British Journal of Healthcare and Medical Research - Vol. 12, No. 01
Publication Date: February 25, 2025
DOI:10.14738/bjhr.1201.18334.
Aguilar, S. I. L., Espinosa, L. D. S., Calvillo, D. S. R., Montiel, O. R., & Carbajal, A. Y. D. (2025). Case Report of Transformation from Multiple Myeloma IgG KAPPA to Primary Plasma Cell Leukemia. British Journal of Healthcare and Medical Research, Vol - 12(01). 341-346.

Case Report of Transformation from Multiple Myeloma IgG KAPPA to Primary Plasma Cell Leukemia

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INTRODUCTION

Plasma cell leukemia (PCL) is a rare and aggressive identity with a prevalence of 1-2%. It is associated with 2-4% multiple myeloma, which is the second most frequent hematologic neoplasm, at an average age of 66 years. The 5-year survival rate from diagnosis of PCL does not exceed 10%. Clonal events are present in cells present; abnormalities in cup number, such as loss or gain of chromosomal regions, as well as loss of tumor suppressor genes, which is the result of deletion of the short arm (p), long arm (q) of chromosome (1p) causes loss of CDKN2C, FAF1 and FAM4GC (also known as TENT5C), of (11q) BIRC2 and BIRC3, of (13q) RB1 and DIS3, and of (17p) TP53. Gain on the long arm of chromosome 1 is found in about 40% of patients, often in association with t(4;14). Common secondary translocations involve MYC, either through t (8;14) or without involving the immunoglobulin heavy chain gene.

Mutation rates in genes of the RAS/MAPK pathway; about 50% of patients have such a mutation (KRAS 22%, NRAS 17%, BRAF 8%). Affected signaling pathways include the NFκB pathway (affected by copy number loss, mutations and translocations) and the PI3K pathway (deregulated in the absence of genetic changes). Dysregulation of the apoptotic pathway occurs, with BCL2 dependence in patients with t(11;14) and MCL1 dependence in other patients. Normal signaling of plasma cell differentiation is altered, with up-regulation of IRF4 occurring through a positive autoregulatory loop and loss of negative feedback of MYC expression through PRDM1. The CD56 antigen presents an aberrant form in the anchorage of plasma cells

to the bone marrow stroma, which is associated with extremomedullary disease, has to be elevated in plasma cell leukemia. The presence of plasma cells can be confirmed by a flow cytometry evolution that is positive for CD38 and CD138. This hematological dyscrasia is characterized by a percentage of circulating plasma cells exceeding 20% in relative number and 2 × 109 cells / l in absolute number. They are classified as primary, when they appear de novo, and have an incidence of 60-70%. Secondary plasma cell leukemia arises from a relapse of preexisting multiple / refractory myeloma. It presents with severe cytopenias, hypercalcemia, osteolytic lesions and renal failure. Also with increased tumor burden, PCL proliferative activity, which manifests with increased levels of B2 microglobulin and lactate dehydrogenase. With extreme manifestations (involvement of lymph nodes, liver, spleen, pleura and CNS). PCL, two common markers are present, such as CD38 and CD138 antigens. With a more mature immunophenotype, more frequently CD20, CD23, CD28, CD44 and CD45 antigens, and less frequently CD9, CD56, CD71, CD117 and HLA-DR antigens [14-16). Secondary plasma cell leukemia has a male:female ratio of 3:2, with a mean age of 50 years at diagnosis. Treatment consists of proteosome inhibitors such as bortezomib, which suppresses the expression of adhesion molecules and is antiangiogenic.

CASE REPORT

We present the case of a 56 year old woman, housewife. Originally from San Luis Potosi, who was diagnosed with primary plasma cell leukemia isotype IgG Kappa, with a history of systemic arterial hypertension of 3 years of evolution. No family history of onco-haematology. The patient 3 months before admission. She presents low back pain, intensity 8/10. As well as paresthesias in lower limbs. Weight loss of approximately 29 kilograms. Diaphoresis at night, accompanied by fever, chills, urinary symptoms, we have bladder. Subsequently with asthenia tendency. Admitted to the emergency department for symptoms. Hemodynamically unstable with tendency to tachycardia of 110 lpm, as well as desaturation to 88%. With blood pressure of 168/78 mmHg. The patient was cooperative and integrated, with pallor of the integuments. With systolic murmur. She had no organomegaly. Blood biometry was performed with evidence of normocytic normochromic anemia grade IV (Hb 5.5 g / dl). Presence of acute renal injury, hypercalcemia of 11g/dl. As well as presence of total protein 10.93, globulin of 5.66, albumin of 3.4. Peripheral blood smear was requested with presence of plasma cells of 13%. During her stay we proceeded to perform a tomographic study with the presence of lytic lesions in “hole punch” at the level of T2-T9 and S1-l5. The patient met the clinical criteria compatible with multiple myeloma. Bone marrow aspirate was performed, again with smear with evidence of hypercellular bone marrow, numerous plasma cells, with more than 10 bone spicules, compatible with multiple myeloma. Presence of > 36% of plasma cells. Serum protein electrophoresis with Gamma monoclonal peak of 4.58g/dl, IgM isotype kappa immunofixation, kappa light chains of 7.3. Beta-microglobulin of 4.0mg/dl. Peripheral blood flow cytometry results showed plasma cell population with CD380+, CD138+ phenotype corresponding to 36.95% compatible with multiple myeloma, with primary plasma cell leukemia. During her hospital stay, four platelet concentrates were transfused, as well as dabopoyetin administration. As well as monitoring of hypercalcemia and acute kidney injury. This was remitted with the use of crystalloids and loop diuretics. Treatment was started with dexamethasone, lenadomide, with application of subcutaneous bortezomib (VRd), with anticoagulation with rivaroxaban. The patient was discharged with hematology outpatient follow-up. Continuing with the same scheme.

