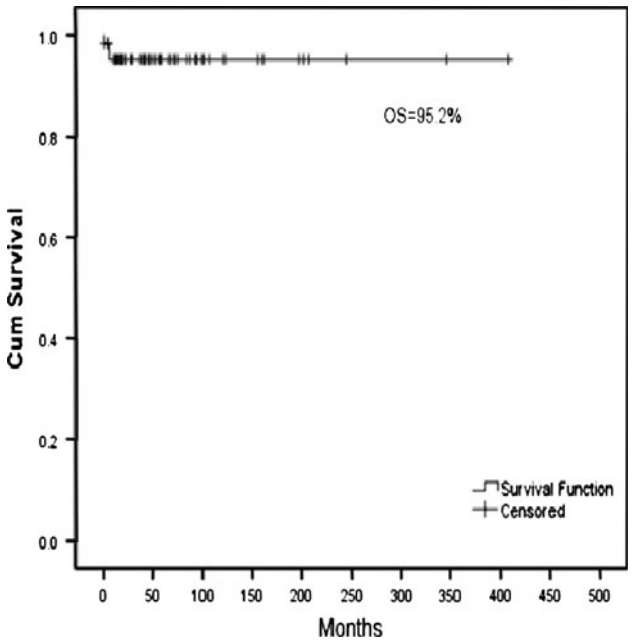

Fig. 1 Overall survival (OS), 65 patients

births. Ten out of the 16 women who conceived were treated with adjuvant chemotherapy (9 BEP, 1 EP), 1 treated with whole abdominal radiation and 5 had no adjuvant therapy.

Discussion

Ovarian dysgerminoma is rare tumor among all ovarian tumors and the majority of cases arise in adolescents and young adults. Patients often present with early stage disease and have excellent long-term outcome. Surgical management is needed for diagnosis, complete surgical staging, and definitive treatment. Given the excellent prognosis and the majority of the patients are young, debate has been raised regarding the extent of surgery and additional therapy required to treat those patients. There is lack of randomized trials due to the rarity of these tumors. This study represents one of the largest series in the literature and provides important information regarding clinical presentation, management of these patients, and the long-term outcome.

The treatment principle for dysgerminoma of the ovary includes surgery with optimal cytoreduction for advanced disease and adjuvant therapy in patients with extraovarian disease. The majority of patients (76.9%) in our study underwent fertility-sparing surgery, and 44 (67.7%) received postoperative chemotherapy or radiotherapy. Only eight (12.3%) patients underwent complete surgical staging including omentectomy, cytology, and lymph node sampling/dissection. Six (9.2%) patients developed recurrence, and all were successfully salvaged and become free of disease on last follow-up. Three patients had relapse at pelvic area and nodal disease, two had contralateral ovary, and one had lung and liver metastasis. Because of successfully salvage therapy at time of recurrence, the question raised in our review and other previous reports [12, 13] about the advantage of early treatment. The long-term effects of adjuvant chemotherapy at young women such as lung toxicity, secondary malignancies should be taken into account when deciding about treatment.

This study confirms an excellent long-term outcome for women with ovarian dysgerminoma. The five-year DFS and OS were 88 and 95%, respectively. In fact, the number of events was too small to detect any difference in overall survival between identified prognostic factors. The fertility-sparing surgery is as effective as radical surgical intervention without compromising the outcome, similar results reported by other studies [9, 14, 15]. Ovarian dysgerminoma is highly sensitive to platinum-based chemotherapy [10, 16]. In our series, adjuvant chemotherapy was associated with significant improvement in DFS (HR, 0.09; 95% CI, 0.01–0.84; $P = 0.034$). As a result, it can be concluded that full complete surgical staging may not play significant role in the outcome of chemotherapy-sensitive tumors. The benefit and the risk of aggressive cytoreductive surgery for metastatic disease must be carefully weighed for this tumor. Even leaving residual disease after cytoreductive surgery in patients with advanced stage, they will have long-term outcome with modern cisplatin-based adjuvant chemotherapy [10, 17]. At our study, of the 18 patients that had residual disease, 16 received chemotherapy, one received radiation, and one died with postoperative complication before adjuvant therapy. Thirteen (72.2%) patients had complete response and remain disease free at the last follow-up.

In our series, all recurrences occurred within 9 months of primary diagnosis. Similarly, Patterson et al. [7] reported all recurrence within 12 months and Danielle et al. [13] reported within 19 months. This raise question about how long patients with ovarian dysgerminoma should be followed up regularly. Only 13 cases reported in a review of the literature to have late recurrence, after 2 years from diagnosis [18].

Sixteen (32%) patients attempted conception, 14 of whom had healthy infants without congenital defects. This confirms the high rate of reproductive function observed in other series. Most women (87%) will resume normal ovarian function after received platinum-based chemotherapy [9, 19, 20]. Older age at initiation of chemotherapy has adverse effect on future gonadal function.

