Original Article

Plasma cell leukemia: A retrospective study of 10 cases

Anshul D Agarwal, Beena S Brahmbhatt, Biren P Parikh, Manoj J Shah

Department of Pathology, The Gujarat Cancer and Research Institute, Ahmedabad, Gujarat, India

Correspondence to: Dr. Anshul Agarwal, E-mail: dranshulagarwal@gmail.com

Abstract

BACKGROUND: Plasma cell leukemia (PCL) is a rare aggressive variant of multiple myeloma (MM) characterized by a fulminant course and poor prognosis. Flow cytometry (FCM) is very useful in the diagnosis of the plasma cell leukemia. Herein, we present 10 cases of PCL. **MATERIALS AND METHODS:** We retrospectively studied immunophenotypic profile of 10 cases of PCL from Jan 2009 to Dec 2013 using 5 parameters, 6 color flow cytometric analysis. We also studied their clinical presentation and other laboratory findings. **RESULTS:** Common clinical features at presentation were weakness, bone pain, anemia, thrombocytopenia and osteolytic lesions. Plasma cell population were identified by strong expression of CD38 and co-expression of CD38 and CD138. CD56 was expressed in 20% cases. CD19 and CD117 were negative in all cases. **CONCLUSIONS:** Immunophenotyping is highly useful to differentiate PCL from other chronic lymphoproliferative disorders with plasmacytoid morphology as well as from non-neoplastic reactive plasma cells. Co-expression of CD38 and CD138 is a best combination to identify the plasma cells by using FCM.

Key Words: Plasma cell leukemia, immunophenotyping, CD38, CD138

Introduction

Plasma cell leukemia (PCL) is a rare neoplastic disorder of plasma cells, accounting for 1-2% of all plasma cell neoplasm[1]. It is defined by an absolute plasmacytosis of greater than 2 × 10^9 cells or greater than 20% plasma cells in the peripheral blood.[1]

Plasma cell leukemia has an aggressive clinical course and is resistant to chemotherapy with a median survival of 6-8 months. However, drugs like bortezomib, cyclophosphamide and dexamethasone have been shown to be more effective for PCL.[2]

Multiparametric flow cytometry (FCM) is generally required in the differential diagnosis of unusual cases of PCD. Availability of newer markers allows us to unequivocally identify plasma cells and also help to discriminate between normal and neoplastic plasma cells.[3]

Materials and Methods

We reviewed an immunophenotypic profile of 10 cases of PCL presented to our laboratory, over a period of five years, from 2009 to 2013. We received peripheral blood (PB) and bone- marrow aspirate (BMA) sample in all the cases. The PB and BMA smears were stained with Wright's stain for morphologic evaluation. For flow cytometric immunophenotyping (FCI), the cells were stained within 24 hours of collection using a whole blood lyze wash technique.

Panel of directly conjugated monoclonal antibodies comprised of CD45 (PerCp), CD3 (PE Cy7), CD5 (PerCp), CD10 (APC), CD19 (APC-H7), CD20 (PE Cy7), CD22 (FITC), CD23 (PE), CD38 (PE), CD56 (APC), CD79b (PE), CD138 (FITC), FMC7 (FITC), Kappa (PE), Lambda (FITC), IgD (PE) and IgM (FITC). Five parameters and 6 color immunophenotyping were performed using a FACS Canto II (Becton, Dickinson). Minimum 10,000 events were acquired using low side scatter *versus* low to high forward scatter gating. Data (collected in list mode) was analyzed with BD FACSDiva software (Becton, Dickinson). Other clinical, hematological and biochemical parameters were correlated.

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Results

Clinical features

Common complaints were weakness, backache, bone pain, fever and loss of weight. Four patients had hepatosplenomegaly. Osteolytic lesions were detected in 8 cases, absent in 1 case and was not available in 1 case.

Laboratory findings

Leukocytosis (mean; 53.3 × 10^9/L, range; 21-88 × 10^9/L), and anemia (mean; 68 g/L, range of hemoglobin; 58-84 g/L), were seen in all cases. Thrombocytopenia (mean; 64.1 × 10^9/L, range of platelets; 29-125 × 10^9/L) was seen in nine cases. In one case platelet count was normal. On manual differential count in PB smear, the plasma cells percentage were more than 20% (range; 22-95%) in all cases except one case (14%), in which an absolute count of the plasma cells was >2000 cell/μl biochemical investigations revealed hypercalcemia (67%), high serum creatinine (70%) and high blood urea levels (90 ml/min)

Immunophenotypic characteristics

The PC population was identified on the moderate to strong expression of CD38 and co-expression of CD38 and CD138. All ten cases were positive for CD38 [Table 1]. Three out of ten cases were negative for CD138 although they were positive for CD38. CD56 expression was seen in two out of ten cases studied (20%). CD117 was expressed in none of the eight cases studied. CD19 was negative in all cases. Other markers including CD45, CD5, CD10, CD11c, CD23, CD25, CD79b, and CD103 were consistently negative in all cases.

