

Therapy Related Chronic Myeloid Leukemia – A Case Report

Dr. Abhilash Menon¹, Dr. Sugeeth MT^{2*}, Dr. Simi C. M³

¹MD., Senior Resident, Department of Medical Oncology, Regional Cancer Centre, Trivandrum 695011, India

²MD, DNB, DM, DNB., Assistant Professor, Department of Medical Oncology, Regional Cancer Centre, Trivandrum 695011, India

³MD., Assistant Professor, Department of Pathology, Regional Cancer Centre, Trivandrum 695011, India

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*Corresponding author: Dr. Sugeeth MT

MD, DNB, DM, DNB., Assistant Professor, Department of Medical Oncology, Regional Cancer Centre, Trivandrum 695011, India

Abstract

Case Report

Therapy-related acute leukemia or myelodysplastic syndrome are well-recognized entities, whereas less is known about the incidence of secondary chronic myeloid leukemia (CML) after cytotoxic treatments, particularly radiotherapy, for a primary malignancy. Here we report a patient who was initially treated 8 years before with concurrent chemoradiation followed by High Dose Rate (HDR) Brachytherapy for FIGO Stage IIB carcinoma cervix, and now while on follow up developed CML.

Keywords: Chronic myeloid leukemia, Cervical cancer, second malignancies, therapy related.

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INTRODUCTION

Progress made in the therapy of several malignant diseases during last decades has improved survival and cure rates for many patients. At the same time second malignancies started emerging as an important late complication. According to Aguiar's analysis, chronic myeloid leukemia (CML) associated with prior chemotherapy and/or radiotherapy constituted 13.3% of the overall cases of therapy-related leukemia, with breast or ovarian cancer as the most frequent primary malignancies [1]. Here we report a rare case of therapy related CML.

CASE PRESENTATION

A fifty eight-year-old- postmenopausal lady was evaluated for excessive fatigue of 3 months duration. There was no history of recurrent infections, bleeding per vagina, loss of weight, abdominal pain or other systemic symptoms. She is a known hypertensive and diabetic on regular medications. She has a past history of discharge per vagina of 3-month duration in January 2012. On per vaginal examination there was, 4 x 4 cm growth involving both lips of cervix and posterior fornix, extending to both parametrium medially but not up to pelvic side wall. Vaginal walls and Rectal mucosa were free. There were no palpable lymph nodes. Biopsy from the growth revealed squamous cell carcinoma, non-keratinising type. She was diagnosed to have FIGO Stage IIB carcinoma

cervix. She was treated with External Beam Radiation (EBRT) 40Gy to pelvis using four field box technique, followed by 10Gy boost to parametrium along with weekly concurrent cisplatin 40mg/m². She also received three sittings of High Dose Rate (HDR) intra-cavitary brachytherapy 7Gy to point A over a period of 3 weeks. Post treatment there was no residual disease and she was on regular follow up.

There was no significant family history. She had an Eastern Co-operative Oncology Group (ECOG) performance status of one. On per abdominal examination she had showed mild splenomegaly of 2 cm below the left costal margin. Per vaginal and pelvic examination showed post radiation changes only. She had a haemoglobin of 10 g/dl, total count of 88700 cells/mm³, platelet count of 6.5 lakh/mm³ with a differential count: Neutrophils – 55%, Eosinophils – 2%, Lymphocytes – 10%, Myelocytes – 21%, Basophils-1%, Promyelocytes – 5%, Myeloblast – 3%, and Band forms – 3%. Peripheral smear showed neutrophilic leucocytosis with shift to left and thrombocytosis. Bone marrow study showed myeloid hyperplasia with mild eosinophilia and the blast percentage was less than five (Figure 1). Peripheral blood analysis for BCR-ABL1 by Polymerase Chain Reaction (PCR) revealed the presence of p210 (b3a2/b2a2) transcript. Fluorescent in situ hybridization (FISH) analysis and karyotyping confirmed presence of BCR-ABL1 translocation. She was diagnosed to have

CML in chronic phase with a low risk EUTO's score of 15. Correlating her present diagnosis with past treatment history, a diagnosis of therapy related CML

was considered. She was started on imatinib at 400mg daily. At 1 month she achieved complete haematological remission.

