Uterine involvement in advanced epithelial ovarian cancer

N. Behtash[1], M. Karimi Zarchi[2], T. Ashraf-Ganjoei[3]

[1]Gynecology Oncology Department, Vali-Asr Hospital, Tehran University of Medical Sciences, Tehran (Iran)
[2]Gynecology Oncology Department, Shahid Sadoughi University of Medical Science, Yazd (Iran)
[3]Gynecology Oncology Department, Kerman University of Medical Sciences, Kerman (Iran)

Summary

Background: With an increasing trend for sparing fertility in gynecologic malignancies, we tried to assess uterine involvement in all stages of epithelial ovarian cancer (EOC) in an evidence-based study. *Method and Material:* From September 1999 to September 2005, 177 patients with epithelial ovarian cancer underwent staging laparatomy in the Gynecologic Oncology Department, Vali Asr University Hospital, Tehran, Iran. Staging data from patient files and pathologic reports were analyzed. *Result:* Of the 177 cases with EOC, 26% of patients were in Stage I, 13.6% Stage II, 53.1% Stage III and 7.3% Stage IV. Uterine Involvement was 17.9% with serosal involvement in 25 cases (78.1%) and myometrial involvement in seven cases (21.9%). Of these cases 84.4% were in Stages III or more and all had omental involvement (Stage IIIa 7.4%, Stage IIIb 14.8%, Stage IIIc 63% and Stage IV 14.8%). Only 15.6% cases of normal appearing omentum had uterine tumoral involvement. *Conclusion:* Only eight cases had myometrial involvement out of 177 cases of EOC (all in Stage III). All the eight patients had omental or gross pelvic tumoral involvement. In this study we found that in the absence of gross pelvic or omental involvement in EOC, there is really none or minimal chance of myometrial involvement. Future multicenter studies with more cases will show whether standard hysterectomy by multiple serosal biopsies could be replaced.

Key words: Epithelial ovarian cancer; Conservative surgery; Uterine involvement; Omental cake.

Introduction

Ovarian cancer is the second most common gynecological cancer and is the leading cause of death from gynecological malignancies [1]. Invasive epithelial ovarian cancer (EOC) accounts for approximately 70% of all ovarian malignancies. The most common type of EOC is serous, which is bilateral in 50% of these patients [2]. At diagnosis about 70% have already spread to the upper abdomen or beyond; however, only 25% of epithelial ovarian cancers are limited to the ovaries at the time of diagnosis [3, 4]. For patients with Stage I to IV disease, conventional therapy consists of total abdominal hypterectomy with bilateral salpingo-oophorectomy and debulking surgery followed by systemic platinum/taxane-based chemotherapy [5, 6].

Ovarian cancer generally affects older women with less than 17% of invasive cancers occurring in women under 40 years of age for whom preservation of reproductive function is an important clinical goal [1]. Ovarian cancer in young women generally compromises definitively reproductive performance with the exception of cases of unilateral salpingo-oophorectomy performed for Stage 1A1 [7].

During the past two decades there has been a trend toward less radical surgery in patients with early-stage breast cancer, cervical cancer, vulvar cancer, and ovarian germ cell malignancies [8]. Benefits of this therapeutic approach include reduced operative morbidity and mortality, enhanced patient self-image, and in the case of ovarian cancer, retention of reproductive function.

The term conservative surgery indicates a surgical procedure that allows removal of the ovarian tumor together with adequate staging. Potential benefits of conservative surgery will include not only the preservation of fertility but also the maintenance of endocrine function. The potential risks are an increase in the probability of recurrence and death, and an increase in further benign surgery. Due to the fear of leaving microscopic contralateral tumor and thereby compromising curability, most authors are reluctant to perform conservative surgery in all other Stage I invasive ovarian cancers. Morice *et al*. showed most recurrent lesions were on the remaining ovary and consequently, the spared ovary was the first recurrence in the majority of patients [6].

