

## Case Report

**Secondary Plasma Leukemia: About a Case and Review of Literature**

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**Abstract:** Plasma cell leukemia (LP) is a rare ailment that is defined by the presence in the peripheral blood smear of 20% plasma cells or circulating plasma cells that is greater than  $2 \text{ G} / \text{L}$ . There are two variants: the primary form occurring de novo, diagnosed directly in the leukemic phase and the secondary form complicating an already known multiple myeloma. We report in this work a case diagnosed in the laboratory of hematology of the CHU Hassan II of Fez of a multiple myeloma transformed into plasma cell leukemia. It is a rare entity but should not be neglected. Secondary plasma cell leukemia maintains most of the characteristics of multiple myeloma in contrast to primitive plasma cell leukemia. Our work aims to show the common characteristics of the primitive and secondary forms of this leukemia and to discuss the peculiarities of each one.

**Keywords:** leukemia, multiple myeloma, Plasma cell.

**INTRODUCTION**

The secondary plasma cell leukemia LP-s is a leukemic transformation of a multiple myeloma previously diagnosed, which represents the terminal stage of chemo-resistance; It is an aggressive form of poor prognosis [1].

It survivals in 1% of patients with multiple myeloma and is less frequent than primary plasma leukemia because it represents only 40% of all plasma cell leukemia [2].

The role of the biologist remains important in the diagnostic orientation; As well as the importance of cytological examination in the follow-up of patients with multiple myeloma.

**CASE REPORT**

A 42-year-old male patient, diagnosed with multiple myeloma initially revealed by rachidian pain with alteration of the general state with no lymphadenopathy or hepatosplenomegaly at the clinical examination. A radiological assessment has been carried out to objectifying a biconcave settlement of the vertebral body of the eighth dorsal vertebra and compaction of the lumbar vertebrae plates with magnetic resonance imaging (MRI). The laboratory studies had shown an inflammatory syndrome, normocytic normochromic aplastic anemia, hypercalcemia, normal renal function and a narrow

spike ( $66 \text{ g} / \text{L}$ ) in the gamma globulin zone on the serum protein electrophoresis of with, at the immunofixation, monoclonal gammopathy type Ig A Lambda. Urinalysis showed a positive Bens-jones protein of the Lambda type. Medullary was infiltrated with 73% of plasma cells.

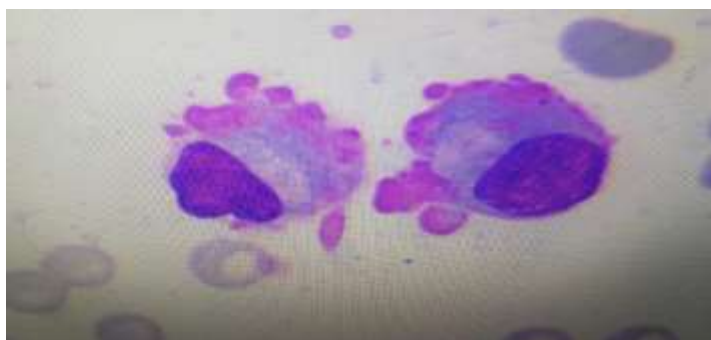
The patient was under on VAD (vincristine, adriamycin, dexamethasone) and a symptomatic treatment with bisphosphonate. The evolution was marked by a persistence of the clinical and biological signs testifying of a chemo-resistance and after a few months the state of the patient has been altered considerably leading to his hospitalization for re-evaluation of his disease objectifying 27% of circulating plasma cells ( $1,269 \times 10^9 / \text{L}$ ) to blood smear (Fig. 1) for level of leukocyte of  $4.700 \times 10^9 / \text{L}$  with massive medullary infiltration with 83% from normal and dystrophic plasma cells (Fig. 2) to a type of flamed plasma cells, of binucleated plasma cells even tri-nucleated, with central nuclei, open chromatin and a low basophil cytoplasm, sometimes vacuolated.

A hypercalcemia with impaired renal function, beta 2 microglobulin at  $6.46 \text{ mg} / \text{L}$ , albuminemia at  $27 \text{ g} / \text{L}$  and LDH at  $900 \text{ IU} / \text{L}$  has also been detected.

The patient's state quickly degraded and he died in the month following his plasma cell leukemia diagnosis.



