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# Three Cases of Plasma Cell Leukemia

**Mouhamed Dieng[1,2*], Atoumane Faye[1], Jules Dabi Gabnon[1], Baïdy Sy Kane[1], Maïmouna Sow[1], Michel Assane Ndour[2], Seynabou Fall[3], Nafi Diagne[1], Awa Cheikh Ndao[1], Demba Diedhiou[2], Boundia Djiba[1], Fatou Samba Ndiaye[3], Maïmouna Ndour Mbaye[2], Anna Sarr[2], Awa Oumar Touré[4], Abdoulaye Pouye[1]**

[1]Division of Internal Medicine, Aristide Le Dantec Hospital, Dakar, Senegal
[2]Division of Internal Medicine, Abass Ndao Hospital, Dakar, Senegal
[3]Division of Clinical Hematology, Dalal Jamm Hospital, Dakar, Senegal
[4]Division of Biological Hematology, Aristide Le Dantec Hospital, Dakar, Senegal
Email: *docmdieng@gmail.com

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## Abstract

**Introduction:** Plasma cell leukemia (PL) is a rare lymphoproliferative disorder characterized by the monoclonal proliferation of plasma cells in the marrow and blood peripheral. It is defined by a blood plasmacytosis greater than 2 G/l or a plasma cell level greater than 20% of leukocytes. It can be primitive or secondary to multiple myeloma (MM). We reported 3 cases of PL. **Observations:** Case 1: A 59 years old woman with fever, anemia with 7 g/dl, hyperleukocytosis 9200/mm$^3$, thrombopenia 86 G/l inflammatory biological syndrome with CRP at 129 mg/l, hypercalcemia at 120 mg/l, renal failure with serum creatinine at 35 mg/l, urea at 0.85 g/l and 24-hour proteinuria at 0.98 g/24h. B2 microglobulin at 10.34 mg/l. The blood smear shows dysmorphic plasma cells at 68% and the bone marrow at 79% of dysmorphic plasma cells. The immunophenotyping of blood cells, the electrophoretic serum protein, shows PL CD38+, secondary of a MM LAMBDA. Case 2: A 65-year-old man with type 2 diabetes presented, right femoral neck, anemia, hyperleukocytosis at 22 G/l, and thrombocytopenia at 99 G/l. There was no hypercalcemia, or kidney failure. The blood smear showed 28% of plasma cells and 9% of blasts. On the myelogram, the marrow was normal richness with significant medullary plasmacytosis (31%) made up of dysmorphic plasma cells. The CT scan showed a settling of the body of D5 with heterogeneous osteocondensation. The patient was transferred to hematology where she was treated with polychemotherapy. The evolution was unfavorable following a death due to malignant hypercalcemia. Case 3: A 62-year-old woman who had a 5-year follow-up of Ig G kappa multiple myeloma was treated with Melphalan, Prednisone, and thalidomide with a therapeutic break for 2 months. She came back to the Internal Medicine department with: severe global dehydration, anemia

with externalized bleeding gingivorrhagia, pain in mechanical bones of the ribs, lower limbs, and pelvis, bilateral pneumonia. The biology found hyperleukocytosis at 99 G/l, anemia at 4.7 g/dl, thrombocytopenia at 31 g/l, hypercalcemia at 190 mg/l, renal failure with creatinine at 34 mg/L, and urea at 1.08 g/l, a biological inflammatory syndrome with CRP 294 mg/l. The smeared blood had shown 93% blood plasma cells and immunophenotyping showed CD38+. The patient died before specific treatment for the disease. **Conclusion:** Plasma cell leukemia is a rare atypical variant, complicating essentially multiple light chain myeloma. She must be suspected especially when there are cytological abnormalities such as major leukocytosis or thrombocytopenia, which are unusual in classical myeloma. Evolution is usually a very bad prognosis, with a median survival of 12 to 14 months for the form primary and 2 to 3 months for the secondary form.

