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ORIGINAL ARTICLE

A retrospective analysis of women's chances to become pregnant after completion of chemotherapy: a single center experience

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Summary

Purpose: *With the improvement in anticancer therapies, the survival of women with malignancies has increased and infertility may affect the quality of life of premenopausal women, who experience temporary or permanent amenorrhea due to chemotherapy. The aim of this study was to review the rate of pregnancies among women with malignancy previously treated with chemotherapy.*

Methods: *We retrospectively recorded 317 women younger than 40 years of age who were treated with chemotherapy (and a number of them with additional radiotherapy/RT) due to several malignancies between 2007-2010. The patients who got pregnant after stopping chemotherapy and during follow-up were analyzed.*

Results: *Among women with breast cancer (n=116), malignant lymphoma (n=85), ovarian cancer (n=26) and colon cancer (n=90), 20 got pregnant after a median 22.9 months (range 10.7-96.5) from the end of chemotherapy. Childbearing was uneventful and newborns were healthy.*

Conclusion: *Women who had previously received chemotherapy for malignancy can get pregnant and deliver healthy newborns.*

Key words: chemotherapy, fertility, malignancies, pregnancy

Introduction

Nearly 20-30% of malignant tumors are seen in women younger than 45 years. Chemotherapy-induced amenorrhea is defined as cessation of menses for more than 12 months. Menstruation return after 1 year of amenorrhea in less than 15% of women [1]. The risk of ovarian failure depends on patients' age and the type and dosage of the chemotherapeutic agents administered [1]. According to the literature, about 10% of breast cancer patients can get pregnant, which is half of the pregnancy rate seen in age-matched groups of women without breast cancer [2].

The optimal timing of pregnancy after the completion of chemotherapy is unclear. It depends on the type of malignancy, prognosis, and stage of disease. It is recommended to delay conception for 2-3 years after the end of chemotherapy [1].

In the current study we reviewed patients who had been treated with chemotherapy for several malignancies and investigated the effects of the mostly used chemotherapy regimens on fertility.

Methods

This retrospective analysis included 317 premenopausal female patients, with 116 (36.5%) of them having breast cancer, 85 (26.8%) malignant lymphomas 26 (8.2%) ovarian cancer and 90 (28.3%) colon cancer. All of them were treated and followed-up at Dr. Lutfi Kirdar Kartal Education and Research Hospital, Department of Medical Oncology, between 2001 and 2009. Twenty (6.3%) of them became pregnant after the end of chemotherapy. Patients with breast, ovarian and colon cancer were administered adjuvant chemotherapy and some of them had additional RT. It was not known how many of them wanted to get pregnant or

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not after the end of adjuvant chemotherapy±RT. Six of the 20 patients had breast cancer, 7 malignant lymphoma, 4 ovarian cancer and 3 colon cancer. Information regarding patient and newborn characteristics including mother's age, tumor type, stage of disease, the type of chemotherapy, delivery, fertility after completion of chemotherapy, newborn weight, congenital anomalies, and prematurity were obtained from the medical records of the patients after informed consent was taken. The state of children was evaluated by taking their history from the mothers who were followed-up at the Oncology department. Median follow-up time of patients who got pregnant after chemotherapy±RT was calculated from the end of treatment to the last follow-up visit.

Results

The median patient age that became pregnant was 25.5 years (range 16-37). Their characteristics are shown in Table 1.

Modified radical mastectomy and axillary lymph node dissection (MRM-ALND) was carried out for breast cancer patients. Four patients had TNM stage IIA, one stage IIB and the other one stage IIIB breast cancer. Adjuvant chemotherapy including anthracycline (FEC: 5-FU, epirubicin, cyclophosphamide) was administered to all of them, and one patient received docetaxel combined with FEC. Because of axillary nodal involvement all of them were treated with adjuvant RT and 4 of them received also tamoxifen as adjuvant hormonotherapy.

