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Case Report Open Access

Plasma Cell Leukemia Remains Like an Incurable Disease? A Rare Presentation of an Aggressive Case of Secondary Plasma Cell Leukemia

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Abstract

Secondary plasma cell leukemia is an aggressive variant of multiple myeloma characterized by the presence of more than 2×10^9/L plasma cells on peripheral blood. We reported an unusual presentation of this entity. The diagnosis of secondary plasma cell leukemia was done by cytological and immunophenotypic characteristics of plasma cells. On the blood smear examination was visualized a high number of plasma cells (46.3×10^9/L) and plasmablastic cells. Conventional chemotherapy and bortezomib regime led to a complete remission, but the patient's condition deteriorated very quickly and she died of sepsis. The prognosis of secondary plasma cell leukemia remains unfavorable and the early diagnosis needs to be done in order to provide a better choice of treatment and increase the survival of patients with plasma cell leukemia.

Keywords: Plasma cell leukemia; Multiple myeloma; Imunophenotyping; Prognosis

Introduction

Plasma Cell Leukemia (PCL) is a rare disease and the most aggressive presentation of plasma cell neoplasm, accounting for 2–4% of all plasma cell disorders [1,2]. The diagnostic is based on degree of plasmacytosis (plasma cells >20% and an absolute count greater than 2×10^9/L in peripheral blood examination [3-5].

Primary PCL (pPCL) is defined as a malignant Plasma Cell (PC) proliferation first diagnosed in the leukemic phase, while secondary PCL (sPCL) arises in the context of a pre-existing refractory or relapsing myeloma disease [6,7].

In addition, the high numbers of circulating PCs proliferation leads to deposits in extramedullary sites (liver, spleen, lymph nodes), organomegaly and bleeding tendency were common in primary PCL younger myeloma patients, but not in secondary PCL, while patients with sPCL have shown recurrent bone pain and advanced bone disease with osteolytic lesions [8,9].

Myeloma cells show an expression of some antigens: $CD138^{+++}$, $CD38^{++}$, $CD56^{++}$ and $CD45^{+}$. CD56 present in 60%-70% of myeloma cases. The surface phenotype of PCs in plasma cell leukemia is different from that bone marrow PCs in patients with multiple myeloma (MM) [10]. On the other hand, a lack of CD56 expression is considered to be an immunophenotyping characteristic of leukemic cells in PCL. Besides, the appearance of a decreased CD56 expression on bone marrow plasma cells is considered an unfavorable factor and a hallmark of leukemic transformation of MM. CD20 antigen displayed higher reactivity in clonal plasma cells of patients with PCL and it's differentially expressed in circulating plasma cells when compared to bone marrow plasma cells in myeloma patients [9-12].

sPCL rarely responds to polychemotherapy, because patients have already received previous treatment for myeloma patients. Bortezomib treatment is highly effective in MM, therefore, chemotherapy regimens with bortezomib in patients with PCL hasn't showed the same efficiency in myeloma patients yet [13,14].

The purpose of this study was to report a rare and aggressive case of secondary PCL treated with high-dose chemotherapy and bortezomib followed by fast relapse.

Case Report

A 63-years-old female patient, assisted at an outpatient oncology service with complaints of weakness, weight loss and bone pain with radiation to the leg, which does not respond to any antialgic or muscle relaxants medication. Magnetic resonance image revealed the presence of a solid tumor on the left leg and the biopsy was compatible with plasmacytoma. Complete blood count presents bicytopenia: anemia, hemoglobin: 8.8g/dL, thrombocytopenia, platelet count: 87×10^9/L and increase of the white blood cells: $59.4 \geq 10^9$/L with plasmocytosis, 46.3×10^9/L. These leukemic plasma cells represented 78% of all white blood cells. Blood smear also revealed the presence of immature cells with delicate chromatin and nucleoli (plasmablastic cells) and erythrocytes in rouleaux (Figure 1). Bone marrow examination exhibited hypoplasia of erythrocyte (3%), granulocytic (7%), megakaryocytic sectors (4%) and hyperplasia of lymphoplasmacytic cells (4% lymphocytes and 82% of plasma cells). Her biochemical profile showed increase of serum creatinine (3.8 mg/dL), lactate dehydrogenase (LDH, 1502 U/L), β2-microglobulin (β2M, 5.57 μg/mL), calcium (12.8 mg/dL) and decrease in albumin (3.0 mg/dL). The immunophenotyping by flow cytometry revealed a high number of

peripheral plasma cells that expressed $CD138^{+++}$, $CD38^{++}$, $CD45^{+}$, $CD56^{-}$, $CD117^{-}$, $CD10^{-}$, $CD15^{-}$, $CD16^{-}$, $CD19^{-}$, $CD20^{-}$, $CD22^{-}$, $CD23^{-}$, $CD25^{-}$ and cytoplasmatic lambda light chain was positive (Figure 2). Conventional cytogenetic demonstrated only a deletion of chromosome 13 in 70% of cells. Serum protein electrophoresis exhibited M component (IgG 3.850 mg/dL) and urine Bence Jones was absent. The diagnosis of MM IgG lambda IIB/secondary plasma cell leukemia was done. After that, the patient underwent chemotherapy (Vincristine, Bortezomib, Cyclophosphamid, Mephalan and Dexamethasone), that achieved complete response. However, 4 months later, the patient was admitted with relapse, atypical cells with plasmacytoid characteristics prior to bone marrow transplantation and the patient died from septic shock.

