

Letter to the Editor

Bone marrow limited diffuse large B-cell lymphoma following prolonged immunosuppressive therapy with methotrexate and corticosteroids

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Dear Editor,

Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphomas (NHL) globally. Although bone marrow involvement is noted in up to 60% of advanced stage patients, PBM limited DLBCL (PBM-DLBCL) is very rare. The WHO 2016 classification of lymphoid neoplasms does not recognize PBM-DLBCL as a separate entity.^[1] Further studies and research are required to delineate the clinical and natural history of this rare entity.

We report a 57-year-old female with seropositive rheumatoid arthritis and autoimmune hemolytic anemia. For these, she was on weekly oral methotrexate 10 mg and daily oral prednisolone 10 mg continuously for 6 years. She presented to us with fever, weakness, exertional dyspnea, and weight loss. Blood investigations revealed pancytopenia with hemoglobin 6.5 g/dl, total WBC 2400/mm³, neutrophils 55%, lymphocytes 30%, and platelets 78,000/mm³. Bone marrow aspiration and biopsy revealed diffuse infiltration by sheets of large lymphoid cells which were strongly positive for CD45, CD20, PAX5, BCL-2, and focal positive for MUM1. The Ki67 proliferation index was 40%. Cells were negative for TdT, CD3, CD5, and CD7. Baseline positron emission tomography [Figure 1] showed diffuse hypermetabolic activity of whole of the skeleton without the involvement of lymph nodes, spleen, or liver.

Thus, the patient was diagnosed to have bone marrow limited DLBCL. She was treated with six cycles of R-mini CHOP chemotherapy because of poor performance status. Bone marrow evaluation after chemotherapy showed normal cellularity with no features of lymphoma. She is on regular follow-up with normal blood counts and no evidence of disease 12 months from the end of treatment.

DLBCL comprises 31% of all NHL in Western countries and 37% of B-NHL worldwide. Median age at presentation is the 6th decade.^[2] PBM-DLBCL is a very rare entity, and hence, the clinical, pathologic, and prognostic aspects of this subtype of lymphoma have not been clearly established. Available literature shows that it is associated with dismal prognosis and poor outcome. The WHO classification of lymphoid neoplasms divides DLBCL in to four site-specific subtypes, namely primary central nervous system lymphoma, primary effusion lymphoma, DLBCL

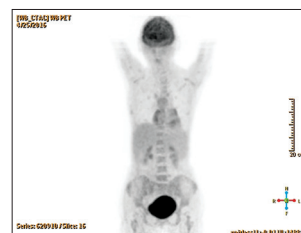


Figure 1: Positron emission tomography whole body

of leg type, and primary mediastinal B-cell lymphoma.^[1] This updated classification does not recognize DLBCL exclusively affecting the bone marrow as separate disease entity.^[1]

The diagnostic criteria for PBM lymphoma are as follows (1) isolated bone marrow infiltration by lymphoma cells regardless of peripheral blood involvement, (2) no evidence of lymph nodal or extranodal disease detectable by physical examination or imaging, (3) no evidence of localized bone tumors, (4) no features of bone trabeculae destruction in the trephine biopsy, and (5) exclusion of leukemias and lymphomas that primarily involve the bone marrow.^[3] In a retrospective review conducted by the International Extranodal Lymphoma Study Group, 21 cases fulfilling the criteria were found, of which the subtypes noted were DLBCL ($n = 15$), follicular lymphoma ($n = 4$), and peripheral T-cell lymphoma not otherwise specified (NOS) ($n = 2$).^[3] In our patient, all the above criteria for the diagnosis of PBM-DLBCL were fulfilled. A literature search for arthritis associated with PBM-DLBCL identified only one report where a patient with seronegative polyarthritis developed bone marrow limited high-grade NHL.^[4] Due to the extreme rarity of PBM-DLBCL, at present, these patients are managed similar to those with DLBCL-NOS with R-CHOP chemotherapy. The possibility that prolonged use of methotrexate and steroids may have altered the characteristics of DLBCL in our patient should be considered. Whether the distribution of DLBCL in the marrow rather than lymph nodes and spleen has any adverse bearing on the prognosis and whether alternative chemotherapy regimens are required for such patients are as yet unclear.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

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Conflicts of interest

There are no conflicts of interest.

**Pravesh Dhiman, Parameswaran Anoop,
Channappa N Patil**

Department of Medical oncology and Hematology, Apollo Hospitals, Bengaluru,
Karnataka, India

Correspondence to: Dr. Pravesh Dhiman,
E-mail: pravesh_dhiman@yahoo.in

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