Pregnancy after Cancer Treatment and Pregnancy Associated Cancer: A Single Center Experience with 96 Cases

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ABSTRACT

OBJECTIVE: The objective of our study was to evaluate our experience on pregnancies after cancer treatment and pregnancy-associated cancer.

STUDY DESIGN: The clinical records of 96 pregnant women including previously received treatment for cancer and association of cancer with pregnancy who admitted to our department were enrolled between 2002 and 2012. Demographics, pregnancy outcomes, maternal and fetal complications, perinatal outcomes, cancer types and treatments performed were evaluated.

RESULTS: The study group was consisting of 96 cases, 59 out of 96 were cancer survivors and 37 were pregnancy-associated cancer patients. Of those thirty seven, 25 were synchronous with the pregnancy and 12 were metachronic. Pregnancies resulted in 77 healthy newborns, 7 abortions and 12 medical terminations. The most common type of cancer was the breast cancer in 25 patients, followed by thyroid, leukemia, osteosarcoma, lymphoma and ovarian cancer. Patients were treated for their cancer with different modalities including surgery, chemotherapy and radiotherapy. We encountered maternal mortality in 8 cases, all occurred after delivery.

CONCLUSIONS: Since management of a pregnancy of a cancer survivor and pregnant woman with cancer a hard work, multidisciplinary approach involving gynecologists, pediatricians, oncologists is essential. Interval between cancer and pregnancy and timing of initiation of therapy in cases of pregnancy associated cancer are important issues in the perspective of fetal/neonatal well-being.

Keywords: Cancer, Metachronous tumor, Synchronous tumor

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Introduction

Cancer is the second most common cause of death among women in the childbearing period worldwide.[1] With the raise in participation of women in the society, the age of childbearing is postponed, contributing to the increase of pregnancies associated to cancer.[2] The most common malignancies in women 15 to 34 years old are malignant melanoma, breast cancer, leukemia, cervical cancer, central nervous system tumors, and non-Hodgkin lymphoma. Lung, colorectal, and ovarian cancer also are common in 35-to 54-year-old women.[3]

Pregnancy-associated cancer (PAC) is defined as a malign neoplasm diagnosed during or within 12 months after pregnancy. Women with cancer at the time of the pregnancy were classified as synchronic and those within 12 months after birth as metachronic.[4] PAC has been reported in 0.02-0.1% of all pregnancies and it is estimated that 1/1.000-1.500 births are associated to a malignancy in the mother.[1] When we evaluate issue of pregnancy after cancer treatment, reports dealing with this subject are limited. This may be because the proportion of reproductive aged women with cancer is relatively low. In addition, cancer survivors may not attempt pregnancy, due to fertility problems and/or fear of recurrence. Beside this, the possible hazardous effect of exposure to chemotherapeutics and pelvic radiation on the future pregnancies and fetuses is a concern. The multidisciplinary approach is mandatory for optimal results for both PAC and pregnant of cancer survivors.

The objective of our study was to evaluate our experience on pregnancies after cancer treatment and PAC, describing the

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demographic characteristics, type of cancer, treatments performed and maternal/fetal outcomes.

Material and Method

In this study, a retrospective analysis was carried out 96 pregnant women including previously received treatment for cancer and with association of cancer during pregnancy who admitted to our department. We reviewed prenatal data and postnatal medical records of these patients that were diagnosed cancer between January 2002 and September 2012. Of those 96 cases, 59 were cancer survivors and 37 were PAC patients. Of those thirty seven, 25 were synchronous with the pregnancy and 12 were metachronic. Clinical characteristics including demographics, pregnancy outcomes, type of cancer, treatments performed, oncological outcome, maternal and fetal complications and perinatal outcomes including gestational age, birth weight and perinatal mortality were evaluated. Therapeutic abortion is the termination of a pregnancy to preserve the maternal health before 22 completed weeks of pregnancy. Preterm delivery is defines as birth before 37 weeks of gestation. Late preterm delivery is birth between 34 and 37 weeks of gestation. Low birth weight is defined as a birth weighting less than 2500 gr. Statistical analysis was performed with the SPSS package 17 edition.

