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Teaching cases

CD20-negative low-grade B cell lymphoma showing immunophenotypic and genotypic features resembling plasma cell myeloma

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ABSTRACT

Here we demonstrate a unique case of CD20-negative low-grade B cell lymphoma showing immunophenotypic and genotypic features resembling multiple myeloma.

The female patient had no abnormal masses, splenomegaly, swelled lymph nodes, or bone lesions. Although serum levels of IgG, IgA, and IgM were decreased without M protein, κ-type Bence–Jones protein was observed. In bone marrow, monotonous proliferation of small to medium-sized lymphoid cells was observed without classical myeloma cells, the same histological findings as lymphoplasmacytic lymphoma. The cells were CD38+, CD138+, CD43+, CD44+, CD3−, CD4−, CD5−, CD7−, CD8−, CD10−, CD11b−, CD19−, CD20−, CD21−, CD23−, CD24−, CD25−, CD27−, CD40−, CD45−, and CD56−. Surface or cytoplasmic IgM, κ, or λ were all negative. Chromosomal analysis demonstrated t(11;14)(q13;q32).

The present case may belong to a new entity of low-grade B cell lymphoma with the same histological findings as lymphoplasmacytic lymphoma, mainly proliferated in bone marrow whose immunophenotype and genotype are similar to plasma cell myeloma.

Introduction

Lymphoplasmacytic lymphoma (LPL) is a B-cell neoplasm composed of small lymphocytes, plasmacytoid lymphocytes, and plasma cells, involving bone marrow (BM), lymph nodes (LNs), and spleen, which does not fulfill the criteria for any other B-cell neoplasm with plasmacytic differentiation, defined in the 2008 WHO [4]. Waldenström's macroglobulinemia (WM) is defined as BM infiltration primarily by LPL along with IgM monoclonal gammopathy. On the other hand, it is well known that myeloma cells are morphologically various. Some of them, especially multiple myeloma (MM) with (11;14)(q13;q32) translocation, show lymphoplasmacytic morphology [5,7].

Here we demonstrate a unique case of CD20-negative low-grade B cell lymphoma with the same histological findings as LPL, showing immunophenotypic and genotypic features resembling MM.

Clinical history

A 91-year-old woman was referred to our hospital because of general fatigue and anemia. She had been treated for Parkinsonism for 2 years and had a history of severe iron deficiency anemia due to a gastric ulcer 4 years previously. Upon admission, superficial LNs were not palpable in the cervical, axillary, or inguinal regions, and neither hepatosplenomegaly nor skin lesions were present. Abnormal masses, splenomegaly, or swelled LN were not observed in the chest or abdominal areas by computed tomography (CT). Bone lesions were not detected by X-ray, CT, or bone scintigraphy. Laboratory findings revealed decreased levels of WBC (2.47×10^9/l) with 27.5% of abnormal cells, RBC (1.85×10^{12}/l), hemoglobin (6.9 g/dl), and platelets (110×10^9/l). Her reticulocyte count was normal, and direct antiglobulin test was negative. Serum chemistry revealed almost normal levels for AST, ALT, alkaline phosphatase, lactic dehydrogenase, calcium, C-reactive protein, soluble IL-2 receptor, vitamin B12, folic acid, haptoglobin, and thyroid function, except for elevated serum β2-microglobulin (7.5 mg/dl; normal, <2.4) and ferritin (636 ng/ml; normal, 2.3–121). Autoantibodies examined were negative for anti-nuclear antibody, anti-SS-A, anti-SS-B, anti-thyroglobulin, or platelet-associated IgG. Neither cryoglobulin nor hepatitis C antibody was detected. Serum levels of total protein (5.7 g/dl; normal, 6.7–8.3), IgG (505 mg/dl; normal, 870–1700), IgA (34 mg/dl; normal, 110–410), and IgM (7 mg/dl; normal, 35–220)

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were decreased. Although M protein was not detected in the serum, κ-type Bence–Jones protein (BJP) was observed.

BM aspiration was performed, and she was diagnosed as CD20-negative low-grade B cell lymphoma with the same histological findings as LPL, showing immunophenotypic and genotypic features resembling BJP-MM.

Her general condition was ameliorated by transfusion with red blood cells accompanied by the administration of low dose (10 mg/day) prednisolone. However, she died 8 weeks later of gastro-intestinal bleeding.

Materials and methods and results

Histopathology

BM aspiration demonstrated a nuclear cell count of $19.1 \times 10^4/\mu l$ with 94.7% of abnormal cells (Fig. 3a) which had slightly basophilic cytoplasm and round to oval nuclei with indistinct nucleoli without perinuclear hof (Fig. 3b). Three lineages of normal hematopoietic cells were severely decreased. On a clot section, monotonous proliferation of small to medium-sized lymphoid cells was observed. Classical myeloma cells were not seen (Fig. 3c)

