Case report
Plasma cell leukemia, a case report and literature review
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ABSTRACT

The plasma cell leukemia (PCL) is an extremely rare malignant blood disorder with a pejorative prognosis. It is defined by the presence of at least 20% of plasma cells in the peripheral blood or an absolute number of circulating plasma cells greater than 2 giga/L. It appears under two variants: secondary PCL that complicates known multiple myeloma and primitive PCL that is immediately leukemic. We report the case of a 56 years old male patient who presented 2 months before his hospitalization diffuse bone pains with asthenia. The CBC revealed a normochromic normocytic anemia (Hb: 8.5 g/dL) and a leukocytosis. The blood smear objectified 3 giga/L circulating plasma cells. The bone marrow exam noted a rich cellularity and a marrow invaded up to 60% by dystrophic plasma cells. The clinical presentation of the plasma cell leukemia, its cytological smear characteristics, immunophenotypical, pathophysiological, therapeutic approach and outcome will be reminded in this article.

1. Introduction

Plasma cell leukemia (PCL) is a very rare variant but the most aggressive of monoclonal gammopathy. [1] We retain two forms: the original form occur de novo in patients without multiple myeloma (MM) existing and readily diagnosed by blood dissemination and the secondary PCL, corresponding to a late event in patients with MM. We report a case of primary PCL with quickly pejorative evolution.

2. Observation

This is a Moroccan patient aged 56, without significant pathological history, admitted in the Mohammed V military hospital in Rabat for bone pain of the right arm, resistant to usual analgesics, lasting for 3 months, in a context of impaired general condition (weight loss of 11 kg, fatigue and night sweats).

On physical examination, the patient was not febrile and has a cutaneous pallor with pain mobilization and pressure of the right arm. There was no bleeding, infection or tumor syndrome. Radiological assessment showed lytic picture of the right humerus, but also in the skull and pelvis.

Laboratory tests revealed the presence in the blood count for anemia normochromic normocytic non regenerative to 85 g/dL and thrombocytopenia 100 giga/L associated with leukocytosis 16 giga/L. The blood smear showed the presence of circulating plasma cells in 19% (3 giga/L) (Figure 1).

Bone marrow examination objectified rich marrow invaded by 60% dystrophic plasma cells (Figure 2).

In biochemical tests, there was an inflammatory syndrome with high CRP to 150 mg/L, an hyperprotdemia at 100 g/L, hypercalcemia 120 mg/L, renal failure (creatinine clearance measured at 16 mL/min), and on protein electrophoresis a monoclonal peak at 59 g/L in gammaglobulin area. Immunofixation confirms the presence of IgG immunoglobulin kappa light chains. Cytogenetic analysis was conducted, and revealed an hyperdiploidy, 57 chromosomes who has a standard prognosis in multiple myeloma. (Figure 3)

Therapeutically, patients received chemotherapy according Velcade-Dexamethasone -Thalidomide protocol with monthly injections of bisphosphonates associated with symptomatic treatment. The evolution was marked by achieving a very good partial response after 6 treatments. This response was consolidated by a therapeutic intensification of melphalan with autologous stem cell support. Eight months after autograft the patient had a relapse explosive. A remedial treatment was initiated with Revlimid-dexamethasone, but unfortunately the patient died during course in an array of septic shock.

CASE REPORT:

HISTORY

A 53 years old Philippine male patient live in Saudi Arabia since 1993, referred electively through OPD because he was complaining of skin legions since two years.

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Discussion

PCL has been described for the first time by Gluzinski Reichenstein, there are more than a century. This is a rare form that represents only 2-4% of multiple myeloma patients and 0.9% of all acute leukemia [1]. It results from a monoclonal proliferation of plasma cells and is defined by the presence in the circulation of plasma cells with a rate higher than 2 giga / L or greater than 20% of leukocytes [1]. Sometimes, additional assessments should eliminate causes reaction to infection, autoimmune disease or neoplastic. In the case of our patient, these investigations have not been carried out before such a clear picture.

In Morocco, the notification registry Rabat cancers shows that the incidence of MM in 2005 was 22 per million population (pmp) per year for men and 9.4 pmp for women [2]. These figures give us a rough estimate of the PCL in our context, as they complicate 2-4% of MM.

The median age of onset of LAP is between 52 and 65 years (approximately 10 years younger than the median age observed in MM) and sex ratio is 1 [3]. Our patient fits perfectly within this range.

The clinical presentation of the PCL is more aggressive than MM and combines fatigue, bone pain, anemic syndrome and bleeding. Important frequency of extramedullary damage is noted, especially liver (52%) and spleen (40%) [4].

Biologically, the frequency and severity of anemia and thrombocytopenia appear higher in the PCL than in MM. Regarding the monoclonal immunoglobulins, IgA forms are less common than in patients with MM. In primitive PCL, there are a high percentage of light chains to form explaining the frequency of renal disease. Cytologically, plasma cells are typically well differentiated, in our patient, they were instead dystrophic. The hypercalcemia, renal failure and elevated serum $\beta_2$ microglobulin are frequent as the case in our observation. The PCL and like MM, the plasma cell express CD38 and CD138 antigens on the surface in the flow cytometry [5]. Unlike the MM, a CD54 over expression on plasma cells facilitates their extramedullary migration promoting tumor dissemination. Also there is an over expression of antigens CD28 and low expression of CD9, CD117, CD56 and HLA-DR [6]. Secondary PCL is characterized by the acquisition of CD28 responsible of increased cell proliferation and progression of the disease [6]. An important expression of chemokine receptors (CCR1, CCR2 and CXCR4) is involved in the development of the PCL [7]. In the end, the cytometry in flow can sit immunological diagnosis in exceptional cases of plasma cells with cytoplasmic projections mimicking hairy cells [8, 9].

Cytogenetic and molecular biology can identify many abnormalities without any of them actually reveals specific. The hypodiploidy, deletions of chromosome 13 and monosomy represent the most abnormalities found. Monosomy 7, rarely reported in case of MM was noted in the PCL. Abnormalities of chromosome 1 are also common particularly the 1q21 amplification and 1p21 deletion. The loss of TP53, mutation or
deletion was observed in 56% of primary PCL against 83% of secondary PCL. Translocation (11; 14), délétion1p13.1 and monosomy 13 were considered poor prognostic markers [4, 10]. In our patient cytogenetic analysis revealed an hyperdiploidy.

Prognostic of the PCL is one of hematological pejorative prognosis. The historical median survival (before the 2000s) ranged from 4 to 12.6 months with a survival rate at 5 years less than 10% in many series. With the advent of new therapies and the use of increasingly autologous hematopoietic stem cells, the median survival is much improved (recently over 3 years).

Treatment of LAP is an emergency and must be implemented quickly. Currently, protocols based on proteasom inhibitors are recommended during the induction phase and enable rapid cytoreduction. This result must be consolidated by an intensification therapy and the support of autologous or allogeneic stem cells.

Conclusion

The PCL is a very serious but fortunately extremely rare. The diagnosis is simple based on the discovery of circulating plasma cells in the blood smear by an experienced biologist.

Despite the encouraging therapeutic results especially for protocols including new drugs, the road is still far to better control and cure this disease.

REFERENCES