As this study represents a retrospective chart review, the Local Ethical Committee permission was not sought. However, all patients signed an informed consent that allows our institution to use their clinical data.

Results

During the period of 2002-2012, 96 pregnant patients were enrolled to our study group. Mean age of the study group was 31.4±5.7 (range 19-43). 59 of them (61,5%) were pregnant after treatment for cancer, 25 tumors (26,0%) were synchronous with the pregnancy (26,0%) and 12 tumors (12,5%) were metachronic. The most common type of cancer was the breast cancer in 25 patients, followed by thyroid, leukemia, osteosarcoma and ovarian cancer. In the breast patients all of them were invasive ductal carcinoma and in thyroid all of them were papillary type thyroid carcinoma. In the ovary group 4 were diagnosed as borderline epithelial carcinomas and treated with fertility sparing surgery before pregnancy, the other 2 were diagnosed as malign neoplasms at the time of cesarean section and staging surgery was performed. The other cancer types are shown in Table 1.

Mean age of cancer survivors at delivery was 31.8±5.7 (range 19-42 years) years. The median interval between diagnosis and date of delivery was 6.7±5.0 (range 1.0-26.0 years) years. In cancer-treated group 13 (22,0%) were childhood cancers including leukemia and lymhpoma, 12 (20,3%) were breast cancer, 9 (15,3%) were thyroid cancer, 5 (8,5%) were cancer originating from neural tissue, 4 (6,8%) were ovarian cancer and rest 16 (27,1%) were the other types of adenocarcinomas. From this group 45 (76%) had healthy newborns, 7 (12%) medical termination and 7 (12%) abortions were encountered. 45 newborns did well in the routine postnatal follow-up without congenital malformations with a mean birth weight of 2985.3±689.3 gr (range 1250±4400 gr). Six out of 45 (13,3%) were low birth weight, slightly higher than the general population (10%). Details are given Table 2. Eleven out of 45 patients (22,2%) in this cohort had preterm delivery, higher than the general population with an early and late preterm ratio of 7/4. In this group, cesarean section rate was 71%. Medical terminations were performed for maternal indications such as advanced disease, plan of chemotherapy or surgery. Beside this, the abortion rate (12%) was not different from the general population. Twenty one women had been treated with chemotherapy only before pregnancy and 5 treated during pregnancy. None of this cohort received radiotherapy alone. Eleven women had received chemo-radiotherapy before pregnancy, 3 received during pregnancy. There were 3 maternal mortalities in this cohort, all occurred after delivery with a median interval of 12.3±6.5 (range 6-19 months) months.

Mean age of synchronous tumor group was 30.2±6.1 (range 20-43 years) years. In synchronous tumor group 7 (28,0%) were breast cancer, 4 (16,0%) were osteosarcoma, 2 (8,0%) were lymphoma, 2 (8,0%) were ovarian cancer, 2 (8,0%) were bladder cancer and rest 8 (32,0%) were the other types of adenocarcinomas. In 25 synchronous cases we found that cancer was diagnosed at the seventh week of the pregnancy at the earliest and up to the cesarean section. The mean gestational week at diagnosis was 31.0±9.8 (range 7-40) weeks. Three out of 25 were diagnosed in the first, 7 were diagnosed in the second and 15 were diagnosed in the third trimester. From this group of patients, 12 had a cesarean section, 8 vaginal deliveries and 5 medical terminations. Medical terminations were performed due to maternal indications such as advanced disease, plan of chemotherapy or surgery. Twenty newborns were healthy without congenital anomalies with a mean birth weight of 2796.5±598.8 (range 1280-3910 gr) gr. Five out of 20 (25%) were low birth weight, 2,5 times more than the general population (10%). Ten out of 20 patients (50%) in this cohort had preterm delivery, much higher than the general population, mostly late preterm (8/10) and induced due to plan of chemotherapy. Five women treated with chemotherapy alone during pregnancy and in 9 chemotherapies were postponed after delivery. None of this cohort received radiotherapy alone. One woman received chemo-radiotherapy during pregnancy, 8 received after delivery. 2 patients of this cohort received neither chemotherapy nor radiotherapy, one was a papillary type thyroid carcinoma, and the other was an advanced stage uterine lymphoma ended up with maternal mortality after a month of delivery. We encountered 5 maternal mortalities in this cohort, all occurred after delivery with a median interval of 11.2±8.5 (range 1-24 months) months. Details are given Table 3.

