

## Meningeal Syndrome as the Debut of Multiple Myeloma, Case Report

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### ABSTRACT

Multiple myeloma (MM) is a monoclonal gammopathy characterized by malignant proliferation of plasma cells. Considered the second most common hematological neoplasm. Symptoms result from infiltration of plasma cells and secreted monoclonal proteins or interaction of plasma cells with their microenvironment. The classic CRAB criteria (Hypercalcemia, renal failure, anemia and lytic lesions), with renal failure being one of its most frequent complications, are necessary to establish the diagnosis. Our report presents the case of a man in his seventh decade of life, who presented with meningeal syndrome, which motivated the study approach, reaching the conclusion that this entity was due to a state of immunosuppression secondary to multiple myeloma, whose diagnostic suspicion was a finding that was obtained when doing a comprehensive study of the disease, since reaching the diagnosis in this case was a cause of controversy as it had an unusual presentation. This is a good case to discuss differential diagnoses and teaches us that in medical practice we deal with patients and not with diseases, since these debut in a particular way in each individual.

**KEYWORDS:** Multiple myeloma, meningeal syndrome.

### ARTICLE DETAILS

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### INTRODUCTION

Multiple myeloma (MM) is a monoclonal gammopathy characterized by malignant proliferation of plasma cells and monoclonal protein in serum and/or urine associated with target organ damage <sup>[1, 2]</sup>. It is the second most common hematological neoplasm, corresponding to 10% of hematological neoplasms and 1% of all neoplasms <sup>[3]</sup>. It is considered a disease of older adults, the median age at the time of diagnosis is 65 to 74 years, being more common in men than in women, and among people of African American descent <sup>[2]</sup>. The typical picture is characterized by the frequency of presentation of anemia 73%, bone pain 58%, elevated creatinine 48%, generalized fatigue/weakness 32%, hypercalcemia 28%, weight loss 24%. On the other hand, the less common ones (<5%) include paresthesias 5%, hepatomegaly 4%, splenomegaly 1%, lymphadenopathy 1% and fever 0.7% <sup>[2]</sup>.

The presence of infections is a frequent finding and is attributed to a defect in humoral immunity <sup>[3]</sup>. The infection rate in patients with MM is much higher than in the general population, with bacterial and viral infections predominating. The most common infections are meningitis, septicemia, pneumonia, osteomyelitis, cellulitis and pyelonephritis <sup>[4]</sup>. It should be noted that central nervous system involvement in multiple myeloma (leptomeningeal myelomatosis) is not

common and has been reported in only 1% of patients <sup>[1]</sup>. The acronym "CRAB" is sometimes used to remember myeloma-defining events that are used for its diagnosis: C - Calcium Elevation; R - Kidney failure; A - Anemia; and B - Bone lesions <sup>[2]</sup>. After diagnosis and risk stratification, all patients are evaluated for eligibility for autologous hematopoietic cell transplantation (HCT). Because in the absence of treatment, symptomatic patients die in a median of six months <sup>[6]</sup>.

### CASE REPORT

A 70-year-old male, employed as a taxi driver, with a chronic degenerative history of long-standing systemic arterial hypertension undergoing treatment. He denies any history of fractures. Family history refers to the presence of three brothers with cancer (hepatic and gastric).

The condition began six months ago with bone pain predominantly in the proximal extremities that was tolerable with the ingestion of analgesics. A month ago, edema was added to the face and pelvic extremities, so they went to a private doctor detecting alterations in kidney function. Relatives report that he recently began to experience asthenia, adynamia, fatigue, dyspnea on medium effort and generalized weakness that lasts throughout the day, adding fever (Quantification with a mercury thermometer at 38 ° C). However, the symptoms worsened to the point of total loss of

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muscle strength and deterioration of the neurological status with lethargy, and the patient went to the emergency department finding himself in a state of encephalopathy.

Three days later, with progression of neurological deterioration and the presence of Cheyenne Stokes respirations, orotracheal intubation was decided. The most relevant analytical data at the time of admission were:

Blood chemistry: Urea 65 mg/dl, BUN 30.37 mg/dl, creatinine 2 mg/dl (6 months ago it was normal), glucose 109 mg/dl. Albumin 3.2 g/dl, total proteins 9.1 mg/dl.

Serum electrolytes: Sodium 143 mmol/l, potassium 3.4 mmol/l, chlorine 100 mg/dl, calcium 14.5 mg/dl (ionic: 5.5 mg/dl), phosphorus 4 mg/dl and magnesium 2.2 mg/dl.

