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Plasma Cell Myeloma with Unusual Expression of CD19, CD10, CD45 and Surface Light Chain in a Human Immunodeficiency Virus Positive Patient

Julia Adams and Jiehao Zhou*

Department of Pathology and Laboratory Medicine, Indiana University School of Medicine, Indianapolis, USA

Abstract

A 52-year-old male with a history of Human Immunodeficiency Virus (HIV) infection presented with acute renal failure, hypercalcemia, anemia, and cervical lymphadenopathy. Serum protein electrophoresis demonstrated an IgG kappa monoclonal protein and bone scan demonstrated multiple lytic bone lesions. Given patient history/clinical presentation of HIV infection and cervical lymphadenopathy, differential diagnosis includes plasma cell myeloma, B cell lymphoma with extensive plasmacytic differentiation, plasmablastic lymphoma and HHV-8 associated large B cell lymphoma.

Flow cytometry of the bone marrow aspirate showed a CD19 positive/CD20 negative population with high side scatter and co expression of CD45, CD10, CD56, and surface kappa light chain.

Bone marrow biopsy/clot showed sheets of atypical plasmacytic cells. Immunohistochemical stains showed these atypical plasmacytic cells were positive for CD138, CD79a, CD56, MUM-1, CD19, CD10 and kappa light chain; negative for CD20, PAX-5, HHV-8, EBV and EBER in situ hybridization. Ki-67 demonstrated a low proliferation index in these atypical cells. Cytogenetic study showed a normal male karyotype. All things considered, including clinical presentation, morphologic and immunophenotypic features, it represents a unique case of plasma cell myeloma with unusual expression of CD19, CD10, CD45, and surface light chain.

Keywords: Plasma cell myeloma; Surface light chain; CD45; CD10; CD19; HIV

Case Report

A 52-year-old male with a past medical history of human immunodeficiency virus (HIV), hepatitis C virus, coronary artery disease, chronic obstructive pulmonary disease, and hypertension was admitted with acute renal failure and hypercalcemia. On physical exam, the patient was found to have an enlarged, 1.5-cm right cervical lymph node. No other lymphadenopathy or splenomegaly was identified. The complete blood count was: WBC 7.4 k/µl, Hgb 7.7 g/dL, MCV 90.7 fL, RDW 27.2%, and platelets 170 k/µl. Serum creatinine was elevated to 4.8 mg/dL. Serum free light chain analysis demonstrated a kappa to lambda

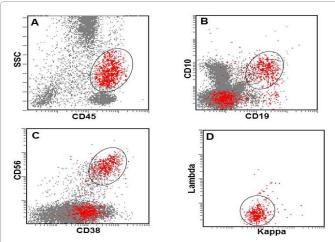


Figure 1: Flow cytometry analysis showed a distinct monoclonal cell population with high side scatter and expression of CD45 (bright), CD19, CD10, CD38, CD56 and surface immunoglobin kappa light chain. (A) CD45 versus side scatter plot; (B) CD19 versus CD10 plot; (C) CD38 versus CD56 plot; (D) Kappa versus Lambda plot (gated on CD19+ cells).

free light chain ratio of approximately 22:1. Serum immunoglobulin studies showed increased IgG at 6914 mg/dL, decreased IgM at 29 mg/ dL, and normal IgA at 94 mg/dL. Serum protein electrophoresis showed an IgG kappa monoclonal protein measuring 3.5 g/dL. Urine protein electrophoresis with immunofixation demonstrated two abnormal bands in the gamma region, one abnormal band with free kappa light chain and one abnormal band with IgG kappa. Bone scan demonstrated multiple lytic bone lesions.

Fine needle aspiration was performed on the enlarged cervical lymph node and demonstrated atypical plasmacytoid cells, suspicious for malignancy. Concurrent flow cytometry with a limited panel due to low cell count showed a small monoclonal CD19 positive population with high side scatter and expression of CD19, CD10, CD45 and surface kappa light chain. The CD5 and CD23 antigen expression were negative.

Bone marrow evaluation was performed. Flow cytometry analysis on bone marrow aspirate showed a population of cells with high side scatter and bright CD45 as well as co expression of CD10, CD56, CD38 and surface kappa light chain (Figure 1). T-cells were immunophenotypically unremarkable and blasts were not increased.

Evaluation of bone marrow biopsy and aspirate demonstrated

*Corresponding author: Jiehao Zhou, Department of Pathology and Laboratory Medicine, Indiana University Health Pathology Laboratory, Indiana University, Indianapolis, USA, Tel: 317-491-6563; Fax: 317-491-6509; E-mail: zhouji@iupui.edu

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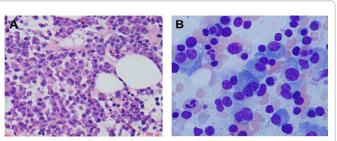


Figure 2: Morphology evaluation of bone marrow.