In our 12-year experience of EOC surgery, we observed that gross uterine involvement in all stages is relatively uncommon even in the presence of diffuse omental or peritoneal disease. This study is an evaluation of uterine pathologic data in EOC patients during the last six years in our department.

Method and Materials

Subjects for this investigation included all patients with invasive EOC who were treated with radical surgery at Gynecologic Oncology Department of the Vali-Asr University Hospital, Tehran, Iran, between 1999 and 2005. Hospital records and available histological material for each patient were used as sources for patient data. Pathology slides were reviewed by one pathologist to confirm cell type, histologic differentiation, and stage of disease. Tumors were classified histologically according to the World Health Organization (WHO) system and were staged according to the International Federation of Gynecology and Obstetrics (FIGO) system. Statistical analysis of the data

Revised manuscript accepted for publication March 5, 2009

was performed using univariate and multivariate analyses. Proportions were compared using the chi-square statistic from the corresponding contingency tables. Statistical significance was determined at the 0.05 level.

Results

Patient demographics and tumor characteristics in cases studied are shown in Table 1. The mean age of the patients was 47.7 years (range 18-82 years). Of the patients 28.8% were young (≤ 40 years) and 45% of these cases were in Stage I-II.

As shown in Table 2 there was uterine involvement in 17.9%, serosal involvement in 25 cases (78.1%) and myometrial involvement in seven cases (21.9%). Of these cases 84.4% were in Stage III or more and all had omental involvement (Stage IIIa 7.4%, Stage IIIb 14.8%, Stage IIIc 63% and Stage IV 14.8%). Only15.6% cases of normal appearing omentum had uterine tumoral involvement.

Table 1. — *Patient demographics and tumor characteristics in studied cases (N = 177).*

Stage	Percent of patients	Total
I	26	
II	13.6	
III	53.1	
IV	7.3	100%
Cell type		
Serous	74.7	
Mucinous	7.2	
Endometrioid	7.7	
Clear cell	2.1	
Mixed serous mucinus	2.1	
Poorly differentiated adenocarcinoma	5.2	
Other	1	100%

Table 2. — *Characteristics of patients with uterine involvement.*

Stage	No. of patients	No. of patients with uterine involvement
I	42	0
II A	8	1 (12.5%)
II B	13	4 (30.8%)
II C	3	0 (0%)
III A	13	2 (15.4%)
III B	123	4 (25%)
III C	66	17 (25.8%)
IV	13	4 (30.8%)

Discussion

Although the incidence of epithelial ovarian cancer increases with age, reaching a maximum in the seventh decade of life, it does occur in women of childbearing age as well. Approximately 17% of all epithelial ovarian cancer occurs in women ≤ 40 years of age [9].

The standard management of epithelial ovarian cancer involves primary surgery including total abdominal hysterectomy and bilateral salpingo-oophorectomy, tumor debulking, omentectomy, pelvic/paraaortic lymph node biopsies, and multiple peritoneal biopsies and washings of the pelvis and abdomen.This is followed by adjuvant chemotherapy, and second-look surgery in selected cases. Many young women with early-stage ovarian cancer wish to maintain reproductive capability [9].

Fertility-sparing surgery in the face of a frankly malignant epithelial cancer requires formal staging to determine whether conservative surgery is contraindicated (e.g., by occult peritoneal or lymph-node spread). In the absence of such spread following thorough staging, conservative surgical management can be an option for those women who are highly motivated and desire to preserve their childbearing potential. Chemotherapy has been efficient in treating the microscopic lesions. When these Stage IA epithelial cancers are high grade, adjuvant chemotherapy is typically advised [10].

Women with frankly malignant epithelial cancers can be managed with fertility-sparing surgery when disease is confined to one ovary. In such instances the opposite ovary should be inspected carefully for occult metastasis or a synchronous tumor. When the histology is other than mucinous, for which bilaterality is uncommon, bivalving the opposite ovary might be prudent [10]. Colombo *et al*. [11] analyzed the outcomes of 99 women under the age of 40 with Stage I ovarian carcinoma, 56 of whom (including 36 Stage IA, 1 Stage IB, and 19 Stage IC patients) were treated by conservative surgery. Relapse occurred in three Stage IA (grades 1-3) patients, but only one occurrence was in the residual ovary, and that case was remedied by a second operation [10].

