Case Report

Breast cancer as second malignant neoplasm after acute myeloid leukemia: A rare occurrence

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ABSTRACT

Cancer survivors after successful treatment of hematological and lymphoid malignancies are at an increased risk for second malignant neoplasms. As the overall survival has increased in these cancers, solid tumors are emerging as a serious long-term complication. In this article, we describe such a rare occurrence, in literature, of breast cancer after the treatment of acute myeloid leukemia.

Key words: Acute myeloid leukemia, breast cancer, chemotherapy, second malignant neoplasm

INTRODUCTION

People can have more than one cancer in their lifetime. Patients who survive cancer, especially hematological and lymphoid malignancies with successful treatment, are at an increased risk for second malignant neoplasms (SMNs). As the survival times have increased in these cancers, second solid tumors are emerging as a serious long-term complication. Not all second cancers are due to cancer treatment. Certain inherited gene changes such as BRCA 1 and BRCA 2 can increase a woman's risk for both breast and ovarian cancers.[1] Exposure to certain cancer-causing substances, such as tobacco smoke, puts a person at higher risk for different cancers such as cancers of the lung, larynx, throat, and mouth.[2]

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CASE REPORT

We report an unusual case of a woman treated for acute myeloid leukemia (AML) 7 years ago who presented to us with newly diagnosed breast cancer. She was diagnosed as AML - M2 in the year 2007 after a complete workup. She was treated with the standard induction chemotherapy regimen of 3 + 7 daunomycin and cytarabine. As she did not achieve complete remission (CR) after the first induction, she received a second induction chemotherapy regimen with daunomycin, cytarabine, and mitoxantrone. After the second induction, her bone marrow showed CR. She was further given four cycles of consolidation with high-dose cytarabine with growth factor support. She successfully completed her treatment in December 2007. She was on regular follow-up for the next 7 years and was asymptomatic. During her follow-up, her hemogram was normal on all the subsequent visits. In February 2014, she noticed a lump in the left breast, about the size of a lemon. On examination, the mass was found to be outer quadrant

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of the left breast, measuring around 2 cm × 2 cm. It was not associated with pain or discharge from the nipple. There was no associated swelling in the left and right axilla. Fine-needle aspiration cytology was done from the lump which showed duct carcinoma. She underwent left modified radical mastectomy, with axillary lymph node dissection. Histopathology report showed invasive duct carcinoma, grade 2, with clear margins and no lymphovascular emboli. Her hormonal receptor status was triple negative. Following the surgery, she received adjuvant chemotherapy with three cycles of FEC and three cycles of docetaxel given thrice weekly. She is at present on regular follow-up after the completion of adjuvant treatment and is disease-free till the date of writing this article.

DISCUSSION

The second- and higher-order malignancies comprise about 18% of all cancers. Solid tumors comprise a leading cause of mortality among long-term survivors, including patients with Hodgkins lymphoma (HL), non-HL (NHL), and acute leukemias.[2] The occurrence of SMNs is influenced by various factors such as late effects of cancer therapy, genetic predisposition, environmental factors, and shared etiological factors with the primary cancer such as obesity and host factors.

In this article, we report the rare occurrence of breast cancer as a second malignancy after the treatment of leukemia with anthracyclines and cytarabine. In literature, the occurrence of AML following the adjuvant treatment of breast cancer with anthracyclines and taxanes is more commonly reported, and the vice versa is not mentioned so far.[2-4]

The treatment of AML has improved over the past few decades. Aggressive induction with more potent intensification regimens with chemotherapy alone or chemotherapy plus stem cell transplantation (SCT) has improved the treatment results.[1-7] The present risk stratification based on cytogenetics has tailored the treatment of AML and prognosis is better. However, patients who have received cytotoxic therapy with chemotherapy drugs such as anthracyclines, epipodophyllotoxins, and/or radiotherapy are at a risk for long-term complications, especially the occurrence of a second cancer. SMNs are a known complication of chemotherapy and irradiation treatment for patients with HL, NHL, and have also been reported after SCT.[8-12] Risks for selected SMNs are also modified by age at exposure and attained age.[4] Travis *et al.* categorized SMNs into three major groups according to the predominant etiologic factor: Treatment-related, syndromic, and due to shared etiologic influences.[8] Although a causal link has not been proven, these neoplasms are thought to be a direct consequence of mutational events caused by cytotoxic therapy. Both ionizing radiation and many chemotherapy drugs alter cellular DNA. Such an alteration of DNA might involve a single base change, deletion or inactivation of a growth suppressor gene, or changes in the expression of certain critical oncogenes or growth factor receptor genes.

Secondary malignant neoplasms have been reported especially in the context of cranial irradiation and administration of epipodophyllotoxins. Long-term cumulative incidences of second malignancies have been estimated between 1.5% and 5.9%.[13]

Earlier studies showed an increased risk of new malignancies after the treatment of childhood ALL.[13] Hematologic malignancies develop relatively early, but solid cancers have a longer latency period. In a study among adult ALLs, the median time from the diagnosis of ALL to the diagnosis of the second malignancy was 1.7 years for AML/myelodysplastic syndrome (MDS), whereas it was 6.9 years and 3.7 years for skin tumors and other solid tumors, respectively. The risk for developing a solid tumor increased over time and was highest among patients who had undergone transplantation as postremission therapy. Patients who have undergone SCT have an increased risk for secondary cancers compared with the general population of patients. The risk of secondary neoplasm in adult ALL survivors may be influenced by genetic or other predisposing factors as well as by the treatment given for the primary disease, as shown in Table 1.

Chemotherapy-related malignancies

Multiagent chemotherapy used as part of a multimodality therapy for malignant disease has increased the difficulty of assessing which agents might play a causative role in the development of SMNs. Alkylating agents and DNA-topoisomerase II inhibitors have been linked to the development of secondary AML and MDS. Alkylating agents and irradiation both possess strong mutagenic

Table 1: Etiological factors of multiple primary cancers and second malignant neoplasms

Modifiable	Nonmodifiable
Lifestyle	Host factors
Tobacco	Age and sex
Alcohol	Genetics
Diet	Immune function
Others	Hormonal and others
Environment	Interactions and other influences
Contaminants	Gene-environment
Occupation	Gene-gene
Viruses	
Others	
Interactions and other influences	
Gene-environment	
Gene-gene	

activity. Treatment-related leukemia typically occurs in the first 10 years after treatment after which risk tapers a little. Other drug classes with leukemogenic potential include topoisomerase II inhibitors, leading to secondary leukemia characterized by 11q23 chromosomal abnormalities and platinum-based chemotherapy.[2,3,5] In addition to leukemia risk, alkylating chemotherapy has been related to solid tumors, notably lung cancer, gastrointestinal cancer, sarcoma, and bladder cancer.[5] Furthermore, the use of rituximab along with high-dose therapy and autologous SCT for lymphoma has been implicated as a possible risk factor for the development of subsequent solid tumors.

CONCLUSION

Second neoplasms may result from a specific combination of age, genetics, first malignancy, and therapy. The biologic characteristics of the malignant cells may be associated with the development of malignancy. Therapy-related secondary neoplasms have been identified in patients receiving radiotherapy, chemotherapy, or combined modality therapy for a variety of primary neoplasms and need to be constantly watched for in follow-up.

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Conflicts of interest

There are no conflicts of interest.

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