Three patients with stage IIB and IIIB Hodgkin's lymphoma (HL) were treated with a median of 6 cycles (range 4-6) of ABVD combination chemotherapy (doxorubicin, bleomycin, vinblastine, dacarbazine) and 4 patients with stage IIA, IIIB, and IV non-Hodgkin's lymphoma (NHL) received CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone; 2 patients) and rituximab-CHOP (R-CHOP; 2 patients) for a median of 6 cycles (range 6-8). Additional RT was given to 2 stage II HL and one stage IIA NHL patients after the completion of chemotherapy.

Ovarian cancer patients had undergone fertility-sparing surgery with unilateral salpingo-oophorectomy. Two of them had stage IA, grade I epithelial ovarian cancer and were followed-up without chemotherapy. The remaining 2 patients with stage I and III ovarian dysgerminoma were treated with BEP combination chemotherapy (bleomycin, etoposide, cisplatin) after fertility-sparing surgery.

Table 1. Patient characteristics

Cases	*Malignancy*	*Stage*	*Age (years)*	*CT*	*RT*	*Operation*	*Fetal weight (grams)*	*Patient age during pregnancy*	*Delivery*	*Pregnancy after treatment (mo)*	*OS (mo)*
1	breast cancer	IIA	28	FEC	Yes	MRM+ALND	3620	36	N	108	120
2	breast cancer	IIB	27	FEC	Yes	MRM+ALND	3380	35	N	96	120
3	breast cancer	IIA	35	FEC	Yes	MRM+ALND	3760	36	N	6	40
4	breast cancer	IIA	32	FEC	Yes	MRM+ALND	3800	38	N	36	48
5	breast cancer	IIA	33	FEC	Yes	MRM+ALND	3300	34	C/S	5	18
6	breast cancer	IIIA	37	FEC-T	Yes	MRM+ALND	3400	38	C/S	18	42
7	HL	IIB	30	ABVD	Yes	–	3300	31	N	12	145
8	HL	IIB	32	ABVD	No	–	3200	34	N	22	22
9	HL	IIIB	22	ABVD	Yes	–	3500	30	N	87	91
10	NHL	IIA	34	R-CHOP	Yes	–	3500	36	N	30	44
11	NHL	IIIB	25	R-CHOP	No	–	3500	26	N	15	22
12	NHL	IIIB	16	CHOP	No	–	3000	20	N	43	60
13	NHL	IV	37	CHOP	No	–	3400	38	N	21	42
14	ovarian cancer	IIIB	24	BEP	No	ULSO	3150	25	N	27	10
15	ovarian cancer	I	20	–	No	ULSO	3550	21	N	16	14
16	ovarian cancer	I	26	–	No	ULSO	3780	27	C/S	31	17
17	ovarian cancer	II	28	BEP	Yes	ULSO	3300	31	N	49	42
18	colon cancer	I	24	–	No	hemicolectomy	3450	26	N	30	33
19	colon cancer	III	17	FUFA	Yes	hemicolectomy	3500	23	N	71	87
20	colon cancer	III	36	FLOX	Yes	hemicolectomy	3450	38	C/S	32	35

NHL: non -Hodgkin's lymphoma, HL: Hodgkin's lymphoma, CT: chemotherapy, FEC: 5-FU+epirubicin+ cyclophosphamide, FAC: 5-FU+adriamycin+cyclophosphamide, AC: adriamycin+cyclophosphamide, ABVD: adriamycin+bleomycin+vinblastine+dacarbazine, CHOP: cyclophosphamide+adriamycin+vincristine+prednisolone, R-CHOP: rituximab+CHOP, RT: radiotherapy, BEP: bleomycin+etoposide+cisplatin, MRM-ALND: modified radical mastectomy+ axillary lymph node dissection, ULSO: unilateral salpingo-oophorectomy, C/S: cesarian section, N: normal vaginal delivery, OS: overall survival, mo: months

Three patients with colon cancer underwent hemicolectomy; one was diagnosed as carcinoid tumor and the other 2 had adenocarcinoma. Because both patients with colon adenocarcinoma had stage III disease, they received FLOX (5-fluorouracil-oxaliplatin combination) and FUFA (5 fluorouracil-folinic acid) as adjuvant chemotherapy.

