Small-lymphoid cells and myeloid antigen expression in a patient with IgG myeloma: A case report

PENJUN JIANG*, WEN XIA*, XUEMEI SUN, XINGBIN DAI and LIN LI

Department of Hematology, Affiliated Hospital of Nanjing University of Traditional Chinese Medicine, Nanjing, Jiangsu 210029, P.R. China

Received March 2, 2015; Accepted December 18, 2015

DOI: 10.3892/ol.2016.4197

Abstract. Multiple myeloma is defined as a malignant proliferation of a single clone of plasma cells resulting in monoclonal immunoglobulin production. Due to the number of plasma cell morphological variants, difficulty is often faced during morphological diagnosis. The current study describes the case of a 49-year-old woman presenting with atypical plasma cell morphology detected by a bone marrow examination. Flow cytometric immunophenotyping determined the nature of the neoplastic cells as monoclonal myeloma cells with myeloid antigen expression. Serum electrophoresis with immunofixation and subsequent clinical findings confirmed this diagnosis. Therefore, the immunophenotyping of plasma cells in myelomas may be useful for the diagnosis of cases with atypical plasma cell morphology.

Introduction

Multiple myeloma (MM) accounts for ~1% of all tumors and 13% of hematological malignancy cases (1). The median age of patients at myeloma diagnosis is 66 years, with diagnosis being particularly rare in individuals <40 years of age (1). The diagnosis of normal MM is commonly determined through a combination of clinical, pathological and radiological techniques and the subsequent findings (2). MM is often associated with extensive skeletal destruction, anemia, hypercalcemia, infections and renal failure (2). However, certain cases presenting with atypical features may be challenging for hematopathologists to diagnose (3). The current study describes a case of immunoglobulin G (IgG) myeloma presenting with small lymphoid cells. Diagnosis of the case based on morphology alone proved to be challenging, with flow cytometric immunophenotyping confirming the cells as monoclonal myeloma cells with myeloid antigen expression. The patient obtained complete remission following combination chemotherapy and received thalidomide as maintenance therapy. Several months later, the patient suffered a relapse and eventually succumbed to the disease.

Case report

In May 2012, a 49-year-female was admitted to the Department of Hematology, Affiliated Hospital of Nanjing University of Traditional Chinese Medicine (Nanjing, China), presenting with dizziness, episodic tiredness and a lack of motivation. Physical examination was unremarkable, with the exception of a cough, chest tightness and pallor. The hemoglobin and red blood cell counts were 72 g/l (normal range, 110-150 g/l) and 2.34x10¹² cells/l (normal range, 3.5x10¹²-5.0x10¹² cells/l) respectively, whilst the white blood cell and platelet counts were within normal ranges. Immunology tests indicated that the IgG paraprotein and β-2-microglobulin levels were 66 g/l (normal range, 6.94-16.20 g/l) and 3,879 µg/l (normal range, 1,035-1,945 µg/l), respectively. Additionally, on serum free light chain evaluation, the k light chain concentration measured 7,960 mg/l (normal range, 629-1,350 mg/dl) and the λ light chain level measured 30 mg/l (normal range, 313-723 mg/dl), with a k/λ light chain ratio of 265.33. Osteoporosis was revealed by computed tomography and X-ray examination.

A bone marrow aspiration was performed and the sample underwent cytological study. Small lymphoid or lymphoplasmacytic-like plasma cells were observed, and accounted for 22.5% of all nucleated cells in the bone marrow. The cells had round nuclei of a uniform size, the chromatin was dense and coarse, and the cytoplasm was slightly basophilic and scanty, wrapping closely around the nucleus (Fig. 1). The antibody expression in the cells was measured using a multiparameter flow cytometer (FC500 Flow Cytometer; Beckman Coulter, Inc., Brea, CA, USA). The results demonstrated that the cells (Fig. 2A) expressed cluster of differentiation (CD)38 (Fig. 2B) and CD33 (Fig. 2C). There was also κ light chain restriction (κ/λ = 13.1) (Fig. 2D, E and F). The majority of the CD138⁺ myeloma cells expressed CD19, but lacked CD56 expression (Fig. 2G and H). The abnormal cells were negative for CD117, CD10, CD20, CD22, CD34 and CD13 expression (data not presented). Interphase fluorescence in situ hybridization (FISH) analysis

Correspondence to: Miss. Xuemei Sun, Department of Hematology, Affiliated Hospital of Nanjing University of Traditional Chinese Medicine, 155 Hanzhong Road, Nanjing, Jiangsu 210029, P.R. China, E-mail: wokibb@gmail.com

