

Primary Bone Marrow B-cell Non-Hodgkin's Lymphoma Successfully Treated with R-CHOP

Liren Qian¹, Zhi Zhang², Jianliang Shen¹, Yi Liu¹

ABSTRACT

Primary isolated bone marrow disease as a presenting feature of lymphoma is very rare. We describe the case of a Chinese with isolated bone marrow small B-cell lymphoma as a first manifestation. A 55-year old woman was admitted to our hospital with fever. Her peripheral blood smear and laboratory findings were suggestive of bicytopenia. Bone marrow specimen showed diffusely distributed small-sized lymphocytes. Combined with immunophenotypic and chromosomal analysis, a diagnosis of primary bone marrow B-cell non-Hodgkin's lymphoma was made. The patient was treated with R-CHOP (rituximab and cyclophosphamide, epirubicin, vindesine, and prednisone) regimen for six cycles. She had complete remission and is still alive without relapse. We concluded that primary bone marrow mature small B-cell lymphoma is a rare but distinctive subtype of lymphoma. The prognosis for this entity is poor but rituximab-based treatment is promising for improving its outcomes.

Keywords: Bone marrow, B-NHL, bone lymphoma, non-Hodgkin's lymphoma

Linfoma Primario No Hodgkin de Células B en la Médula Ósea Tratado con R-CHOP

Liren Qian¹, Zhi Zhang², Jianliang Shen¹, Yi Liu¹

RESUMEN

La enfermedad aislada primaria de la médula ósea como rasgo de manifestación del linfoma es muy rara. Describimos el caso de una paciente china con linfoma aislado de células B pequeñas en la médula como una primera manifestación. Se trata de una mujer de 55 años que ingresara a nuestro hospital con fiebre. El frotis de sangre periférica y los hallazgos de laboratorio apuntaban a una bicitopenia. El espécimen de la médula ósea mostró la presencia de linfocitos de pequeño tamaño distribuidos de manera difusa. En combinación con un análisis inmunofenotípico y un análisis cromosómico, se realizó un diagnóstico de linfoma primario no Hodgkin de células B de la médula ósea. La paciente recibió como tratamiento un régimen de seis ciclos de R-CHOP (rituximab, ciclofosfamida, epirubicina, vindesina, y prednisona). Esto le permitió alcanzar una remisión completa, y todavía está viva sin que se haya producido recaída alguna. Concluimos que el linfoma primario de células B pequeñas maduras de la médula ósea es un subtipo raro pero particular de linfoma. La prognosis para esta entidad es pobre, pero el tratamiento a base de rituximab re-basado resulta promisorio en cuanto a mejorar su evolución clínica.

Palabras claves: Médula ósea, B-NHL, linfoma óseo, linfoma no Hodgkin

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From: ¹Department of Haematology and ²Department of Emergency, Navy General Hospital, Fucheng Road, Beijing, PR China.

Correspondence: Dr Liren Qian and Jianliang Shen, Department of Haematology, Navy General Hospital, Fucheng Road, 100048, Beijing, PR China. E-mail: qlr2007@126.com and shenjianliang@csc.org.cn, respectively.

INTRODUCTION

Primary bone marrow non-Hodgkin's lymphoma (PBNHL) is rarely seen (1) compared with secondary non-Hodgkin's lymphoma (NHL) in bone marrow (2). To date, up to a total of 34 cases have been reported in the English literature (3–10). In

these cases, bone marrow biopsy revealed infiltration of lymphoma cells with a diffuse or interstitial pattern. Morphologically, mature small lymphocytes or medium to large-sized lymphoid cells were seen. Also, based on immunohistochemical stains, most cases were classified as lymphoma of B-cell or T-cell lineage. Among B-cell lymphomas, nine cases were diagnosed as diffuse large B-cell lymphoma (DLBCL), but the other B-cell lymphoma cases could not be further classified due to lack of specific findings. Here, we report a case of PBNHL associated with bicytopenia.

CASE REPORT

A 55-year old woman was hospitalized with a febrile illness for 10 months. On physical examination, no physical sign was observed. No specific previous medical history and family history were observed. Laboratory findings on admission were as follows: haemoglobin, 9.9 g/dL, platelet, $67 \times 10^9/L$, white blood cells, $7.67 \times 10^9/L$ (45.44% neutrophils, 23.64% lymphocytes without any atypical lymphocytes, 2.38% monocytes), serum lactate dehydrogenase (LDH), 456 U/L (reference range, 109–245 U/L), ferritin, 943.5 (reference range, 12–200 ug/L), β_2 -microglobulin (BMG), 3.3 mg/L (reference range, 0–2.2 mg/L), C-reactive protein, 93 mg/L (reference range, 0–8.2 mg/L), erythrocyte sedimentation rate (ESR), 120 mm/h (reference range, 0–20 mm/h). Tests for viruses including hepatitis A (HAV), hepatitis C (HCV), hepatitis B (HBV), and human immunodeficiency virus (HIV) were negative. Other laboratory findings of infection, tumour and autoimmune disease were negative. Chest and abdominal computed tomography (CT) did not demonstrate either lymph node enlargement or hepatosplenomegaly. Magnetic resonance imaging (MRI) of the head was normal. Positron emission tomography-computed tomography (PET/CT) showed mild increased FDG uptake at the site of the femur and ilium.