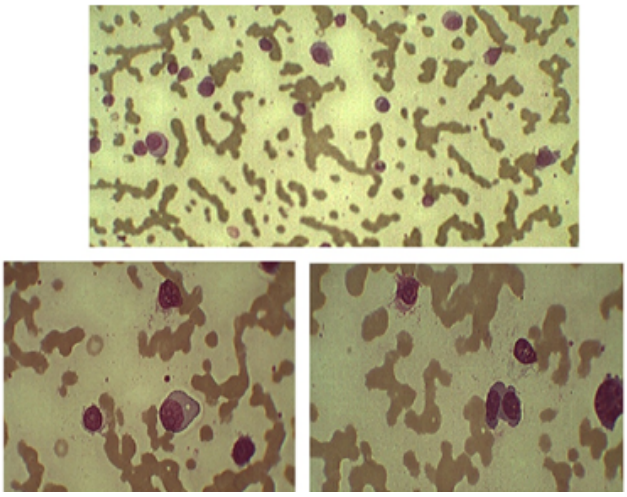

Figure 1: A- Plasmocytosis in blood smearof patient with secondary plasma cell leukemia. B-Plasmablastic cell with increased hiperbasophilia in cytoplasm, multiple nucleoli and erythrocytes in rouleaux (May-GruwaldGiemsa stain 1000x). C- Clonal plasma cell division in pheripherical blood (May-GruwaldGiemsa stain 1000x)

Discussion

Plasma Cell Leukemia (PCL) is a rare and aggressive plasma cell dyscrasia. Different studies recognize the sPCL as a variant of plasma cell myeloma, characterized by the expansion of a clone of immunoglobulin-secreting terminally differentiated mature B-cells. Mechanisms contributing to the pathogenesis and development of PCL are not fully understood [1,3,5].

Immunophenotypically, PCL is typically positive for CD38, CD138, CD20 (more common in PCL than multiple myeloma). CD56 N-CAM (neuronal adhesion molecule) may be presented in plasma cell myeloma [10]. Moreover, patients with sPCL tend to exhibit several clinical findings, such as extramedullary disease, bone marrow failure, advanced stage disease and expression of distinct immunophenotypic markers, such as lack of CD56 and presence of CD20 [10-12]. CD20 is usually negative in normal PCs and has shown to be positive in 30% cases of MM [9,10]. On the other hand, the expression of the CD20 antigen is associated with a poor prognosis in patients with PCL, but their absence does not show any association with prognosis.

The French Study Group of MM provides risk groups based on two variables: β2M and changes of chromosome 13 and defined that patients with β2M ≥ 2.5 mg/dL and deletion chromosome 13 presented high risk of developing advanced disease and short survival [15].

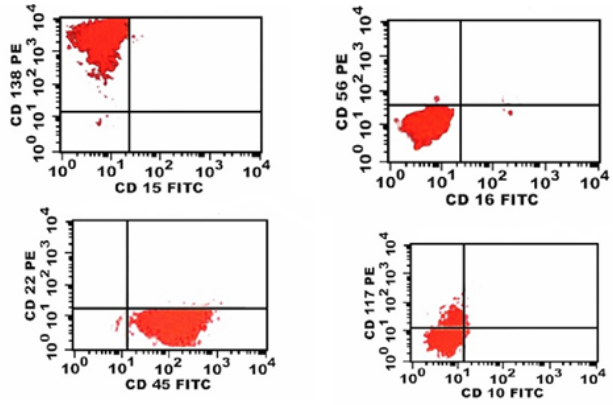

Figure 2: Immunophenotyping of circulating plasma cells. The clonal plasma cells are tagged in red. The graphs shows that the plasma cell are positive for CD138, CD117, CD45 and negative for CD15, CD16, CD56, CD22 and CD10 (PE, phycoerythrin, FITC, fluorescein.

Our study revealed a common clinical finding of MM such as weakness, fever and bone pain. Moreover, the presence of high number of circulating plasmablastic cell, increase of serum LDH and β2M, deletion of 13 chromosome and the absence of CD56 (N-CAM) in circulating PC may be associated with release of bone marrow PC and should be involved in leukemic transformation. Furthermore, the CD20 antigen was absent, but this finding cannot be associated with a better prognosis. The immunophenotyping by flow cytometry also proved to be extremely indispensable on diagnosis of sPCL, because it was able to characterize the circulating PCs. Besides, we recommend that β2M levels, deletion of chromosome 13 and absence of CD56 should be used to classify the most advanced stages of the disease in patients with plasma cell leukemia.

PCL is an extremely aggressive disease with no standard treatment regime so far due to the rarity of the disease. Melphalan/Prednisolone (MP), Vincristine, Doxorubicin and Dexamethasone (VAD) or Thalidomide/Dexamethasone regimes have been tried but the outcome has been dismal. Prognosis is generally very poor with a median survival of 2–8 months [16-18].

Katodritou et al. (2014) showed that patients treated with bortezomib versus conventional therapies had a higher survival of 13 months versus 2 months. The same study also demonstrated that treatment of PCL with bortezomib induces high response rates and prolongs survival over conventional therapies. The combination of new drugs such as bortezomib, Lenalidomide and dexamethasone as part of the induction regimens and bone marrow transplantation (autologous and allogeneic approaches) can improve the prognosis of patients with PCL [19,20]. Our case also presents a fast progression of the disease with short survival and drug resistance. The poor therapeutic response to bortezomib, probably happened due to a late

diagnosis of sPCL and delay to start this treatment, resulting in rapid evolution to death.

This study highlights the importance of early diagnosis and attempt to understand the behavior of this rare and aggressive disease to improve the therapeutic outcomes and increase survival of patients with secondary plasma cell leukemia.

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