Table 1: Cancer types and frequencies

Cancer type	n	%	Cancer type	n	%
Breast	25	26	Soft tissue	2	2,1
Thyroid	10	10,4	Skin	2	2,1
Leukemia	10	10,4	Endometrium	1	1
Lymphoma	8	8,3	Choriocarcinoma	1	1
Bone/Cartilage	8	8,3	Uterine lymphoma	1	1
Over	6	6,3	Leiomyosarcoma	1	1
Intracranial	5	5,2	Lung	1	1
Cervix	3	3,1	Esophagus		
Bladder	3	3,1	1	1	
Nasopharynx	3	3,1	Gastric	1	1
Renal	2	2,1	Pheochromocytoma	1	1
			Parathyroid	1	1
			Total	96	100

Table 2: Obstetric outcomes of the patients

	Previous cancer	Synchrone	Metachrone
Patient number (%)	59 (61.5%)	25 (26,0%)	12 (12,5%)
Mean age (years)	31.8±5.7	30.2±6.1	31.4±4.7
Live birth (%)	45 (76%)	20 (80%)	12 (100%)
Birth weight (gr)	2985.3±689.3	2796.5±598.8	3260.8±546.3
Cesarean birth rate (%)	71	60	50

Table 3: Therapeutic modalities

Case No.	Maternal age	Cancer type	Tumor type	Chemotherapeutics	Surgery	Radiotherapy
1	36	Breast	Cancer survivor	CAF	before pregnancy	absent
2	30	Lymphoma	Synchronous tumor	CHOP	absent	during pregnancy
3	30	Lymphoma	Cancer survivor	CHOP	absent	during pregnancy
4	39	Breast	Cancer survivor	CAF	before pregnancy	absent
5	34	Lymphoma	Cancer survivor	CHOP	absent	absent
6	33	Nasopharynx	Synchronous tumor	Cisplatin	absent	during pregnancy
7	43	Breast	Cancer survivor	CAF	before pregnancy	before pregnancy
8	28	Choriocarcinoma	Synchronous tumor	EMA/CO	absent	absent
9	26	Leukemia	Synchronous tumor	Hydroxyurea	absent	absent
10	23	Breast	Synchronous tumor	CAF	during pregnancy	during pregnancy
11	24	Lymphoma	Synchronous tumor	Methotrexate	absent	absent

CAF: Cyclophosfamide, adryamycin and 5-Fluoracile, CHOP: Cyclophosfamide, adryamycin, vincristine and prednisone, EMA/CO: Etoposide, methotrexate, and dactinomycin alternating with cyclophosphamide and vincristine

Mean age of metachronous tumor group was 31.4±4.7 (range 24-40 years) years. The median interval between the date of delivery and diagnosis was 5.3±3.0 (range 1.0-26.0 months) months. In this cohort 6 (50,0%) were breast cancer, 3 (25,0%) were cervix and rest 3 (25,0%) were the other types of adenocarcinomas. From this group of patients, half had a cesarean section and the other half vaginal delivery. 12 newborns were healthy without congenital anomalies with a mean birth weight of 3260.8±546.3 (range 2350-4300) g. Four out of 12 received chemo-radiotherapy, the others underwent surgery.

Discussion

Cancer and pregnancy association is a great concern both for the physicians and mother. It is reported that approximately one in four of cancer cases were women in childbearing age (15-44 years).[4] In our institute, in the period of study a total of 4,200 women in those ages were diagnosed as cancer, our study group represented 2.28% of our female population in that age range.

