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Plasma Cell Leukemia: Clinicopathological Profile of Five Cases

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Abstract

Aims: Plasma cell leukemia (PCL) is a rare disorder which develops spontaneously (primary PCL) or evolves in patients with multiple myeloma (secondary PCL). It is defined by the presence of 2×10^9/L peripheral blood plasma cells and plasmacytosis accounting for more than 20 % of the differential white cell count[1]. This study aims to analyze the clinical, morphologic and immunophenotypic profile of cases of Plasma cell leukemia and determine the significance of peripheral blood smear, bone marrow aspiration, serum protein electrophoresis and flow cytometry in the diagnosis. *Methods:* All cases diagnosed as Plasma cell leukemia during the period January 2012 to January 2015 were included in this study. Giemsa (MGG- May Grunwald Giemsa) stained smears of peripheral blood smears and bone marrow aspiration were examined. Serum protein electrophoresis (SPE) and immunophenotyping by flow cytometry were also subsequently done. *Results:* There were five cases of PCL diagnosed during this period which included four males and one female. *Conclusion:* Plasma cell leukemia is an aggressive disease. Peripheral blood smear examination, bone marrow aspiration, serum protein electrophoresis and immunophenotyping (flow cytometric analysis) are very useful in the diagnosis of PCL.

Keywords: Plasma Cell Leukemia; Peripheral Blood Smear; Bone Marrow Aspiration; Serum Protein Electrophoresis; Immunophenotyping.

Introduction

Plasma cell leukemia is defined by the presence of 2×10^9/L peripheral blood cells and plasmacytosis accounting for more than 20% of the differential white cell count [1]. Primary PCL is defined as a malignant Plasma cell proliferation first diagnosed in the leukemic phase, while secondary PCL corresponds to the leukemic transformation of a previously diagnosed multiple myeloma (MM), probably as consequence of clonal transformation [2,3]. Clinical presentation is characterised by nonspecific symptoms, such as fatigue, weight loss and bone pain. The prognosis of PCL is poor with a median survival of 7-11 months. Survival is even shorter when PCL occurs in the context of refractory or relapsing MM [4].

Materials and Methods

Between January 2012 and January 2015, 5 diagnosed cases of Plasma cell leukemia were studied. These included four males and one female. Peripheral blood smear and bone marrow aspirate smears of the patients were studied. These smears were stained with Giemsa (MGG- May Grunwald Giemsa) stain for morphologic evaluation. Serum Protein electrophoresis and Flow cytometry were outsourced to a reference laboratory. The chief complaints of the patients were noted. The following

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biochemical parameters were determined at diagnosis for each patient: serum calcium, serum creatinine, serum urea and serum uric acid.

Results

Leucocytosis was noted in all the five cases, and anaemia was seen in all the cases. Thrombocytopenia was noted in 4 patients. One patient had normal platelet counts. All the patients had bone pain, history of weight loss and fatigue alongwith non-specific symptom such as malaise. Differential leucocyte count on peripheral blood smear examination showed the plasma cell percentage more than 20% (range 25-52%) in all 5 cases (Figure1& 2). Bone marrow aspirate smears revealed bone marrow involvement by increased number of plasma cells (range 38-88%). Biochemical investigations revealed hypercalcaemia, increased blood urea, high serum creatinine and uric acid levels. M-band was detected on serum protein electrophoresis.

Immunophenotypic Characteristics

Flow cytometry in all five cases was done. All of these cases showed moderate to strong expression of CD 38. Co-expression of CD 38 and CD 138 was also noted. CD 20 positivity was noted in three cases. CD 56 was positive in two cases. However, all five cases were negative for CD 19 and CD 117 (Table 1).