## Keywords

Plasma Cell Leukemia, Multiple Myeloma

## 1. Introduction

Plasma cell leukemia (PL) is a rare lymphoproliferative disorder characterized by the monoclonal proliferation of plasma cells in the marrow and blood peripheral [1] [2]. It is defined by a blood plasmacytosis greater than 2 G/l or a plasma cell level greater than 20% of leukocytes. She may be primary (pPL) in 70% of cases occurring de novo in patients without pre-existing multiple myeloma (MM), diagnosed at the outset in phase leukemic, or secondary (sPL) corresponding to the terminal course of MM [3]. PL is characterized by an aggressive clinical picture with localizations frequent extra-marrow and laboratory abnormalities (anemia, thrombocytopenia, renal failure, and hypercalcemia) more severe than in MM. She remains one incurable disease despite the emergence of new therapies coupled with transplantation of hematopoietic stem cells which seem promising avenues for improving patient survival and quality of life [2]. We report a series of 3 cases of plasma cell leukemia diagnosed quite incidentally in the Internal Medicine Department of Aristide Le Dantec Hospital between 2013 and 2018 and handled in conjunction with the hematology department at Dalal Jamm Hospital.

## 2. Observations

Case 1:

A 59-year-old woman with no reported pathological history was hospitalized in the internal medicine department for the exploration of diffuse bone pain inflammatory and paraparesis. She had a fever of 40˚C and was hemodynamically stable. Biologically, we noted: anemia at 7 g/dl aregenerative normochromic normocytic, hyperleukocytosis 9200/mm$^3$, thrombocytopenia at 86 G/l, an in-

flammatory syndrome with ESR at 103 mm at the first hour, CRP at 129 mg/l, hypercalcemia at 120 mg/l, renal failure with serum creatinine at 35 mg/l, urea at 0.85 g/l and 24-hour proteinuria at 0.98 g/24 h. B2 microglobulin at 10.34 mg/l. The blood smear shows dysmorphic plasma cells at 68% (**Figure 1**). Immunophenotyping of circulating blood lymphocytes confirmed the CD38+ plasma cell proliferation. The medullogram confirmed leukemia in plasma cells showing 79% dysmorphic plasma cells. Electrophoresis serum proteins and urine protein immunofluorescence allowed confirming of light chain myeloma of the LAMBDA type with hypogammaglobulinemia at 3.6 g/l. It was leukemia with plasma cells revealing light chain myeloma complicated by medullary epiduritis. The patient was treated with multidrug therapy based on COP + Alkéran and the evolution has been unfavorable.

Case 2:

A 65-year-old man with type 2 diabetes who had a pathological fracture of the right femoral neck 3 months previously was admitted to the medical department Internal. He presented: anemia at 5.5 g/dl complicated by anemic heart, lower back pain in the hemi-girdle without bone marrow involvement, thrombocytopenia 99 G/l, hyperleukocytosis at 22 G/l. There was no hypercalcemia, kidney failure, or proteinuria. The blood smear showed a 28% plasmacytosis and 9% blastosis. On the myelogram, the marrow was normal richness with significant medullary plasmacytosis (31%) made up of dysmorphic plasma cells. The CT scan showed discreet settling of the body of D5 with heterogeneous osteocondensation. The patient was transferred to hematology where she was treated with polychemotherapy. The evolution was unfavorable following a death due to malignant hypercalcemia.

Case 3:

A 62-year-old woman with hypertension and regularly monitored, who has

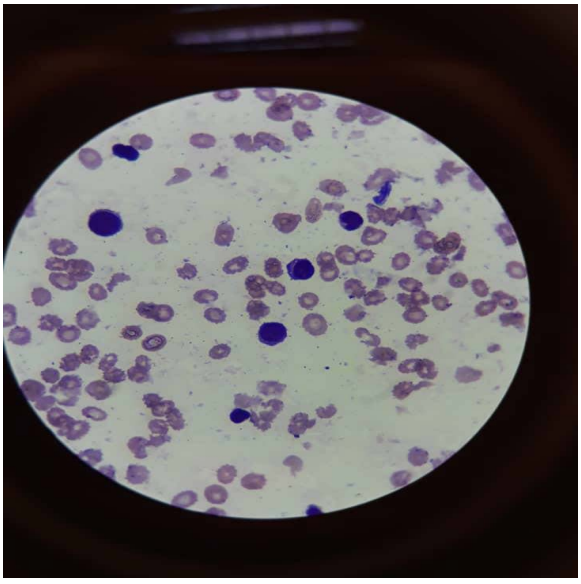

**Figure 1.** Dysmorphic plasma cell of blood smear (×100).

5-year follow-up of Ig G kappa multiple myeloma treated with Melphalan, Prednisone and thalidomide with a therapeutic break for 2 months. She came back in emergency in the Internal Medicine department with: severe global dehydration, anemia with externalized bleeding gingivorrhagia, pain mechanical bones of the ribs, lower limbs and pelvis, a bilateral pneumonia. In biology, we had hyperleukocytosis at 99 G/l, a anemia 4.7 g/dl, thrombocytopenia 31 g/l, hypercalcemia 190 mg/l, hyponatremia at 123 mEq/L, renal failure with creatinine 34 mg/L and urea at 1.08 g/l, a biological inflammatory syndrome with CRP 294 mg/l. The smear blood had shown 93% blood plasma cells. The patient died before specific treatment of the disease.

## 3. Discussion

PL represents between 2% and 4% of patients with plasma cells [4] [5] [6] [7]. pPL is a rare form of leukemia which occurs immediately at diagnosis unlike the sPL which corresponds to the unfavorable course (in 2% to 4% of cases) of advanced MM. Within sPL, 60% - 70% are pPL and 30% - 40% are sPL [8]. More recent data suggest an increase in the proportion of sPL around 50% [7]. The physiopathological basis is more or less the same. In the MM, tumor cells are mainly localized in the marrow bone and they depend in part on the microenvironment for their development, survival and protection against induced apoptosis by therapeutics. Plasma cells in leukemia plasma cells also accumulate in the bone marrow but have an increased ability to migrate into the bloodstream peripheral, which explains the extra-medullary manifestations of sickness. This blood circulation is the result, on the one hand, modification of surface molecules and cytokine receptors but also an inhibition of apoptosis and an escape vis-à-vis the immune surveillance system. The loss of expression of a number of adhesion molecules seem to be involved in the pathophysiology of PL, whether primary or secondary. Through example, t (14; 16) would lead to increased synthesis of metalloprotease MMP-9, responsible for destruction of the matrix extracellular [9].

The majority of pPL affects men with an M/F ratio of around 3/2. The median age at diagnosis of pPL ranges from 49.5 to 65 years depending on the series [4] [5] [7] [10] [11] [12]. An epidemiological study of 291 patients diagnosed between 1973 and 2004, however, found an average age 67 years old [6]. This average age is higher than the age at diagnosis of MM or sPL. Due to the low incidence and prevalence of PL, what is known about this pathology is mainly based on cases reported in the literature and retrospective studies concerning a small cohort of patients. The clinical picture of PL is more aggressive than that of MM. Patients may have extra plasma cell infiltration medullary responsible for a tumor syndrome which can. Associate hepatomegaly, splenomegaly, peripheral lymphadenopathy, neuromeningeal invasion, pulmonary involvement or other localizations tissue, usually in a higher proportion than in the MM. On the other hand, bone lesions are less described in the pPL than in MM or sPL [7]. We find

more frequently renal failure and hypercalcemia in pPL than in MM, and very often in the sPCL. This can partly be explained by a higher proportion of light chain diseases [7] [13]. A bone marrow failure with anemic syndrome and thrombocytopenia is the rule due to a bone marrow plasmacytosis much higher than in the MM.

