

Borderline ovarian tumors, fertility-sparing surgery and pregnancy outcome

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Abstract. – BACKGROUND: Borderline ovarian tumors (BOTs) represent a type of epithelial tumors having a biologic intermediate behavior between clearly malignant and straight benign tumors. Most of BOTs interest women during fertile age, for which it is necessary to consider a fertility sparing surgery.

AIM: To evaluate the clinical aspects and pregnancy rate of women affected by borderline ovarian tumors who have undergone fertility sparing surgery.

PATIENTS AND METHODS: A study of 22 patients affected by BOTs who have been treated with a fertility sparing surgery was conducted between January 2005 and October 2011 at Sant'Andrea Hospital, "Sapienza" University of Rome. The patients' characteristics analyzed were: age, histological type, tumor size, adnexal surgery, pre-operative serum CA-125, diagnostic circumstances, number of patients who became pregnant and number of overall pregnancies.

RESULTS: Among the 22 patients treated with a fertility sparing surgery, only sixteen wanted to get pregnant. Eleven patents out of 16 accomplished it. The pregnancy rate was 68.7%.

CONCLUSIONS: Fertility sparing surgery can be considered a safe procedure for young women affected by borderline ovarian tumors.

Key Words:

Borderline ovarian tumors, Fertility sparing surgery, Pregnancy outcome.

interest women aged since 30 to 50 years old and they represent the 10-15% of all epithelial ovarian tumors³. Prognosis is better than their malignant counterpart with reference to the stadium disease. After 10 years, disease free-survival is: 99% for stadium I, 98% for stadium II, 96% for stadium III, 77% for stadium IV⁴⁻⁵. The following features histologically define BOTs: cellular stratification, nuclear atypia, mitotic figures in absence of stromal invasion. The histological subtypes are: serous BOT, mucinous BOT, Brenner BOT, clear cells BOT, endometrioid BOT⁶⁻⁷. Guidelines for surgical treatment of BOTs are similar to those for ovarian cancer and they include: hysterectomy, bilateral salpingo-oophorectomy, omentectomy, four quadrant peritoneal washing, multiple biopsies (including pelvic and peri-aortic lymphonode sampling) and tumor debulking. Since BOTs interest also young women of reproductive age, it would be appropriate to consider fertility sparing surgery. Fertility sparing laparoscopic surgery consisted in: unilateral cystectomy or unilateral salpingo-oophorectomy with a possible contralateral cystectomy or bilateral cystectomy⁸⁻⁹.

The purpose of our study is to evaluate the different issues of the BOTs and the pregnancy rate of women in fertile age who have undergone conservative surgery.

Introduction

Borderline ovarian tumors (BOTs) represent a type of epithelial ovarian tumor, having a biologic intermediate behavior between the clearly malignant ovarian tumor and straight benign tumor. FIGO Committee¹ defined this tumor as a "low malignant potential tumor" in 1971, while WHO² defined it as BOTs in 2003. Most of BOTs cases

Patients and Methods

This study concerned 22 cases of BOTs identified between January 2005 and October 2011 at the Sant'Andrea hospital of Rome. The histological diagnosis of BOTs has been carried out by the same pathologist and staged according to FIGO criteria; the histological criteria used were the following: cellular stratification, nuclear

atypia, and mitotic figures in absence of stromal invasion. The characteristics of patients evaluated were: age, histological type, tumor size, adnexal surgery, pre-operative serum CA-125, diagnostic circumstances, number of patients who became pregnant and number of overall pregnancies. All the patients have been subjected to a fertility sparing surgery, consisting of: unilateral salpingo-oophorectomy (USO) or USO and unilateral cystectomy (UC). All patients underwent surgery for the first time. The surgery procedure has been completed with an accurate staging including: peritoneal washing with cytology, multiple peritoneal biopsy and, for mucinous BOT, appendectomy. In addition, the post-surgical follow-up included: clinical examination, trans-vaginal ultrasonography and serum CA-125 levels. They were carried out every three months for the first two years, every 6 months for the next three years and then annually.

Results

Twenty-two patients, aged since 25 to 37 years old, met our inclusion criteria. All the women enrolled were Italian with the only exception of a South American woman. Table I shows the characteristics of patients with BOTs. The symptoms reported from our patients were: persistent pelvic

pain, in 81.8% of cases and pelvic pain associated to abdominal distension and persistent pollachiuria (only one patient). Three patients out of twenty-two were asymptomatic. Pre-operative CA-125 level was systematically dosed in all patients: in 13 women out of 22 (59.1%) the value was > 35 U/I, while in 9 women out of 22 (40.9%) was < 35 U/I. The maximum value was 140 U/I. The 77.2% of patients have been treated with USO because the stage was Ia, while five patients (22.7%) with stage Ib have been treated with USO and UC. The 68.2% of patients (15/22) were affected by serous type BOT while the other 7 (31.8%) had a mucinous type BOT. All patients with mucinous type underwent appendectomy for a complete staging. The median tumor size was 6 cm (range 4-17 cm): in 18 patients was < 10 cm while in 4 patients was $>$ than 10 cm. After surgery, 16 patients expressed the desire to conceive and 11 of them (68.7%) became pregnant. Table II summarizes the pregnancy outcomes.

The mean period of follow-up to pregnancy was 18.5 months (range 13-24 months). The total amount of pregnancies was sixteen: 14 patients delivered with normal spontaneous vaginal delivery (NSVD), while 2 patients had spontaneous abortion (SA).