Discussion

The median age at diagnosis of primary PCL is 55 years, approximately 10 years younger than for myeloma.[4]

The Plasma cells are morphologically easy to identify in BM; however, they are often missed on PB smear examination owing to its resemblance to plasmacytoid lymphocytes, monocytoid cells or erythroid precursors and rarely hairy cells. Rarely PCL can also be misdiagnosed as acute leukemia.[5] In addition, a few plasma cells may

Table 1: Immunophenotypic profile of all cases of plasma cell leukemia

Case no.	CD38%	CD138%	CD38/CD138 Dual positive%	CD19%	CD56%	CD117%
1	99	98	97.7	Neg	Neg	Neg
2	99	28	0	Neg	Neg	Neg
3	97	Neg	2.8	Neg	Neg	Neg
4	88	86	41.7	Neg	Neg	Neg
5	97	Neg	0.4	Neg	Neg	Neg
6	99	94	93.7	Neg	Neg	Neg
7	86	73	72.8	Neg	Neg	Neg
8	65	Neg	0.1	Neg	Positive	Neg
9	85	30	30	Neg	Positive	NA
10	94	88	86	Neg	Neg	NA

Neg=Negative, ND=Not done

be seen in peripheral circulation in various inflammatory conditions. Our study is limited by its retrospective nature and the small sample size, which is due to the rarity of PCL.

A variety of approaches based on CD38, CD138 (syndecan-1) and/or CD45 expression are being used. Combined use of CD38, CD138 and CD45 together with light scatter characteristics has been recommended by European Myeloma Network.[6] We used light scatter (forward scatter vs side scatter) characteristics and CD45 expression for gating of the plasma cells. Neoplastic plasma cells traditionally have been identified by their strong CD38 and negative or dim CD45 expression pattern on FCM.[7] It has been shown that strong CD38 and negative or dim CD45 gating alone might fail to identify myeloma composed largely or partly of CD45 positive PCs. The CD38 is a nonspecific marker that can be detected on hematopoietic stem cells, myeloid cells and lymphocytes. Neoplastic plasma cells typically express CD38 at a lower intensity than normal plasma cells and might be indistinguishable from contaminating T or B cells. With the introduction of specific monoclonal antibody for plasma cells (CD138), plasma cell is best determined by multiparameter FCM using at least CD138, CD38 and CD45.

CD19 is usually expressed in non-neoplastic plasma cells while they are absent in neoplastic cells. Thus it cannot be used for gating as in other chronic lymphoproliferative disorders

Entities such as chronic lymphocytic lymphoma with plasmacytoid features, lymphoplasmacytic lymphoma, and diffuse large B-cell lymphoma with plasmacytoid differentiation often are in the differential diagnosis. CD19 is an especially useful antigen to separate these processes, being expressed in fewer than 1% of myeloma cases, in contrast with its nearly universal expression by B-cell lymphomas and leukemias.[8]

Normal plasma cells do not express CD56 antigen, which has been considered to have an important role in anchoring PCs to the bone arrow stroma. However, most of the myeloma cells aberrantly express CD56. Pellat-Deceunynck *et al*.,[8] have reported that the malignant cells of PCL (primary or secondary) do not express or weakly express CD56 in contrast to patients with MM. Lack of CD56 expression might be associated with more aggressive disease and extramedullary dissemination.

Flow cytometry is useful to differentiate PCL from other chronic lymphoproliferative disorders with plasmacytoid morphology as well as from non-neoplastic reactive plasma cells. Co-expression of CD38 and CD138 is a best tool to identify the plasma cells in flow cytometry. The complementary effects of CD138 and CD38 permit inclusion of plasma cells with total or partial expression of antigens that are biologically or therapeutically relevant. While aberrant antigen expression is helpful for the diagnosis of myeloma, it might also be helpful for the detection of minimal residual disease, given the similar incidence of marker expression in treated *vs* untreated patients. Inclusion of antibodies against antigens like CD19, CD56, and CD117 in the panel not only helps to diagnose their aberrant expression by PCL, but also helps in prediction of prognosis.

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