In conclusion, the long-term outcome of patients with pure ovarian dysgerminoma is excellent. Most of the patients are detected at early stage. Complete surgical staging is required for diagnosis, staging, and treatment.

However, the benefits and risks of aggressive cytoreductive surgeries for advanced disease must be carefully weighed for these highly chemotherapy-sensitive tumors. Fertility-preserving surgery can be done safely with favorable outcome. The majority of recurrences occurred early within 2 years of diagnosis and can be successfully salvaged with platinum-based chemotherapy. So that five-year follow-up duration for ovarian dysgerminoma is adequate, since the advantage of longer follow-up is questionable. Good reproductive function can be achieved in patients treated with conservative surgery and adjuvant platinum-based chemotherapy.

Conflict of interest None.

References

1. Talerman A. Germ cell tumours of the ovary. In: Kurman RJ, editor. Blaustein's pathology of the female genital tract. New York: Springer; 1994. p. 849.
2. La Vecchia C, Morris HB, Draper GJ. Malignant ovarian tumours in childhood in Britain, 1962–78. Br J Cancer. 1983;48:363–74.
3. Thomas GM, Dembo AJ, Hacker NF, et al. Current therapy for dysgerminoma of the ovary. Obstet Gynecol. 1987;70:268–75.
4. De Palo G, Pilotti S, Kenda R, et al. Natural history of dysgerminoma. Am J Obstet Gynecol. 1982;143:799–807.
5. Kumar S, Shah JP, Bryant CS, et al. The prevalence and prognostic impact of lymph node metastasis in malignant germ cell tumors of the ovary. Gynecol Oncol. 2008;110:125–32.
6. Dark GG, Bower M, Newlands ES, et al. Surveillance policy for stage I ovarian germ cell tumors. J Clin Oncol. 1997;15:620–4.
7. Patterson DM, Murugaesu N, Holden L, et al. A review of the close surveillance policy for stage I female germ cell tumors of the ovary and other sites. Int J Gynecol Cancer. 2008;18:43–50.
8. Smith HO, Berwick M, Verschraegen CF, et al. Incidence and survival rates for female malignant germ cell tumors. Obstet Gynecol. 2006;107:1075–85.
9. Zanetta G, Bonazzi C, Cantu M, et al. Survival and reproductive function after treatment of malignant germ cell ovarian tumors. J Clin Oncol. 2001;19:1015–20.
10. Gershenson DM, Morris M, Cangir A, et al. Treatment of malignant germ cell tumors of the ovary with bleomycin, etoposide, and cisplatin. J Clin Oncol. 1990;8:715–20.
11. Brewer M, Gershenson DM, Herzog CE, et al. Outcome and reproductive function after chemotherapy for ovarian dysgerminoma. J Clin Oncol. 1999;17:2670–5.
12. Casey AC, Bhodauria S, Shapter A, et al. Dysgerminoma: the role of conservative surgery. Gynecol Oncol. 1996;63:352–7.
13. Vicus D, Beiner ME, Klachook S, et al. Pure dysgerminoma of the ovary 35 years on: a single institutional experience. Gynecol Oncol. 2010;117:23–6.
14. Cicin I, Eralp Y, Saip P, et al. Malignant ovarian germ cell tumors: a single-institution experience. Am J Clin Oncol. 2009;32:191–6.
15. Low JJ, Perrin LC, Crandon AJ, et al. Conservative surgery to preserve ovarian function in patients with malignant ovarian germ cell tumors. A review of 74 cases. Cancer. 2000;89:391–8.
16. Culine S, Lhomme C, Kattan J, et al. Cisplatin-based chemotherapy in the management of germ cell tumors of the ovary: The Institut Gustave Roussy Experience. Gynecol Oncol. 1997;64:160–5.
17. Dimopoulos MA, Papadopoulou M, Andreopoulou E, et al. Favorable outcome of ovarian germ cell malignancies treated with cisplatin or carboplatin-based chemotherapy: a Hellenic Cooperative Oncology Group study. Gynecol Oncol. 1998;70:70–4.
18. Jeyakumar A, Cabeza R, Hindenburg A. Late recurrence in ovarian dysgerminoma with successful response to standard adjuvant chemotherapy: a case report and review of the literature. Gynecol Oncol. 2001;81:314–7.
19. Gershenson DM, Miller AM, Champion VL, et al. Reproductive and sexual function after platinum-based chemotherapy in long-term ovarian germ cell tumor survivors: a Gynecologic Oncology Group Study. J Clin Oncol. 2007;25:2792–7.
20. Tangir J, Zelterman D, Ma W, et al. Reproductive function after conservative surgery and chemotherapy for malignant germ cell tumors of the ovary. Obstet Gynecol. 2003;101:251–7.