Discussion

The borderline ovarian tumors are common in young women and according to the literature, the median age of our series was 31.8 years at the time of diagnosis. Romagnolo et al¹⁰, reported in their multicentric study, that the youngest patient was 20 years old and 53 out of 113 (46.9%) women were younger than 40 years. In our series, the main histological type was serous BOT (68.2%), unlike the situation in Western Countries: in fact in the study of Park et al¹¹ and in the study of Song et al¹² the percentages of mucinous BOT were the 68% and the 59.4% respectively. The standard treatment for BOTS follows FIGO guidelines for invasive ovarian carcinomas: total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, four quadrant peritoneal washing, multiple biopsies (including pelvic and peri-aortic lymphonode sampling) and tumor debulking. Appendectomy is recommended for mucinous BOT. The fertility-sparing surgery is an acceptable option for patients with stage I and in women of reproductive age. Con-

Table I. Patient characteristics.

No. of patients	22
Age (years), (mean $\pm$ SD)	30.5 $\pm$ 3.7
Histological type	n (%)
Mucinous	7/22 (31.8%)
Serous	15/22 (68.2%)
Tumor size (cm)	n (%)
< 10 cm	18/22 (81.8%)
> 10 cm	4/22 (18.2%)
Adnexal surgery	n (%)
Unilateral salpingo-oophorectomy	17/22 (77.2%)
Unilateral salpingo-oophorectomy + unilateral cystectomy	5/22 (22.7%)
Pre-operative serum CA 125	n (%)
> 35 U/I	13/22 (59.1%)
< 35 U/I	9/22 (40.9%)
Diagnostic circumstances	n (%)
Large pelvic mass	3/22 (13.6%)
Pelvic pain	18/22 (81.8%)
Routine gynecologic exam	1/22 (4.5%)
Pregnancy outcomes	n (%)
Number of overall pregnancies	16
Number of pregnant patients (Pregnancy Rate)	11/16 (68.7%)

Table II. Pregnancy outcome after conservative treatment.

Case	Age	Pregnancy outcome	Histological type	Adnexal surgery	Pre-operative CA-125 (U/l)	FIGO stage	Months between surgery and pregnancy
1	32	2 X NSVD1 SA	Serous	USO + UC	16.30	IB	15
2	25	1 NSVD	Serous	USO	34.50	IA	24
3	29	1 NSVD1 SA	Serous	USO + UC	140	IB	22
4	37	2 X NSVD	Mucinous	USO	16	IA	14
5	27	1 NSVD	Mucinous	USO	135	IA	24
6	34	2 X NSVD	Mucinous	USO + UC	66.10	IB	16
7	33	1 NSVD	Serous	USO + UC	25	IB	18
8	36	1 NSVD	Serous	USO	90	IA	13
9	29	1 NSVD	Serous	USO	110	IA	20
10	30	1 NSVD	Serous	USO	74	IA	18
11	31	1 NSVD	Serous	USO	20	IA	14

NSVD: normal spontaneous vaginal delivery. SA: Spontaneous abortion; USO: Unilateral salpingo-oophorectomy; UC: Unilateral cystectomy.

servative surgery may consist in unilateral cystectomy, bilateral cystectomy or unilateral salpingo-oophorectomy with possible contralateral cystectomy. Song et al¹² have demonstrated that the recurrence ratio is higher in the patients submitted to a fertility sparing surgery (7.7%), than in the patients submitted to a radical treatment (4.9%). Whereas, Park et al¹¹ have shown that the recurrence ratio was similar between the two groups: 4.9% in the patients underwent a radical treatment, 5.1% in the patients underwent a fertility sparing surgery. The principal aim of conservative surgery is to preserve the fertility of the women willing to have childbearing. In our series, 16 patients attempted to be pregnant and 11/16 (68.7%) accomplished it after a fertility sparing surgery: the pregnancy rate was 68.7%. This result is lower compared to the report of Song et al¹² (pregnancy rate: 88%) while is higher than pregnancy rate of Kanat-Pektas et al (52.3%)¹³. Women who conceived were younger than women who did not conceive: in the study of Fauvet et al¹⁴ the conception percentage was 42% in patients under 35 years old, 22% in patients between 35 and 40 years old, 0% in patients older than 40 years. In our study the pregnancy rate in patients under 35 years old was 81.8% while in patients between 35 and 37 years old was 18.18%. It can be stated that half of the patients undergone conservative treatment became pregnant, except for patients older than 40 years, for who the conception rate is very low. We compared the surgical procedures (USO or USO + UC) with the period (months) between

surgery and pregnancy and the pregnancy rate: in patients underwent USO the median was 18 months (range 15-22) and pregnancy rate was 60%, while for women underwent USO+UC the median was 17 months (range 14-24) and pregnancy rate was 40%. In the study of Boran et al¹⁵ in the group of patients underwent USO, the median period between the surgical treatment and the pregnancy was 9.5 months (range 3-36) and pregnancy rate was 60%, while in patients underwent UC the median period was 26 months (range 4-41) and the pregnancy rate was 40%.

Conclusions

The Borderline Ovarian Tumors affect young women for who it is necessary to consider a conservative treatment. Fertility sparing surgery is the best option to preserve childbearing capacity because it does not condition fertility and pregnancy rate. Our study confirms that fertility sparing surgery can be considered a safe treatment in patients with stage I borderline ovarian tumor who desire future childbearing. After the conservative surgical treatment, pregnancy outcomes are promising and most pregnancies are achieved spontaneously. Once reproductive program is finished, removing the rest of the ovary remains still an uncertain point.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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