Most common cancer types in pregnancy are breast, thyroid, cervical cancers, lymphoma, and melanoma. These types account for at least 85 percent of malignancy in pregnant women.[5] Our study results are consistent with the literature. Breast and thyroid cancer is the most frequent cancers in present study. Cervical carcinoma was relatively low. Because,

low incidence of cervical cancer that is associated with sexual and reproductive factors and the oncogenic subtypes of the human papilloma virus is the pattern observed in Muslim countries. Similarly, HPV and cervical cancer incidences in Turkey are lower than other developed countries.[6,7]

Cancers in pregnancy are often categorized by the time of diagnosis: those discovered during the antenatal period, at the time of delivery, or up to 1 year after birth. More than 50% of cancers complicating pregnancy are found within 1 year after delivery, and more than 25% are found in the antenatal period. Few are found at delivery.[5] In this study, we found similar results consistent with recent literature. Most of the PAC cases were synchronous tumors (25/37).

There is no consensus about pregnancy outcome in cancer survivors. However, pregnancy outcomes from 1953 women in the The Childhood Cancer Survivor Study, who had a total of 4029 pregnancies, have been reported no increasing adverse outcomes.[8,9] But, a Scottish study reported that 917 first pregnancies in cancer survivors had slightly higher rates of preterm birth and postpartum hemorrhage.[10,11] Our study results are consistent with the literature. When we compare the birth weights, perinatal mortality, congenital malformations of synchronic-metachronic tumor groups' and cancer survivors groups' neonates there were no significant difference.

In conclusion, since management of a pregnant woman with cancer and pregnancy of a cancer survivor is a hard work, multidisciplinary approach involving gynecologists, pediatricians, and oncologists is essential. Timing of initiation of therapy in cases of PAC and interval between cancer and pregnancy is an important issue in the perspective of fetal/neonatal well-being.

Kanser Tedavisi Sonrası Gebelik ve Gebeliğe Eşlik Eden Kanser: 96 Hastayı Kapsayan Tek Merkez Deneyimi

ÖZET

AMAÇ: Çalışmamızın amacı kanser tedavisi sonrasındaki veya gebeliğe eşlik eden kanserlerin gebelik sonuçlarının değerlendirilmesidir. .

GEREÇ VE YÖNTEM: 2002-2012 yılları arasında bölümümüzce takip edilen kanser tedavisi sonası gebe kalan veya gebeliğinde kanser tedavisi alan hastaların kayıtları gözden geçirildi. Demografik veriler, gebelik sonuçları, maternal ve fetal komplikasyonlar, perinatal sonuçlar, kanser tipleri ve tedavi yöntemleri değerlendirildi.

BULGULAR: Çalışmamız 96 hastadan oluştu. 59 hasta tedavi sonrası iken 37 hasta gebelikle birliktelik gösteren grupta idi. Bu 37 hastada 25 senkron tümör mevcutken 12 hastada metakron tümör vardı. Gebeliklerin 77'si sağlıklı doğum ve 7'si düşük ile sonuçlanırken, 12 gebelik tıbbi nedenlerle sonlandırıldı. En sık kanser tipi 25 hasta ile meme kanseri iken bunu sırasıyla tiroid, lösemi osteosarkom, lenfoma ve over kanserleri izledi. Hastalarda kanserlerin tiplerine göre cerrahi, kemoterapi ve radyoterapi gibi değişik tedavi modaliteleri uygulanmıştı. Olguların 8'inde maternal mortalite meydana geldi ve bunların tümü doğum sonrasında gerçekleşti.

SONUÇ: Kanser tedavisi sonrasında gebe kalan veya gebeliğinde kanser saptanan hastalarda obstetrisyen, pediatrist ve onkoloji uzmanının katkısı ile multidisipliner yaklaşım temeldir. Gebelik ile ilişkili kanser vakalarında tedavinin başlatılma zamanlaması fetal/neonatal iyilik açısından önemlidir.

Anahtar Kelimeler: Kanser, Metakron tümör, Senkron tümör

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