In our cases we decided to conserve the uterus. Classical surgical treatment of Stage 1C ovarian cancer includes hysterectomy. The oncological efficacy of removing the uterus in such early cases can reasonably be doubted. Our decision to keep the uterus is to preserve the reproductive performance of these patients. The advantages of removing the uterus are minimal. Serous metastatic microscopic implants can be present but the uterine peritoneum is a small part of all pelvic peritoneum. Endometrial metastasis is infrequent in early stages and may be detected eventually by curettage. Chemotherapy could also be considered efficient in this type of metastasis. Conservation of the uterus for reproductive performance can be proposed in young women without impairing their vital prognosis, thus showing that bilateral salpingo-oophorectomy does not affect uterine function or vascularization.

In conclusion, in early-stage ovarian cancer Stage 1C, conservation of reproductive performance should include uterine conservation, thus permitting subsequent oocyte donation.

References

[1] Brinton L.A., Lamb E.J., Moghissi K.S., Scoccia B., Althius M.D., Mabie J.E., Westhoff C.L.: "Ovarian cancer risk after the use of ovulation-stimulating drugs". *Obstet. Gynecol*., 2004, *103*, 1194.
[2] Gershenson D.M.: "Conservative management of ovarian cancer". *Curr. Probl. Obstet. Gynecol. Fertil*., 1994, 168.
[3] 25th FIGO annual report on the results of treatment in gynecological cancer. *Int. J. Gynecol. Obstet*., 2003, *83* (supp. 1), 124.

[4] Douglas N.C., Fan L., Pothuri B., Herzog T.J., Sauer M.V.: "Fertility sparing therapy for ovarian cancer has inherent risks and benefits". *Arch. Gynecol. Obstet*., 2005, *272*, 304.
[5] Monk B.J., DiSaia P.J.: "What is the role of conservative primary surgical management of epithelial ovarian cancer: the United States experience and debate". *Int. J. Gynecol. Cancer*, 2005, *15* (suppl. 3), 199.
[6] Morice P., Leblanc E., Reyl A., Baron M., Querleu D., Blanchot J. *et al*.: "Conservative treatment in epithelial ovarian cancer: results of a multicentre study of the GCCLCC (Groupe des Chirurgiens de Centre de Lutte Contre le Cancer) and SFOG (Société Française d'Oncologie Gynécologique)". *Human Reproduction*, 2005, *20*, 1379.
[7] Pouly J.L., Janny L., Pouly-Vye P., Canis M., Curé A., Déchelotte P.: "Case report-successful oocyte donation after Stage 1C serous ovarian cancer". *Hum. Reprod*., 1977, *12*, 1589.
[8] Plante M.: "Fertility preservation in the management of gynecologic cancers". *Curr. Opin. Oncol*., 2000, *12*, 497.
[9] Schilder J.M., Thompson A.M., DePriest P.D., Ueland F.R., Cibull M.L., Kryscio R.J. *et al*.: "Outcome of reproductive age women with stage IA or IC invasive epithelial ovarian cancer treated with fertility-sparing therapy". *Gynecol. Oncol*., 2002, *87*, 1.
[10] Berman M.L.: "Future directions in the surgical management of ovarian cancer". *Gynecol. Oncol*., 2003, *90* (suppl.), S33.
[11] Colombo N., Chiari S., Maggioni A., Bocciolone L., Torri V., Mangioni C., Williams T.J.: "Controversial issues in the management of early epithelial ovarian cancer: conservative surgery and role of adjuvant therapy". *Gynecol. Oncol*., 1994, *55*, S47.

Address reprint requests to:
N. BEHTASH, M.D.
Gynecologic Oncology Department
Vali-e-Asr Hospital, Imam Khomeini Hospital Complex, Tehran (Iran)
e-mail: nadbehtash@yahoo.com