Table 1: Immunophenotypic characteristics of five cases of PCL

Case no.	CD 38	CD 138	CD 20	CD56	CD 19	CD 117
1.	+	+	+	+	-	-
2.	+	+	-	-	-	-
3.	+	+	+	+	-	-
4.	+	+	-	-	-	-
5.	+	+	+	-	-	-

Abbreviations:
PCL- Plasma Cell leukemia
CD - Cluster of Differentiation

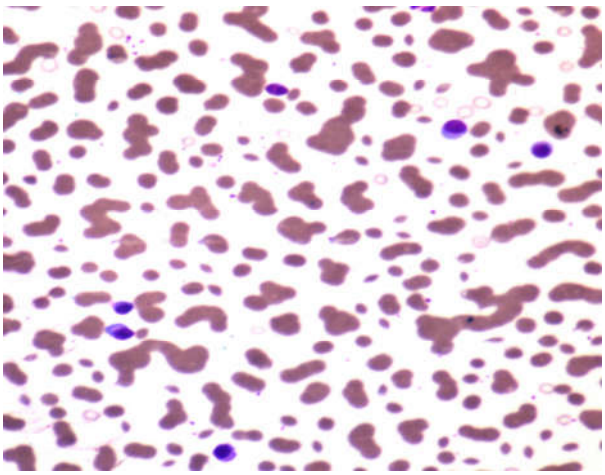

Fig. 1: MGG Stained peripheral blood smear showing circulating plasma cells in Plasma cell leukemia (100X)

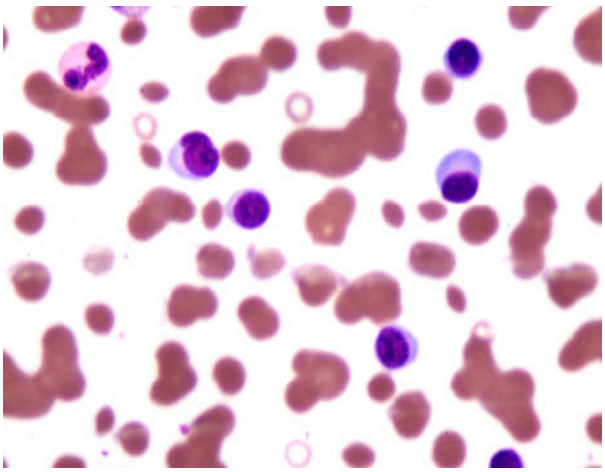

Fig. 2: MGG Stained peripheral blood smear showing circulating plasma cells in Plasma cell leukemia (400X)

Discussion

PCL is a rare disorder representing less than 5% of malignant plasma cell diseases [5]. PCL is a rare and aggressive variant of myeloma characterized by the presence of circulating plasma cells. It is classified as either primary PCL occurring at diagnosis or secondary PCL in patients with relapsed/ refractory plasma cell myeloma. Primary PCL is a distinct clinic-pathological entity with different cytogenetic and molecular findings. The clinical course is aggressive with short remissions and survival duration. The diagnosis is based upon the percentage (20%) and absolute number (2×10^9/L) of plasma cells in peripheral blood [6].

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 CD 138 is the best tool to identify the plasma cells [7].

Plasma cell leukemia is the most aggressive presentation of plasma cell neoplasm characterized by plasma cells circulation in peripheral blood, immaturity and heterogeneity of proliferating cells, acute course, extramedullary involvement and poor prognosis. PCL presents more often extramedullary involvement, anemia, thrombocytopenia, hypercalcemia, as well as impaired renal function. Cytogenetic abnormalities and mutations observed in PCL lead to escape from immune surveillance and independence from the bone marrow microenvironment with changes in expression of adhesion molecules or chemokines receptors. The outcome of PCL has improved with combination approaches with novel agents (including bortezomib and immunomodulatory drugs, such as lenalidomide) and with autologous stem cell transplantation.

Conclusion

Plasma cell leukemia is an aggressive disease. Peripheral blood smear examination, bone marrow aspiration, serum protein electrophoresis and immunophenotyping (flow cytometric analysis) are very useful in the diagnosis of PCL.

Conflict of Interest

None

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