The diagnosis of PL is based on a blood plasmacytosis greater than 2 × 109/L and a circulating plasma cell level greater than 20%. This definition established in 1974 by Noel and Kyle has never been evaluated prospective and recent work by the international myeloma working group (IMWG) considers it too restrictive. So only one of the two criteria would be sufficient to establish the diagnosis of leukemia plasma cells [14]. The current definition, even when only one of the two criteria is required, probably underestimates the real frequency of this pathology. The diagnosis is initially based on cytology and it is important that an experienced biologist examine the smear blood so as not to ignore the presence of plasma cells. Associate clinically, it is a sign of an aggressive disease and highly proliferative. In this context the IMWG proposes to assess whether lower values such as blood plasmacytosis > 5% and/or a circulating plasma cell level ≥ 0.5 × 109/L have the same impact prognosis than historical criteria. Plasmacytosis in the blood of PL differs from a plasmacytosis reactive to an infectious event or immunological by its monoclonal character. In this context, flow cytometry has its place to demonstrate the clonality of plasma cells and exclude other syndromes lymphoproliferative, especially lymphoplasmacytic lymphoma. Especially since the expression profile of plasma cells CD38+ or CD138+ is abnormal in CD19+ or CD56-type PL. The exception of the plasma cell marker is CD138 (also expressed in the pPL, the sPL and the MM), we find many differences in the expression phenotype in flow cytometry of cells of pPCL and sPL compared to those of MM. We observe decreased expression of CD38 (plasma cell marker) between MGUS, the MM and the sPL, thus suggesting a dedifferentiation in the phenotype of plasma cells [15]. The CD56 antigen also called NCAM [neural cell adhesion molecule] is important for adhesion of plasma cells to the medullary stroma. We observe the loss expression of this antigen on primitive PL cells and secondary, which may explain their migration into the circulation peripheral [5] [16] [17]. The cytogenetic abnormalities described in the pPL are quite heterogeneous, based on small retrospective studies. Over 80% have hypoploidism or diploidism [5], which is a factor in poor prognosis.

The prognosis for PL is grim. According to studies patient survival with PL does not exceed a few months. Five-year survival is less than 10% in all series [7] [11] [12]. There is no specific prognostic score for PL. Prognostic factors unfavorable of the PL are mostly common to those of the MM but their prevalence is higher in PL. They include a rate low albumin, high B2 microglobulin and/or high LDH levels, hypercalcemia, advanced age, low performans status and high number of S phase cells [18]. Disease resistance at initial treatment is also a factor of very poor prognosis. The prognostic value of cytogenetic abnormalities in PL is based

on small retrospective studies, the presence of hypoploidism, a complex karyotype, a del (13q), del (17p), del (1q) are associated with a decreased survival in an Italian study [12]. Tiedemann *et al.* describe a shorter survival in the event of translocation involving the chromosome 14q32 in pPL and sPL, a translocation involving the oncogene Myc is a poor prognostic factor in pPL [7].

The therapeutic management of PL remains very little for the time being satisfactory. PL is usually a very poor prognosis with a median survival of around 12 to 14 months for primary SPL and two to three months for secondary sPL. According to the few series studied, treatment with melphalan-prednisone chemotherapy seems inefficient (response rate of 20% to 30%) than the treatments by multidrug therapy (VAD) (response rate of 40% to 60%). Consolidation treatments by autograft, classic allograft, or more recently, by allografts with attenuated conditioning, are proposed in the literature for responder patients [19] [20]. The usage of immunomodulators such as thalidomide, lenalidomide, and bortezomib revolutionized the MM processing landscape and significantly improved the survival of these patients. Retrospective data and prospective studies seem to suggest an improvement in survival for patients with PL but the data in the literature are contradictory [21].

## 4. Conclusion

Plasma cell leukemia is a rare atypical variant, complicating essentially multiple light chain myeloma. She must be suspected especially when there are cytological abnormalities such as major leukocytosis or thrombocytopenia, which are unusual in classical myeloma. Evolution is usually a very bad prognosis, with a median survival of 12 to 14 months for the form primary and 2 to 3 months for the secondary form.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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