PARACLINICS

Table 1: Blood biometry of the patient during her hospitalization.

Date	Leukocytes (thousands/UL)	Hem oglobin (g/dl)9.1	Hematocrit %	Platelets (thousands/UL)	Reticulocytes % Reticulocytes	Serum Creatinine (mg/dl)	Serum calcium (mg/dl)	Serum albumin (g/dl)	Globulin (g/dl)	Alkaline phosphatase (U/L)	Lactate dehydrogenase
08/07/24	12.65	5.5	17.9	200,000	2.0	1.97					
09/07/24	7.79	5.4	17.5	200,000							
11/07/24	7.72	6.8	20.8	177,000		1.59	10.6	3.44	7.49	75	
15/07/24	13.57	9.1	27.9	186,000		0.9	9.5	3.2	6.59	53	
17/07/24	14.3	9.0	27.7	201,000		0.89	8.8	3.11	6.07	195	136
18/07/24	13.36	9.1	28.2	206,000		0.89	9.0	3.05	5.28	83	
19/07/24	9.82	9.2	28.2	213,000		0.69	9.2	3.43	6.28	55	
22/07/24	11.77	9.4	29.4	259,000		0.69	9.2	3.43	6.28	55	136
16/08/24	5.55	8.7	28.4	279,000		0.78	9.0	3.05	5.28	83	
25/10/24	4.64	11.2	36.1	368,000		0.74				195	176

IMAGES

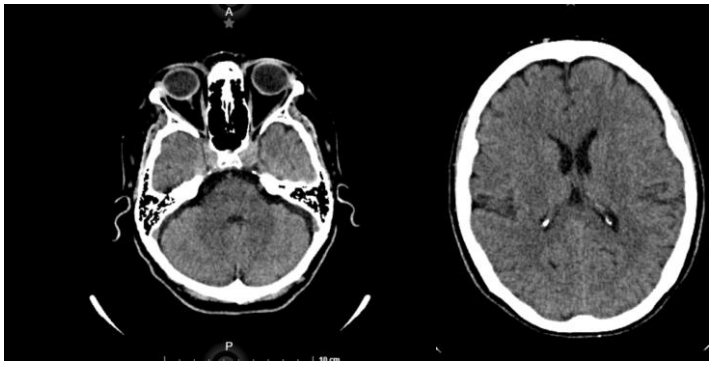
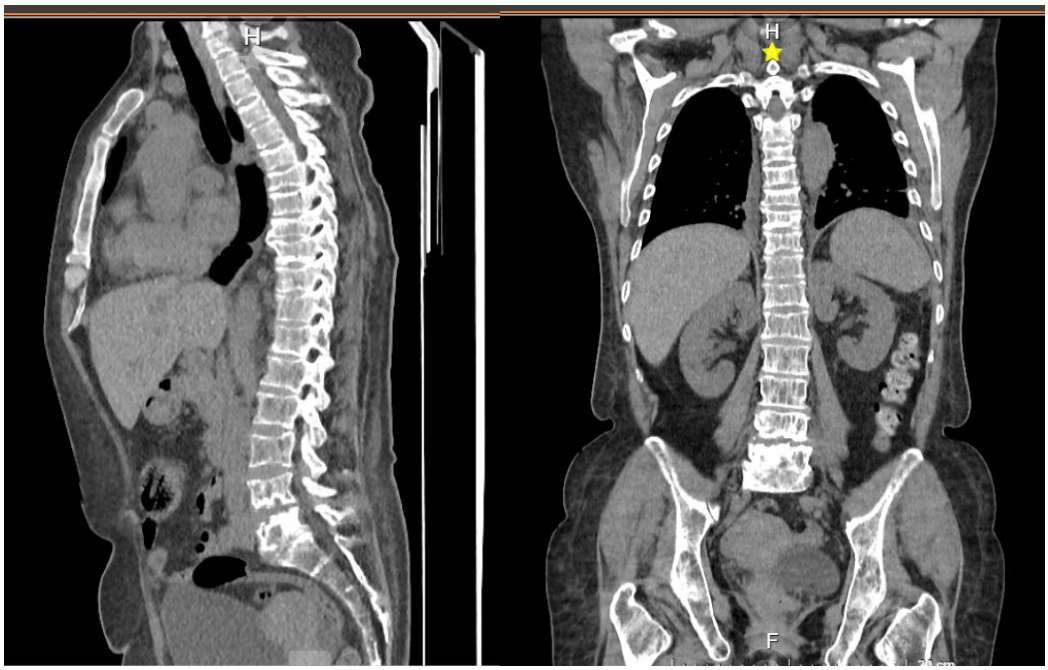


Figure 1 (A)



A) Figure 1(B): Simple thoracoabdominopelvic tomography = Presence of lytic lesions at T2-L5.

