Fertility after ovarian cancer treatment

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Summary: Considering the important improvement of surgical techniques and chemotherapy in the last few years ,it is possible today, in selected cases of patients previously treated for ovarian cancer, to support their desire for motherhood, thus improving the quality of life for them. The major problem for the Gynecologic Oncologist in treating young women for ovarian tumour is the lack of statistically significant experience world-wide, because of the very few cases in which the reproductive function is preserved, and pregnancy is subsequently possible. In this report the problem is discussed, and the results obtained in our Institute are presented.

Key words: Ovarian cancer; Fertility; Therapy.

INTRODUCTION

Still today, tumours of the ovary are considered one of the major problems facing Gynecologic Oncologists, because of the difficulties of early diagnosis of their invasiveness, of the cost of chemo-surgical treatments, and because of the very poor prognosis ([1, 2]).

"Cure without deformity or loss of function must ever be the highest ideal of surgery", Victor Bonney said.

Gynecologists have recognized the importance of fertility and of endocrine function and have striven to preserve both as the mark of their speciality. However, these functions, compared to survival, are obviously of lesser importance ([3]).

For all these reasons, whenever we consider the possibility of pregnancy in patients affected by these tumours, we have to solve some problems:

1) It is essential, particularly when the woman is young, and only one ovary is affected by neoplasia, to make an early diagnosis ([4, 5]). Moreover, the incidence of tumours of the ovary increases with age, except for non-epithelial neoplasias, which are rare and more frequent in fertile females ([4, 5]).

2) Patients affected by neoplasia limited to one ovary and who ask for preservation of their reproductive function present us with a dilemma ([3]). In fact we must consider both the priority of the prognosis and the patient's desire for motherhood. Munnell ([3]), in retrospective study published in 1968, reported 144 patients with unilateral ovarian carcinoma treated with bilateral salpingo-oophorectomy and hysterectomy, compared with 46 patients in whom the controlateral, apparently normal ovary, was preserved. Five years survival rate was slightly higher in the radically treated group, but the difference was not statistically significant, even considering the different histological type and degree of malignancy. Six conservati-

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vely treated patients subsequently had at least 10 successful pregnancies.

On the basis of these considerations, in the last decade a non demolitive surgical approach was preferred, i.e., limited to the removal of the affected ovary with biopsy of the controlateral one, meticulous surgical staging with exploration and frozen biopsies of pelvic organs and washings of Douglas peritoneum for peritoneal cytology and, according to some Authors, omentectomy ([6, 7, 8]). This approach was possible by using combination chemotherapy associated with surgery, according to protocols adopted from time to time ([9, 10]).

3) The third factor we must consider is the possible effect of chemotherapy both on fertility and on determining teratogenic damage of the developing organism, whether the drug administration is performed before or during the pregnancy.

Reviewing current reports and considering our clinical experience, it may be suggested that, in spite of the problem mentioned, it is rational, in selected cases, to support the patient's wish to conceive even though affected by ovarian tumour.

In 1980 Julie Blatt reported a case series of 58 women treated in fertile age for different tumours (not ovarian, but Hodgkin's lymphoma, Ewing etc.). Forty women became pregnant during or after chemotherapy. There were 12 abortions (2 voluntary) and 28 live births. The follow-up of the offspring revealed no major malformations. In addition, growth, development and school performance were normal ([11]).

The major problem for an Oncologist in treating with chemotherapy a young women affected by ovarian tumour, is the lack of statistically significant experience world-wide because of the very few cases treated retaining the reproductive function with subsequent pregnancy.

The chemotherapeutical regimens are different for different Authors and from the same Author for different patients. The most widely used combinations are Vincristine - Adriamycine - Cyclophosphamide, followed by Vincristine - Bleomycine - Cisplatin and then Mitomycine - Methotrexate - Dactinomycine - 5Fluorouracil.

Regarding this problem, Forney ([10]) reported a successful pregnancy following combination chemotherapy and removal of an ovarian endodermal sinus tumour. Ward ([12]) reported another case of term pregnancy, Sessa observed two pregnancies out of 13 patients treated for ovarian cancer ([8]). Concerning germ cell tumours, Schwartz ([14]) has referred two term pregnancies in a patient treated with conservative surgery and combination chemotherapy; Pektasides ([15]) observed 7 pregnancies out of 17 patients treated, and Gershenson ([16]) 22 pregnancies in 11 cases. Finally, Schneider ([5]) and Javaheri ([17]) both report term pregnancies in women affected by immature teratoma of the ovary.

CASE SERIES ANALYSIS

In our case series, out of 548 primary ovarian tumours observed in our Institute from 1963 to 1990, only 145 patients were in stage 0 or in stage A (limited to the ovary) and 141 with monolateral neoplasia (Tabs. 1, 2). Among these cases, 22 patients aged less than 45 years were treated with conservative surgery (Tab. 3).

Only one of the patients who received chemotherapy became pregnant. She was

Table 1. – *Primary ovarian cancers: case series.*

OVARIAN CANCER (case from 1963 to 1990)	
Epithelian tumors	471
Non epithelial tumors	77
Total	548

Table 2. –*Ovarian tumors: Stage distribution.*

	O	A	B	M
Epithelial tumors	12	94	334	31
Non epithelial tumors	–	39	37	1
Total	12	133	371	32

Table 3. – *Managing of limited ovarian tumors.*

Monolateral limited tumors (Stage O-A)
141
↓
Conservative treatment
28
↓
Patients < 45 yrs Age
22
Surgery 9 | Surgery + Chemotherapy 13

treated with 5 cycles of Adriamycine and Cyclophosphamide. Successively she had a second look laparotomy because of positive peritoneal cytology at first operation; at second look a biopsy on the residual ovary resulted negative.

Six other patients became pregnant after the treatment for ovarian cancer and they received only surgical therapy (Tab. 4). No malformations were present in the newborns.

Table 4. – *Pregnancies after treatment (7 cases).*

N. patients	Treatment	Histotype	N. pregnancies
1	Surg. + Chemoth.	Mucinous adenoca.	1
6	Surgery	- Dysgerminoma	1
		- Serous adenoca.	2
		- Mucinous adenoca.	1
		- Adenocarcinoma	1
		- Sero-papilliferous a.	2
		- Mucinous adenoca.	1

In order to complete our case series analysis we would like to report a patient treated with conservative surgery for a serous-papilliferous adeno-carcinoma stage B3, diffused to pelvis, (controlateral negative ovary); she had adjuvant post-surgical chemotherapy and afterwards two pregnancies.

CONCLUSIONS

These data confirm the difficulty, or even impossibility, of calculating the statistical probability of successful pregnancy in these cases and of establishing the best clinical management. This is because the case reports are limited or, even worse, concern histotypes with differing biological features; consequently also the chemotherapeutic regimens are different and cannot be easily compared.

We think that when an ovarian tumour, stage A (limited to the ovary), monolateral, is presented in a young woman who wishes for pregnancy and is willing to accept the risk of recurrence, we must defer to her wishes. In fact today we have the possibility of performing an accurate follow-up of the patient by ultrasonography, computerized axial tomography, magnetic resonance.

We believe that the loss of fertility in a young woman leaves a mark on her life and permanently reduces its quality.

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