Bone marrow aspiration showed hypercellular bone marrow consisting of 11.6% of small-sized lymphocytes with scant cytoplasm. Immunohistochemical studies revealed that the neoplastic cells were positive for CD20, CD38, CD138, Pax5 and MPO and negative for Cyclin D1. Flow cytometric analysis of the bone marrow aspirate revealed 6.5% mature small-sized lymphocytes that expressed CD10, CD20 bri, CD22 dim, CD45 dim, cCD79 admin and HLA-DR bri. Chromosomal karyotype analysis of the bone marrow aspirate revealed 48XX, add (7) (q31), + der (7), t (7;8) (q22; q11.2), -8, add

(12) (p13), + 18, + mar[4]/48. According to these findings, a diagnosis of PBNHL was made.

After two courses of rituximab and CHOP (cyclophosphamide, epirubicin, vindesine, and prednisone), the fever subsided, bicytopenia improved and the laboratory findings of the patient normalized (Table). Platelet counts elevated to about $200 \times 10^9/L$, haemoglobin, 12.2 g/dL, LDH, 139 U/L (reference range, 109–245 U/L), ferritin, 89.9 (reference range, 12–200 ug/L), BMG, 1.91 (reference range, 0–2.2 mg/L), C-reactive protein, 2.1 mg/L (reference range, 0–8.2 mg/L), ESR, 18 mm/h (reference range, 0–20 mm/h). Flow cytometric analysis of the bone marrow aspirate revealed 0.05% mature small-sized lymphocyte. After the third course of R-CHOP, flow cytometric analysis of the bone marrow aspirate revealed 0% mature small-sized lymphocytes.

DISCUSSION

Non-Hodgkin's lymphoma with bone marrow involvement is common. However, primary involvement of non-Hodgkin's lymphoma restricted to the bone marrow is extremely rare, with only 34 fully documented cases in the English literature. The most frequent clinical findings were weakness, fatigue, and B symptoms of NHL according to the Ann Arbor staging system. Most patients had neither hepatosplenomegaly nor lymphadenopathy. At present, to diagnose PBNHL, analysis of lymphoma cells in the bone marrow is required for subtype diagnosis without lymph node specimens. In this patient, the morphology of the lymphoma cells was characterized by small, relatively mature lymphocytes with scant cytoplasm. In this case, morphology of the lymphoma cells is typical of chronic lymphocytic leukaemia (CLL), and makes DLBCL or Burkitt's lymphoma unlikely. However, surface markers were negative for CD23, and peripheral lymphocyte count was not increased. These findings do not match the characteristics of CLL.

This patient had bicytopenia which was consistent with the previous cases of primary bone marrow lymphoma (3–8). The cause of the cytopenia was estimated to be associated with infiltration of lymphoma cells.

The good response to rituximab-based treatment is shown in our present study. Our data suggested that a rituximab-based treatment strategy is more successful than conventional CHOP-like regimens in the treatment of primary bone marrow lymphoma.

In conclusion, we report a case of PBNHL complicated with bicytopenia. Clinical characteristics, therapy, and prog-

Table: Laboratory findings of patient before and after treatment with rituximab and CHOP

	Haemoglobin	Platelet	LDH	Ferritin	β_2 -microglobulin	CRP	ESR
Prior to R-CHOP	9.9 g/dL	$67 \times 10^9/L$	456 U/L	943.5	3.3 mg/L	93 mg/L	120 mm/h
After two courses of R-CHOP	12.2 g/dL	$200 \times 10^9/L$	139 U/L	89.9 ug/L	1.91 mg/L	2.1 mg/L	18 mm/h

R-CHOP – rituximab and cyclophosphamide, epirubicin, vindesine and prednisone, LDH – lactate dehydrogenase, ESR – erythrocyte sedimentation rate, CRP – C-reactive protein

noses of PBNHL are diverse and not well defined. It is sometimes difficult to diagnose subtypes of PBNHL since the criteria for diagnosis are not well established. We report a unique case of PBNHL with bicytopenia as the initial clinical manifestation in a Chinese. In our case, we showed that analysis of cell morphology and infiltration pattern, detailed investigation of immunophenotypic and chromosomal features may be useful for narrowing down the diagnosis.

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