URL: http://dx.doi.org/10.14738/bjhr.1201.18334.

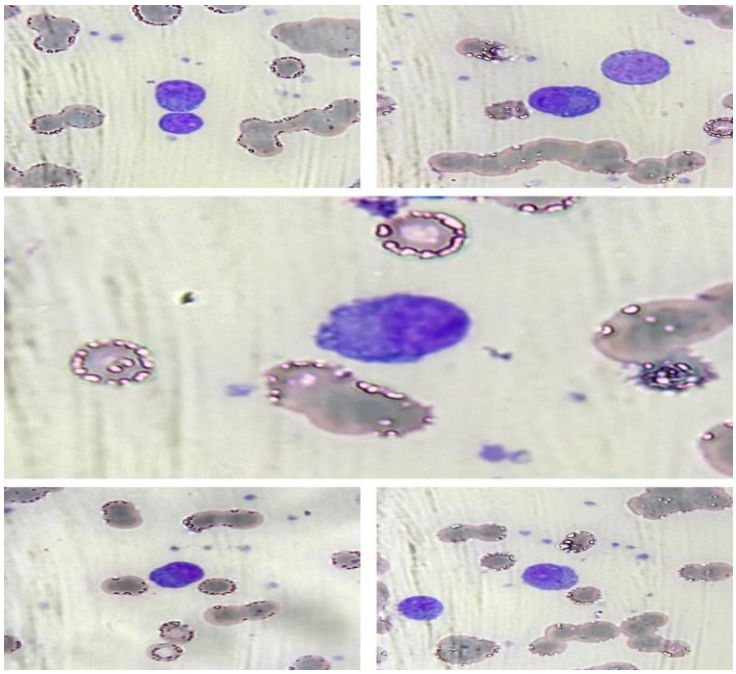


Figure 2: Blood smear: Presence of plasma cells.

DISCUSSION

Plasma cell leukemia (PCL) is a rare but highly aggressive hematologic identity, with a prevalence of approximately 1-2% of cases of hematologic malignancies and a 5-year survival rate of less than 10%. The relationship with multiple myeloma is well established, as 2-4% of patients with myeloma may progress to PCL. The case presented describes a 56-year-old patient with primary PCL of IgG Kappa isotype, which represents an aggressive clinical manifestation of the disease.

The patient's clinical picture included symptoms characteristic of PCL, such as severe low back pain, paresthesias in the lower limbs, fever, chills, asthenia and significant weight loss. In addition, laboratory findings were indicative of advanced disease, with normocytic normochromic anemia grade IV (Hb 5.5 g/dL), hypercalcemia (11 g/dL), acute renal failure and alterations in protein electrophoresis with a monoclonal peak in the Gamma fraction. Peripheral blood smear showed 13% plasma cells, which, together with confirmatory flow cytometry (CD38+ CD138+ CD138+ in 36.95%), supported the diagnosis of primary PCL.

From a cytogenetic and molecular point of view, PCL is characterized by the presence of clonal events such as deletion of the short and long arm of chromosome 1 (1p and 1q), associated with the loss of tumor suppressor genes such as TP53, RB1 and CDKN2C, which favor uncontrolled cell proliferation. In this case, a detailed cytogenetic analysis was not performed, but the elevated tumor burden, evidenced by high levels of beta-2 microglobulin and lactate dehydrogenase, suggests significant involvement of these molecular pathways.

Therapeutic management included the use of a regimen based on bortezomib, lenalidomide and dexamethasone (VRd), with prophylactic anticoagulation with rivaroxaban. Bortezomib, a proteasome inhibitor, is one of the key therapeutic strategies in PCL, as it induces cell apoptosis by interfering with protein degradation and suppresses the expression of adhesion molecules,

which helps to decrease tumor burden. In addition, the patient required transfusion support with platelet concentrates and treatment for hypercalcemia and acute renal failure. The prognosis of primary PCL remains guarded, despite advances in treatment. The rate of complete remission remains low, and long-term survival is limited. In the case of this patient, the response to treatment and long-term course will determine her prognosis. Consolidation therapy with autologous hematopoietic stem cell transplantation has been documented to improve survival and should be considered in patients who achieve partial or complete remission.

Finally, close follow-up at the hematology outpatient clinic is crucial to assess therapeutic response and detect signs of disease progression. Periodic monitoring of biomarkers such as beta-2 microglobulin, lactate dehydrogenase and serum protein electrophoresis, together with clinical and radiological evaluation, is essential for optimizing treatment and improving the quality of life of these patients.

Conflict of interest:
The authors declare no conflict of interest.

Financing:
There was no funding for this work.

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