Blood count: Hemoglobin: 10.7 g/dl, hematocrit 35.1%, erythrocytes 3.51 thousand/ul, platelets 546 thousand, leukocytes 10.93 thousand/ul, neutrophils 6.62 thousand/ul, lymphocytes 1.98 thousand/ul.

During his hospital stay requiring mechanical ventilatory assistance, he showed a torpid evolution. Therefore, it was decided to take a cytological and cytochemical study of the cerebrospinal fluid, which was reported to be transparent, pH 8, glucose 64.5 mg/dl, proteins 0.18 mg/dl, leukocytes 4 u/l, polymorphonuclear cells 100% and erythrocytes 14 U/ul. Same, Chinese ink negative, cerebrospinal fluid culture without bacterial growth. It is considered that the patient presented with a meningeal clinical picture accompanied by systemic inflammatory response syndrome, which is why it was managed as viral meningitis. Subsequently, given the persistence of the three CRAB criteria (anemia, hypercalcemia and renal failure) accompanied by a history of chronic bone pain, indolent multiple myeloma is suspected. Therefore, complementary studies are requested that report:

Urine studies: Creatinine in urine: 68.1 mg/dl, volume 1160 ml, creatinine clearance in 24-hour urine 127.6 mg/dl.

Immunology studies: Immunoglobulin G 2664, Immunoglobulin M 92, Immunoglobulin A 539 (Ig G and Ig A elevated).

PTH 9.25 pg/ml (Normal).

Beta-2 microglobulin 6.109mg/ml (Elevated).

Serum protein electrophoresis and immunofixation: No monoclonal immunoglobulin chains were detected [figure 1].

Electrophoresis and immunofixation of proteins in urine: Total Lambda light chains of monoclonal type.

Chest x-ray, simple complete skull and spine tomography: No evidence of lytic lesions or plasmacytomas.

The medical treatment that the patient received was based on acyclovir, hydration and antihypertensives. When the suspected diagnosis of multiple myeloma was confirmed, treatment with steroids was started.

## DISCUSSION

The pathology of multiple myeloma requires a comprehensive medical approach. Because it is complicated to integrate their diagnosis prematurely, since the clinical picture with which they debut can emulate various diseases

with a higher incidence. This is why it should be suspected in the presence of one (or more) of the following clinical presentations:

Bone pain with lytic lesions discovered on routine skeletal radiographs or other imaging modalities.

Increased concentration of total serum protein and/or a monoclonal (M) protein in serum or urine.

Systemic signs or symptoms suggestive of malignancy, such as unexplained anemia hypercalcemia, which is symptomatic or discovered incidentally.

Acute renal failure with a mild urinalysis or, rarely, nephrotic syndrome due to concurrent primary amyloidosis.

The history should obtain information about bone pain, constitutional symptoms, neurological symptoms, and infections.

The diagnosis of MM requires meeting the following criteria: Clonal bone marrow plasma cells  $\geq 10$  percent or biopsy-proven bone or soft tissue plasmacytoma. Plus one of the following: Presence of impairment of a related organ or tissue (often remembered by the acronym CRAB): End organ damage is suggested by an increased plasma calcium level, renal failure (kidney failure), anemia and bone injuries. To be included as diagnostic criteria, changes in these factors must be felt to be related to the underlying plasma cell proliferative disorder [2].

The risk of infection is due to a multifactorial immunodeficiency caused by the disease itself and the treatment regimens administered during the different phases of therapy [4]. In untreated patients, the main defect is B cell immunodeficiency, manifested by hypogammaglobulinemia. Cytokines released by myeloma cells, such as interleukin IL-6 and IL-10, promote an imbalance in the Th1/Th2 ratio, resulting in a defective Th1 response [4]. The condition in older adults, a population in which immunosenescence and organ dysfunction are additional risk factors for infection [4].

The main comorbidities with which a differential diagnosis must be made are primary amyloidosis (AL) where although, like myeloma, there is a proliferation of plasma cells associated with the overproduction of monoclonal light chains, in amyloidosis it is the deposition of light chains and heavy or both in different compartments of the kidney is responsible for the pathogenesis, due to the presence of tissue deposits of amyloid fibrils or non-fibrillar material that can produce nephrotic syndrome, heart failure, hepatomegaly and other findings that are not observed in MM. On the other hand, we found monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM), Waldenström macroglobulinemia (WM), solitary plasmacytoma, POEMS syndrome and metastatic carcinoma [2,4].

