Primary diffuse large B-cell lymphoma of the bone marrow in a frail and elderly patient successfully treated with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone

TO THE EDITOR: The involvement of bone marrow (BM) in aggressive non-Hodgkin lymphomas (NHLs) usually indicates systemic dissemination. However, although uncommon, extranodal involvement of the BM as an isolated and unique localization of aggressive NHLs [1] such as anaplastic large cell lymphoma [2] or diffuse large B-cell lymphoma (DLBCL) [3-6], has also been reported. In particular, primary DLBCL of the BM is a rare type of extranodal lymphoma with poor prognosis [1, 4]. Approximately 10 cases of primary DLBCL of the BM have been described thus far [3], and few of them have been reported in individuals of very advanced age. Here, we report a case of primary DLBCL of the BM that was successfully treated using rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP chemotherapy; 3-week standard schedule) in a frail 76-year-old woman.

The patient was being treated for pancytopenia and dyspnea on exertion caused by severe macrocytic anemia, which required multiple red blood cells (RBC) transfusions. Her Eastern Cooperative Oncology Group performance status was 2. In terms of comorbidities, she presented with a long-standing history of hypertension, reduced renal function (creatinine clearance as estimated by the Cockroft-Gault formula was 60 mL/min · 1.73 m²), and chronic cerebrovascular disease with slight cognitive and neurological impairment. Her antihypertensive medication consisted of a combination of enalapril and amlodipine. At admission, the patient presented with severe malaise and fatigue. Physical examination revealed pallor and tachycardia, but neither lymphadenopathy nor hepatosplenomegaly was observed. Morphological examination of peripheral blood smears showed marked thrombocytopenia with prominent erythrocyte and platelet anisopoikilocytosis; however, no other abnormalities were detected. Although rare circulating neutrophils were present, no immature or atypical cells were observed.

Myelodysplastic syndrome (MDS) was suspected, and a comprehensive work-up was performed. BM aspiration revealed a dry tap; examination of the BM specimen by trephine biopsy showed involvement of large abnormal lymphoid cells (Fig. 1) and fibrosis. A standard radiological work-up found no other suspected disease localizations. [18]F-fluorodeoxyglucose positron emission tomography (PET) revealed disseminated BM with diffuse uptake with no evidence of disease involvement of other sites. The patient was diagnosed with primary DLBCL. A comprehensive laboratory evaluation showed high levels of lactate dehydrogenase but no other remarkable abnormalities. The age-adjusted International Prognostic Index was 3 (high risk).

Although the prognosis of this type of NHL is poor and requires an aggressive approach, including high-dose chemotherapy with autologous stem cell transplantation (ASCT), which would normally be indicated [1, 3, 4, 8], the patient was considered unsuitable for an intensive therapeutic program. Therefore, standard treatment with R-CHOP and prophylactic granulocyte-colony stimulating factor treatment were given. The patient received six R-CHOP courses with no significant toxicity, although she required RBC and platelet transfusions until the commencement of the third course, the latter administered with prophylactic intent given her extremely low platelet count. After the second R-CHOP cycle, the peripheral blood count improved significantly, and the patient achieved transfusion independence with regard to both RBC units and platelet concentrates.

At the time of completion of the planned program (six R-CHOP courses), BM reevaluation by trephine biopsy showed no remnant lymphoma cells. Results of the PET scan were normal. Complete remission (CR) of DLBCL was therefore demonstrated, and two additional courses of R-CHOP were administered as consolidation therapy. Twenty-four months since the end of the patient’s course of immunochemotherapy, she is well with no sign of disease, as demonstrated by recent clinical reevaluations, including

![Fig. 1.](image-url) (A) Bone marrow biopsy (Giemsa stain, high magnification) showing a neoplastic infiltrate composed predominantly of blastic cells with centroblastic morphology, with minor components composed of small centrocyte-like cells. These findings are indicative of diffuse large B-cell lymphoma with features suggestive of a centrofollicular origin. (B) Immunostaining with CD20L26 antibodies reveals diffuse membrane expression in neoplastic cells. (C) Immunostaining with BCL2 reveals diffuse cytoplasmatic expression by neoplastic cells.
were reported.

Continuous clinical response observed in this case would usually dismal outcome of this type of NHL, the 24-month draw any firm conclusions; however, compared with the in DLBCL cases with poor prognosis such as ours.

line treatment with an efficacy to allow durable CR, even in elderly patients, this case suggests that, similar to other types of DLBCL, this regimen can be a well-tolerated, frontline treatment with an efficacy to allow durable CR, even in DLBCL cases with poor prognosis such as ours.

The follow-up period for this patient was too short to draw any firm conclusions; however, compared with the usually dismal outcome of this type of NHL, the 24-month continuous clinical response observed in this case would be considered a satisfactory therapeutic result. In this context, R-CHOP can be considered a reasonable approach in cases where advanced age, toxicity concerns, and comorbidities may detract from the pursuit of more aggressive treatments such as high-dose chemotherapy and ASCT.

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Late but effective long-term response to splenectomy in the treatment of immune thrombocytopenia

TO THE EDITOR: Splenectomy is the preferred treatment for steroid-refractory immune thrombocytopenia (ITP) [1]. The initial response to splenectomy is rapid and characterized, in most cases, by immediate thrombocytosis; this finding is considered a favorable predictive factor for long-term response to splenectomy in ITP patients [2, 3]. If platelet count does not increase after splenectomy, it may indicate failure of the procedure and lead providers to consider other salvage treatments.

We report a case of a late response to splenectomy in a patient who was diagnosed with ITP at another center in 1991 at the age of 23 years. At primary diagnosis, a comprehensive work-up for underlying disorders was unremarkable, except for slight positivity for antinuclear antibodies (ANA). The patient was initially prescribed prednisone at a dosage of 1 mg/kg body weight/day; after approximately 1 year, the dosage was appropriately tapered and administration of the steroid was eventually stopped. However, shortly thereafter, the patient experienced a relapse of ITP. She refused splenectomy; therefore, prednisone was restarted and continued at the lowest effective dosage (25–30 mg/day) that allowed stable maintenance of a platelet count >30×10^9/L until 2006. During this time, she was followed up at different hematologic centers. In 2006, the patient was reevaluated because of unresponsiveness to prednisone and was found to have heterozygous factor V Leiden mutation, with no other abnormalities. She refused splenec-