2A: Sheet of plasma cells in bone marrow biopsy/clot (H&E) 2B: Increased plasma cells with cytologic atypia in marrow aspirate (Wright



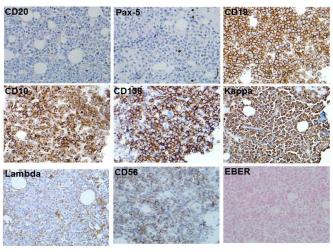


Figure 3: Unusual immunohistochemical features of neoplastic plasma cells.

a variably cellular bone marrow (20-60%) with maturing trilineage hematopoiesis and foci of sheets of atypical plasmacytic cells. No evident lymphoid aggregates were appreciated. These atypical plasmacytic cells showed significant cytologic atypia with frequent large nuclei /prominent nucleolus and binucleation on bone marrow aspirate smear, comprising 36% of total cellularity determined by bone marrow differential (Figure 2). Immunohistochemical stains demonstrated that these plasmacytic cells were positive for CD19, CD10, CD79a, MUM-1, CD138, kappa light chain, and CD56; negative for CD20, and PAX-5 (Figure 3). Ki-67 showed a low proliferation index of less than 10%. Immunohistochemical stains for HHV-8 and EBV, as well as EBER in situ hybridization were negative (Figure 3). Cytogenetic study demonstrated a normal male karyotype and florescent insitu hybridization panel for plasma cell myeloma was negative for abnormalities.

Review of the peripheral blood smear showed normocytic anemia with rouleaux formation, an adequate number of leukocytes with mature morphology and adequate platelets. No circulating plasma cells or atypical lymphoid cells were identified.

Despite of the atypical immunophenotype, in light of the clinical presentation of hypercalcemia, renal failure, anemia, and lytic bone lesions and the fact that morphologic and immunophenotypic examination demonstrated sheets of atypical plasmacytic cells with CD138, CD56 expression and kappa light chain restriction; we believe this case represents a rare case of plasma cell myeloma with unusual CD19, CD10, CD45, and surface light chain expression.

Patient was started on treatment with bortezomib, cyclophosphamide, and dexamethasone but due to extensive comorbidities, including dependence of hemodialysis for renal failure and cardiac dysfunction, the patient was transitioned to treatment with melphalan. Current clinical condition is guarded due to significant comorbidities.

Discussion

Neoplastic plasma cells in plasma cell myeloma typically express bright CD38, CD138, and cytoplasmic light chain. CD38 expression in neoplastic plasma cells, however, is usually dimmer than that of normal plasma cells. Additionally neoplastic plasma cells usually do not show positivity for the normally expressed pan B-cell marker, CD19 (The neoplastic plasma cells in myeloma frequently demonstrate aberrant expression of several markers not seen on normal plasma cells, including CD56, CD117, CD10, CD20, and surface immunoglobulin (Table 1) [1-4]. Of all cases of plasma cell myeloma, less than 1 to 10% show CD19 expression, only 28% show CD10 expression, and approximately one third show surface light chain expression [1-5]. Expression of CD56, however, is seen in approximately 65 to 80% of cases of myeloma, and is only rarely seen in non-neoplastic plasma cells, B-cell lymphomas with plasmacytic differentiation, and plasmablastic lymphoma [1,2].

One of differential diagnoses in our case is B cell lymphoma with extensive plasmacytic differentiation given the expression of CD19, CD45 (bright) and surface light chain detected by flow cytometry. Seegmiller et al. [1]. compared the immunophenotypic features of plasma cells in B cell lymphoma vs. plasma cells in myeloma. He concluded that plasma cells in lymphoma were more likely to express CD19, CD45 and surface immunoglobin than plasma cells in myeloma. However, morphologic evaluation of our case failed to reveal increased lymphoid infiltrates in the bone marrow biopsy, clot and aspirate smear. Immunohistochemical stains confirmed the essential absence of CD20+/ PAX-5+ B cells and negative CD20/PAX-5 staining in plasmacytic cells. In addition, plasma cells in our case were also positive for CD56, which is more commonly seen in plasma cell myeloma. More important, the clinical presentation with hypercalcemia, renal failure, anemia, lytic bone lesions and high levels of kappa IgG paraprotein argue against the diagnosis of B cell lymphoma of plasmacytic differentiation.

One confounding factor making our case interesting and challenging was the fact that our patient was HIV positive, thus raising the differential diagnoses of plasmablastic lymphoma and HHV8-associated large B-cell lymphoma. Plasma cell myeloma and plasmablastic lymphoma can show overlapping morphologic and immunophenotypic features, including plasmacytic markers of CD138 and MUM-1 [2]. To distinguish the two entities in cases with overlapping morphology and immunophenotype, CD56 expression

Antigen	Frequency of expression In plasma
cell myeloma	
C0138	"100%
CD38	-100%
CD19	<1-10%
CO56	65-80%
CD117	20-35%
CD10	28%
CD20	10-30%
Surface immunoglobulin	35-45%
CD45 (LCA)	-40%

 Table 1: Reported frequencies of antigen expression by neoplastic plasma cells in plasma cell myeloma.

and EBER in situ hybridization can be useful. The expression of CD56 is favorable for diagnosis of plasma cell myeloma whereas positivity for EBER is uncommon in myeloma but has a high rate of positivity of up to 86% in plasmablastic lymphoma [2,6,7]. Therefore a negative CD56 with positive EBER makes a diagnosis of plasma cell myeloma unlikely, and a positive CD56 with negative EBER result makes a diagnosis of plasmablastic lymphoma unlikely [8]. Similarly, the negative result of HHV-8 argue against a diagnosis of HHV8- associated large B cell lymphoma.

Overall, in our case, the classic clinical presentation and morphology for plasma cells, along with the immunophenotypic finding of aberrant expression of CD56 and negativity for HHV8 and EBER in situ hybridization ultimately led us to the diagnosis of plasma cell myeloma despite the unusual findings of CD19, CD10, CD45 and surface light chain expression.

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