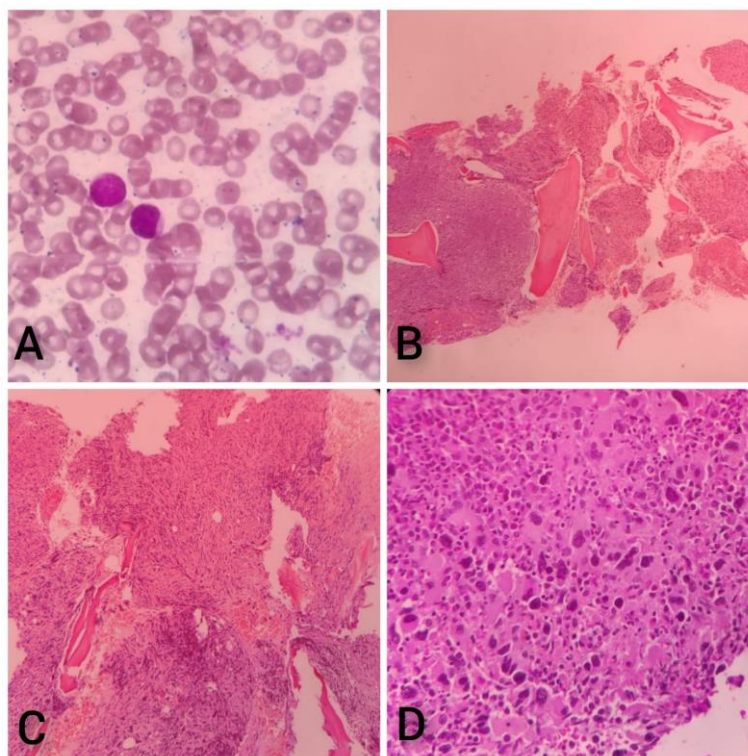


Figure 1: Microphotography finding of the (A)Peripheral smear showing blasts, Bone marrow showing (B) hypercellular marrow 4x, (C)fibrosis 10x, (D)myeloid hyperplasia, megakaryocytes and micro-megakaryocytes 40x

DISCUSSION

The aetiology behind the development of therapy related CML is unclear. Cytogenetic changes associated with chemotherapeutic regimens and/or ionizing irradiation, such as -7 , $-7q$, -5 , $-5q$, *MLL* rearrangement, and complex abnormalities are not reported in therapy related CML suggesting different pathogenesis [2]. It may be multifactorial including coincidence, diminished immune surveillance due to impaired B-cell and T-cell function, hereditary predisposition, direct oncogenic effect of cytotoxic agents or irradiation and therapy induced enrichment of a mutant clone. Therapy-related CML shows a latency (median interval of about 5 years) between that of AML/MDS induced by alkylating agents and/or radiotherapy and that associated with topoisomerase II inhibitors [2]. In our patient also, there was a latency period of 8 years.

Therapy-related CML constitutes a relatively small fraction, the literature is limited to single case reports and small case series. Kaldor *et al* reported two cases of CML from a total of 163 leukemia patients (1.2%) who had been treated for Hodgkin lymphoma [3]. A Japanese study group reported 11 cases of therapy-related CML among 308 patients with CML [4]. In a meta-analysis by Waller *et al.*, the predominant primary malignancy in patients with therapy-related

CML was uterine and cervical cancer, followed by ovarian cancer and Hodgkin lymphoma [2]. A study from China on therapy related CML, 52% had received treatment either for lymphoma or breast carcinoma [5].

In contrast to therapy-related AML/MDS, therapy-related CML demonstrates clinical outcomes similar to that of de novo CML, in line with its pathologic features and cytogenetic profile. Therapy-related CML exhibits a robust therapeutic response to imatinib/ derivatives and favourable clinical outcomes similar to de novo CML.

CONCLUSION

More research is warranted to understand molecular pathology of therapy related CML, especially when the cancer survival increases and so is second malignancies.

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Conflict of Interest – None

REFERENCES

1. Aguiar, R. C. (1998). Therapy-related chronic myeloid leukemia: an epidemiological, clinical and pathogenetic appraisal. *Leukemia & lymphoma*, 29(1-2), 17-26.
2. Waller, C. F., Fetscher, S., & Lange, W. (1999). Treatment-related chronic myelogenous leukemia. *Annals of hematology*, 78(8), 341-354.
3. Kaldor, J. M., Day, N. E., Clarke, E. A., Van Leeuwen, F. E., Henry-Amar, M., Fiorentino, M. V., ... & Stovall, M. (1990). Leukemia following Hodgkin's disease. *New England Journal of Medicine*, 322(1), 7-13.
4. Iriyama, N., Tokuhira, M., Takaku, T., Sato, E., Ishikawa, M., Nakazato, T., ... & Kawaguchi, T. (2017). Incidences and outcomes of therapy-related chronic myeloid leukemia in the era of tyrosine kinase inhibitors: Surveillance of the CML Cooperative Study Group. *Leukemia Research*, 54, 55-58.
5. Yang, L. H., Su, P., Luedke, C., Lu, C. M., Louissaint Jr, A., McCall, C. M., ... & Wang, E. (2018). Chronic myeloid leukemia following treatment for primary neoplasms or other medical conditions: a report of 21 cases and review of the literature. *American Journal of Clinical Pathology*, 150(3), 246-258.