**Fig-1: Blood smear colored with Wright Giemsa stain, magnification x 100 in optical microscope, showing a circulating plasma cell**



**Fig-2: Medullary smear with Wright Giemsa stain, magnification x100 in optical microscope, showing dystrophic plasmocytes with flamed plasma cell types**

## DISCUSSION

The transformation of multiple myeloma into plasma cell leukemia is very rare, it represents 1 to 4% with a median outset of 21 months [1]. The secondary plasma cell leukemia (LP-s) generally has the same characteristics as multiple myeloma (MM), but with a faster tumor extension; however, there are many differences between the primary and secondary form of the leukemia.

The median age of primary plasma cell leukemia (LP-P) is 55 years [3] a decade lower than the LP-s, our patient was 44 years old at the time of diagnosis which represents a very young age seen that the multiple myeloma reach subjects over 40 years old with a peak between 67 and 70 years old [4]. Concerning the sex ratio, we noted a discrepancy among the studies given the limited number of the reported cases.

In the medical literature, the pathophysiology of the transformation of the multiple myeloma into plasma-cell leukemia will be due to the mutation of the genes which codes for the adhesion molecules and the chemokine receptors leading to the passage of plasmocytosteo extra-medullary cells [5]; As well as the presence of several molecular aberrations remains the main explanation for this leukemia [6].

The clinical presentation is comparable to that of the MM but it remains more aggressive; more frequent extramedullary disease in LP-p and predominance of hepatic 52% and splenic 40% but represent less than 20% in the LP-s [7]. Contrary to osteolytic lesions which are rare in LP-p with 18 % against 53 % for LP-s [3]. Our patient presented osteolytic lesions when the diagnosis of multiple myeloma occurred.

The laboratory studies includes many perturbation; Anemia and thrombocytopenia are more frequent and more severe in the LP, with an average of Hb at 8.5 g / dL and 26 000 on platelets, whereas leukocytosis remains variable with an average of 15.7 G / L for the LP-s and 21.5 G / L for LP-p, and even leucopenia can be found [8] hence the requirement of a 20% rate of plasma cell count of the leucocyte formula.

The prognostic factors represented by  $\beta$ 2-microglobulin greater than 6 mg / l and LDH greater than 300 IU / l were found in our patient [9].

The most frequently immunoglobulins ever in the LP are Ig G with 33% followed by Ig A with 20% as the case of our patient [3].

Medullary infiltration is usually massive with plasma cell counts ranging from 76 to 83% [5]; of normal and dystrophic plasma cell.

The average size of the cells in the LP is generally much smaller than in MM. In some cases the majority of cells resemble a normal plasma cell with a basophilic cytoplasm, an eccentric nucleus and an important Golgi zone. In other cases the nuclear contour is irregular with more primitive cells that have a high nucleocytoplasmic ratio, finely dispersed chromatin, prominent nucleololi, limited or absent Golgi zone, corresponding to plasmablasts [10].

Generally, the expression of plasma surface antigens does not differ significantly between primary and secondary LP. To few exceptions: CD28 which is presented in 92% of LP-s for to only 33% of LP-p [5]. The expression of adhesion molecules such as CD11a / CD18 or CD56 may explain the hematogenous diffusion characterizing LP [11].

In cytogenetics, the karyotype is often complex and shows hypodiploidy. With fluorescence in situ hybridization (FISH), a special attention must be given to alterations: t (11; 14) as well as for chromosome abnormalities 1 and 17, in particular 1q + and del17p. Additional molecular research aiming to understand the development of LP-p and the transformation of MM into LP-s is necessary [12]. For our patient the flow cytometry as well as the karyotype were not been archived because it quickly evolved.

The efficacy of conventional therapies is not satisfactory, hence the interest of new treatments: thalidomide analogs and proteasome inhibitors, which aim to prolong survival. The improvement of results with new therapies and Autologous Stem Cell Transplant (ASCT) was observed in LP-p, but with no significant improvement in LP-s [12].

The treatment in relapsed LP-s or LP-p depends on the type of response to previous therapy. Able patients may be candidates to bortezomib-based therapy or intensive chemotherapy (cyclophosphamide, vincristine, doxorubicin, dexamethasone or dexamethasone-thalidomide, cisplatin, doxorubicin, cyclophosphamide, etoposide) followed by appropriate stem cell transplantation [12].

The prognosis of the disease remains very poor with an average of survival of 1.3 months for secondary plasma leukemia and 11.2 months for LP-p [13].

## CONCLUSION

Plasma cell leukemia remains one of the rare lymphoproliferative disorders that requires a fast diagnosis based essentially on the cytological examination of the blood smear especially in the follow-up of a multiple myeloma, hence the biologist importance to make a precise diagnosis even if the use of the immunophenotypic analysis is sometimes necessary.

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