## CONCLUSION

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The patient had various risk factors associated with MM, including gender, age >60 years, overweight (BMI 27.7), smoking and alcoholism. This case is the exception to the typical presentation because it presented as an oncological emergency of a metabolic type and myelosuppression, developing viral meningitis, which debuted as the deterioration of the neurological status and the requirement for respiratory therapy through assisted mechanical assistance. Other infectious sources were ruled out.

Although most of the CRAB criteria were met, which includes hypercalcemia (50%), renal failure (20-40%), anemia (60-70%), and lytic bone lesions (70%), when attempting to demonstrate lytic lesions due to the progressive and chronic bone pain that he reported, these were not identified. Even so, after presenting 3 of the CRAB criteria, immunoglobulins were requested, reporting elevated IgG and IgA, so electrophoresis and immunofixation of proteins in serum and urine, as well as Beta-2 microglobulin, were requested; to confirm the diagnosis.

The report of parathormone at normal levels rules out hypoparathyroidism as a differential diagnosis that justifies high calcium levels. Amyloidosis was ruled out because the patient did not have typical syndromic characteristics of the pathology.

The purpose of the presentation of this clinical case is to demonstrate that we deal every day with patients and not with diseases, since these debut in a particular way in each individual. In the context of this particular case, it was thanks to the results of electrophoresis and immunofixation in urine

of monoclonal light chains, which helped us to complete the diagnosis of multiple myeloma even though we were unable to complete the complete study of the patient, referring to the absence of the bone marrow aspirate due to the fact that he died secondary to meningitis; Just as Beta-2 microglobulin allows us to stage myeloma, by obtaining a value of 6.109 mg/ml, we establish a stage III of the pathology according to the international prognostic system for multiple myeloma (ISS).

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## FIGURES

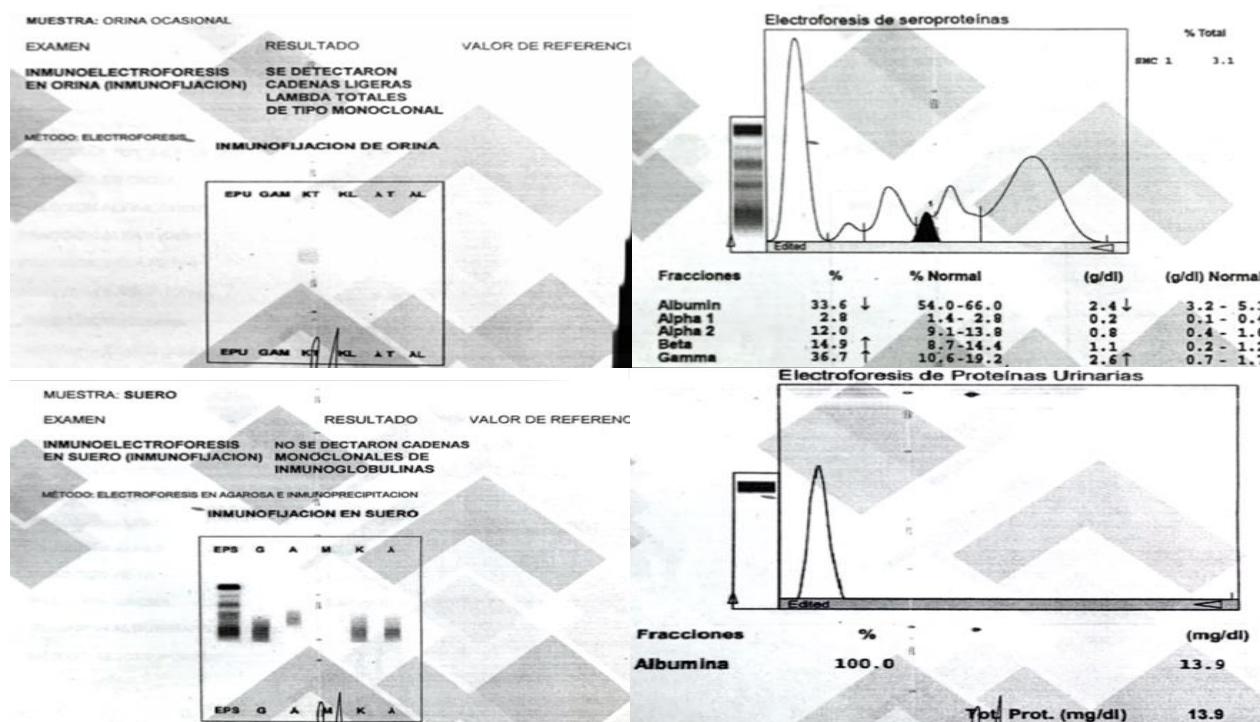


Figure 1. Electrophoresis and immunofixation of proteins in urine and serum.