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CORRESPONDENCE

Treatment Related Acute Myeloid Leukemia in Breast Cancer Survivors: A Single Institutional Experience

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Dear Editor,

Breast cancer is the most common malignancy among Indian women. With the growing population of breast cancer survivors, the oncologists are confronted with plethora of treatment (chemotherapy, radiotherapy) related adverse effects like fatigue, cardiac toxicities, sexual dysfunction, and second malignancies. A SEER data reported an incidence of 1.8% acute myeloid leukemia (AML) among breast cancer survivors treated with chemotherapy after a period of 10 years follow up [1]. Data of treatment related AML (tAML) in breast cancer survivors from our country is limited [2]. Hence, we conducted a retrospective analysis of 7 cases of tAML following breast cancer treatment in medical oncology department of BRA-IRCH from 2006 to 2017. The baseline characteristics and outcome are tabulated in Table 1. The median age of diagnosis of tAML was 60 years. All 7 cases received adjuvant chemotherapy, out of which 5 received 5-fluorouracil 500 mg/m^2, epirubicin 75 mg/m^2 and cyclophosphamide 500 mg/m^2 (FEC) regimen and 2 received FEC and docetaxel 75 mg/m^2. The median interval between breast cancer diagnosis and tAML diagnosis was 41 months. Cytogenetics was evaluated in all the cases and 4 had Del 5q abnormality, 2 had complex cytogenetics and 1 had t (8, 16). An intensive regimen of 3 + 7 (daunorubicin 45 mg/m^2 for 3 days with cytarabine 100 mg/m^2 intravenously for 7 days) was offered for 3 cases, low dose cytarabine (20 mg/m^2 subcutaneously 10 days repeated every 28 days) for 2 cases, decitabine (20 mg/m^2 intravenously for 5 days repeated every 28 days) for 1 case and one patient was given the best supportive care. Out of 6 patients treated, only 1 patient achieved complete remission, 1 had induction related mortality, and 4 continued to have active disease and eventually expired due to disease. The overall survival of our series was 4 months.

Drugs like topoisomerase 2 inhibitors, alkylating agents are established risks for tAML and MDS. Apart from these, studies have reported that granulocyte colony stimulating factor (G-CSF) increase the risk of t AML in breast cancer patients. The proposed hypothesis is antiapoptotic effects of G-CSF result in survival of cytotoxic damaged lineage-specific mutant stem cells, and these mature myeloid cells with chromosomal alterations later predispose to secondary leukemia [3, 4]. Secondly, it is also unclear whether it's a direct stochastic effect or genetic polymorphism in drug metabolism and DNA repair process making the individual susceptible to secondary AML.

Similar to the published literature, our cases were associated with increased high risk cytogenetic abnormalities and poor survival [3, 5]. Our series showed increased incidence in postmenopausal women, predominant 5 q deletion followed by complex cytogenetics which was a distinct finding in our study. Poor performance status and previous therapy with anthracyclines add to the difficulty in managing tAML with high intensity regimens. Only two patients in our study were eligible for high intensity protocol. As conventional therapies have shown a poor outcome across various studies, these patients should be encouraged to enroll in clinical trials.

To conclude, tAML is a rare but dreaded adverse event in breast cancer survivors. With the advent of tests like

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Table 1 Clinical characteristics and outcome of treatment related AML

S. no	Age/sex	Interval to AML (months)	Baseline TLC cells 10^6/L	Cytogenetic abnormality	Treatment for AML	Status
1	60/f	27.60	1500	Del 5q	Low dose Cytarabine	Died
2	47/f	62.30	5600	Del 5q	3 + 7	Died
3	63/f	62.70	34,000	t (8;16)	Decitabine	Died
4	80/f	35.97	3400	Del 5q	Best supportive care	Died
5	74/f	41.63	3300	Del 5q	Low dose Cytarabine	Died
6	49/f	44	14,000	Complex cytogenetics	3 + 7	Alive
7	53/f	30	76,000	Complex cytogenetics	3 + 7	Died

3 + 7: intensive regimen with daunorubicin 45 mg/m^2 for 3 days with cytarabine 100 mg/m^2 for 7 days. Low dose cytarabine: 20 mg/m^2 cytarabine subcutaneously 10 days for every 28 days, decitabine 20 mg/m^2 intravenously for 5 days every 28 days

oncotype DX, mammaprint one can delineate breast cancer patient who could benefit from a cytotoxic therapy and spare a subset of patients from the toxic effects of chemotherapy. Multicenter collaboration to know the incidence and disease characteristics of tAML in our population will help in better management of our patients.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval Institute ethical clearance was obtained for the retrospective study.

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