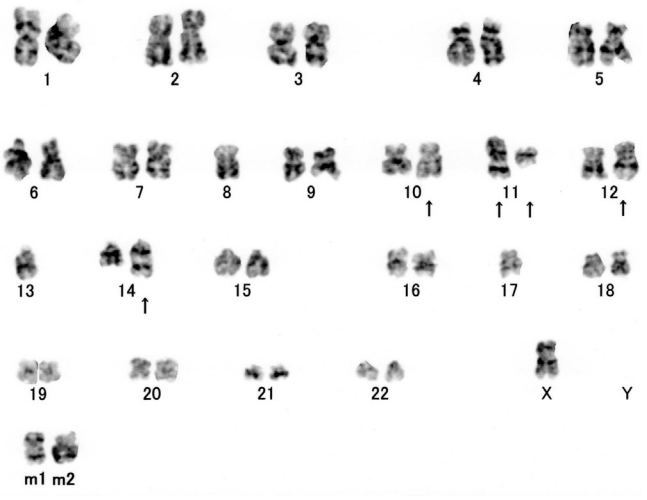

Fig. 1. Karyotype analysis (G-banding) of bone marrow cells. Complex abnormalities were observed in 3 of 20 cells from BM; 44, X, −X, −8, add(10)(q22), add(11)(p15), der(11)t(11;14)(q13;q32), add(12)(p11.2), −13, der(14)del(14)(q24q32)t(11;14), −17,+mar1, +mar2.

Chromosomal analysis and fluorescence in situ hybridization

Chromosomal analysis demonstrated t(11;14)(q13;q32) and -13 in 3 of 20 cells from BM (Fig. 1). Also, the fusion of IgH-BCL1 was observed in 58% of peripheral blood cells by fluorescence in situ hybridization (FISH) analysis (data not shown).

Immunohistochemistry, flow cytometric analysis, and in situ hybridization

On flow cytometric (FCM) analysis of bone marrow cells, the light scatter dot plot showed an abnormal cluster widely distributed from a low to medium forward scatter (FSC) with a low side scatter (SSC) signal. Granulocyte clusters were scarce, lymphocyte clusters were decreased (Fig. 2a). Abnormal cells were positive for CD38, CD138, CD43, and CD44, and negative for CD3, CD4, CD5, CD7, CD8, CD10, CD11b, CD19, CD20, CD21, CD23, CD24, CD25, CD27, CD40, CD45, and CD56. Surface or cytoplasmic IgM, κ, or λ were all negative (Fig. 2b and c).

An immunohistochemical study demonstrated that tumor cells were CD3−, CD5−, CD10−, CD15−, CD20−, CD27−, CD34−, CD38+, CD40−, CD43+, CD56−, CD79a−, cyclinD1+ (Fig. 3d), SOX11−, Bcl-2−, MUM-1+, BOB.1+, Oct-2−, LCA−, PAX-5−, Igγ−, Igμ−, Igα−, Igκ−, and Igλ−. mRNA for Igκ (Fig. 3e) was detected by in situ hybridization (ISH), but Igλ (Fig. 3f), EBER, and HHV-8 were negative by ISH.

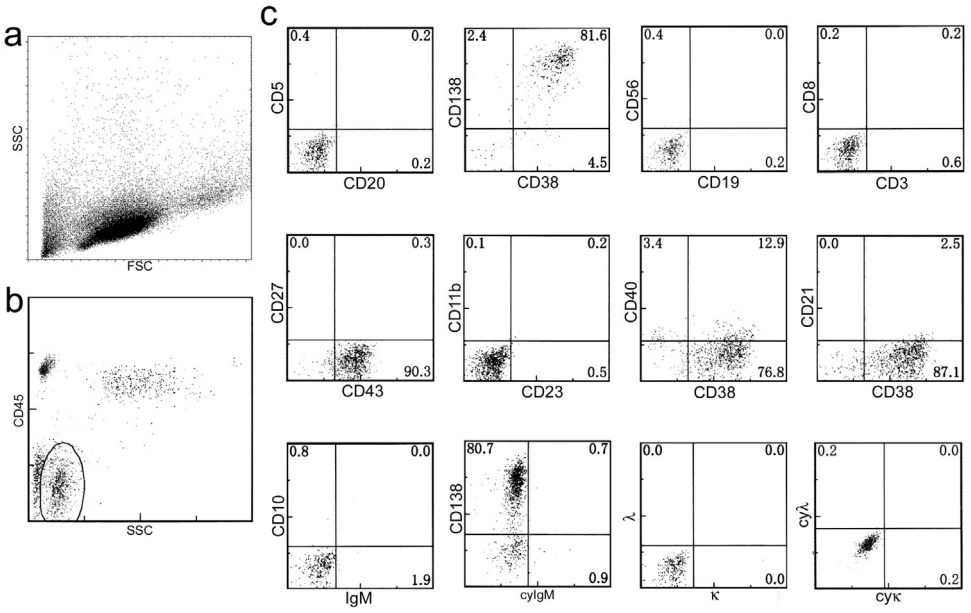

Fig. 2. Flow cytometric (FCM) analysis of BM and peripheral blood cells. (a) FCM analysis of BM cells. BM cells showed a profoundly skewed light scatter profile; i.e. an abnormal cluster widely distributed from a low to medium forward scatter (FSC) with a low to medium side scatter (SSC) signal dominated. (b and c) FCM analysis of peripheral blood cells. Tumor cells with low CD45 and low to medium SSC signal (b) were CD3−, CD5−, CD8−, CD10−, CD11b−, CD19−, CD20−, CD21−, CD23−, CD27−, CD40−, CD38+, CD43+, CD56−, and CD138+. Surface or cytoplasmic IgM, κ, or λ were all negative (c).