*Contributed equally

Key words: immunoglobulin G, myeloma, small lymphoid, myeloid antigen
on the bone marrow aspirate smear, using a probe specific for cyclin D1 (CCND1)/IgH, did not demonstrate a fusion signal, and chromosome analysis revealed a normal karyotype (data not presented). According to the aforementioned findings, the patient of the present case was diagnosed with IgG myeloma. Subsequently, the patient was treated with a vincristine-doxorubicin-dexamethasone regimen that consisted of 1 mg vincristine (days 1-4), 10 mg doxorubicin (days 1-4) and 20 mg dexamethasone (days 1-4, 9-12 and 17-20 for the first cycle and on days 1-4 for the next three cycles). Thalidomide (75 mg per night) was administered as maintenance therapy during each cycle of chemotherapy. The general conditions of the patient improved following the treatment. The lab tests revealed the following results: Bone marrow, 2.5% plasma cells (normal range, 0 - 2.0%); red blood cells, 3.12x10^{12} cells/l (normal range, 3.5x10^{12}-5.0x10^{12} cells/l); hemoglobin, 101 g/l (normal range, 110-150 g/l); IgG κ paraprotein, 15.8 g/l (normal range, 6.94-16.20 g/l); β2-microglobulin, 2,373 µg/l (normal range, 1,035-1,945 µg/l); κ light chain, 1,580 mg/dl (normal range, 629-1,350 mg/dl); λ light chain, 331 mg/dl (normal range, 313-723 mg/dl); and κ/λ ratio, 4.77. Subsequently, consolidate therapy was discontinued by the patient. In May 2013, the patient was admitted to the Department of Hematology, Affiliated Hospital of Nanjing University of Traditional Chinese Medicine complaining of serious bone pain following an injury. The lab tests revealed the following results: white blood cells, 2.4x10^{9} cells/l; hemoglobin, 105 g/l; blood urea nitrogen, 5.19 mmol/l (normal range, 1.70-8.30 mmol/l); creatinine, 47.2 µmol/l (normal range, 44-110 mmol/l); β2-microglobulin, 3.518 µg/l; IgG, 70.7 g/l; and bone marrow, 18.5% plasma cells. The patient was treated with the DECP regimen, which consisted of 20 mg dexamethasone, 100 mg etoposide, 0.6 g cyclophosphamide and 30 mg cisplatinum for 4 days. However, the patient succumbed 18 days later without remission.

Discussion

Diagnosis of typical MM is not often difficult. However, in a small number of cases, unusual morphological variants may pose a challenge when determining a morphological diagnosis, particularly in plasma cell leukemia (2,3). In the current case, the neoplastic cells presented with round nuclei and dense, coarse chromatin. The cytoplasm was scanty and slightly basophilic. Staining, Wright-Giemsa; magnification, x1,000.
CD79α and potent CD38; however, in contrast to normal plasma cells, they are frequently CD19 (5). Additionally, CD56 is abnormally expressed in 67-79% of cases (6,7).

In patients with myeloma, it has been observed that disease aggression correlates with the absence of CD56; CD56 patients were found to exhibit higher levels of β-2-microglobulin, alongside a higher incidence of Bence Jones protein, extra- medullary disease, thrombocytopenia and renal insufficiency when compared with CD56+ patients (7,8). In addition to CD56, it has been reported that CD117 is expressed in the malignant plasma cells of certain patients with myeloma (4). Furthermore, Bataille et al (4) noted that a lack of CD117 was associated with aggressive disease and a significantly shorter survival time compared with CD117+ cases. Pozdnyakova et al (9) reported that the simultaneous assessment of CD56 and CD117 by flow cytometry identified cytogenetically distinct groups of plasma cell myeloma, and CCND1 rearrangement was almost exclusively observed in cases demonstrating CD117 and CD56 negativity.

CD33 is a glycoprotein expressed on myeloid cell surfaces and has a mass of 67-kDa. A small number of studies have observed the expression of CD33 on plasma cell surfaces; however, the reactivity of the marker has been noted in 6.5-12% of patients with myeloma (10,11). The expression of CD33 in such patients is reported to be associated with certain clinical parameters; the CD33+ patient group had a lower survival rate compared to the CD33– patient group, thus indicating the clinicopathological significance of CD33 expression (12).

Certain cases of CCND1+ myeloma are associated with the t(11;14)(q13;q32) rearrangement, involving the CCND1 gene (13). Such cases have been linked with a lymphoplasmacytic morphological appearance and may therefore be misdiagnosed, particularly if CCND1 and CD138 immunohistochemical staining has not been performed (13). However, in the present case, the FISH analysis for CCND1/IgH and the chromosome analysis appeared normal (data not presented). Due to the low frequency of aberrant antigen expression and the unclear association between morphology and myeloid antigenic expression, the possible prognostic indications of these features require further investigation.

In conclusion, forming a conclusive diagnosis for MM patients with unusual morphological appearances, based on morphology only, presents a challenge. In the present study, the flow cytometry technique allowed doctors to ascertain the nature of the neoplastic cells with atypical morphology. The present case possessed small-lymphoid cells and with myeloid antigen expression. Therefore, flow cytometry immunophenotyping may aid the diagnosis and the monitoring of minimal residual disease, particularly for patients that demonstrate no cytogenetical evidence.

References