The median gestational age at delivery was 37 weeks (range 36-41). The median newborn weight was 3450 g (range 3000-3800). No congenital malformations were detected in any newborn. No stillbirths, miscarriages or perinatal death occurred. After completion of the adjuvant treatments, patients became pregnant after a median of 22.9 months (range 10.7- 96.5). The pregnancies ended as normal vaginal delivery in 16 mothers (80%) and with cesarean sections in 4 (20%) of them. Routine follow-up was performed every 3 months and at a median of 43 months (range 12-145) post-labor the patients remain free of disease.

Discussion

About 10% of women diagnosed with breast cancer can get pregnant and this is the half of the pregnancy rate seen in age-matched groups without breast cancer [2]. In our study, the pregnancy rate of breast cancer patients was 5%. Meirow reported that alkylating agents had the greatest risk for inducing ovarian failure among all chemotherapeutic agents [3]. Because the majority of our patients had breast cancer or malignant lymphoma (67%), they received anthracycline-based chemotherapy regimens.

The risk of chemotherapy-induced amenorrhea depends on the patients' age, the chemotherapeutic agents used and the total cumulative dose administered [1]. Older women bear higher risk for chemotherapy-induced amenorrhea because the primordial follicle reserve declines with age [1]. Only 2 of our patients were 37 years old, while all of the others with breast cancer were below 35 years of age.

In the present study, all patients with breast cancer received FEC combination chemotherapy. It has been reported that addition of taxanes to breast cancer chemotherapy didn't play a role in amenorrhea [4]. In our study, with only one patient with breast cancer treated with docetaxel (plus FEC), no conclusion can be drawn. Tamoxifen may cause menstrual disorders or may also stimulate ovulation [2]. In this study, 6 breast cancer patients treated with anthracycline-based chemotherapy became pregnant after a median of 27 months (range 5 -108) after chemotherapy.

Dann et al. analyzed ovarian function of 13 patients with NHL who were treated with 4 cycles of intensified CHOP combined with D-TRP6-GnRH analogue. In a median follow-up of 70 months, 12 patients retained fertility and 8 of them conceived spontaneously [5]. None of our patients received GnRH analogue during chemotherapy and our 4 NHL patients became pregnant spontaneously after they had received standard CHOP or R-CHOP therapy. In a retrospective analysis, 20 out of 103 women treated for HL could get pregnant [6].

Fertility-sparing surgery is a reasonable alternative treatment for young women with stage IA, grade I epithelial ovarian cancer desiring fertility preservation with similar recurrence-free survival compared with standard surgery [7]. Both of our epithelial ovarian cancer patients with median age of 25 years (range 20-26) underwent fertility-sparing surgery without chemotherapy. The other two patients with stage II and IIIB ovarian germ cell tumors were treated with BEP chemotherapy after unilateral salpingo-oophorectomy. In a study, among 52 women with ovarian germ cell tumors 41 underwent fertility-conserving surgery and pregnancy was achieved in 12 of them who attempted conception after BEP chemotherapy without administration of estroprogestative drugs [8].

In a study by Strong et al., less than 20% of women of childbearing age who were diagnosed with colorectal cancer had documentation of counseling for post-treatment infertility and 38% of patients had documented difficulty with pregnancy [9]. In the present study, 3 of 90 colon cancer patients got pregnant after colon cancer treatment. Two of them had received adjuvant 5FUFA and FLOX, respectively.

In our series, 20 patients with a median age of 27 years (range 16-37) were treated for breast cancer, HL and NHLs, ovarian cancer and colon cancer and conceived after a median of 22.9 months (range 10.7-96.5) after the end of adjuvant chemotherapy. Hickey et al. indicated that generally the vast majority of recurrences for all kinds of cancer occur after 2 years of follow-up, so it is recommended to attempt conception after 2 years from the completion of chemotherapy [2]. In our study the earliest pregnancy took place in a breast cancer patient in the 5th month after the end of chemotherapy. In concordance with the literature [10], all children born by mothers who had received chemotherapy were healthy without congenital anomalies.

Infertility after chemotherapy is important because it may affect the patients' quality of life. Despite the retrospective nature of our study and the small number of patients suffering from different malignancies, it is worth noticing that women with cancer who receive chemotherapy may remain fertile, have normal pregnancies and deliver healthy newborns.

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