Multiple myeloma-amyloidosis presenting as pseudomyopathy

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ABSTRACT

Amyloidosis is a generic term that refers to the deposition of amyloid fibrils in bodily tissues. Its onset is usually after 40 years of age, with localized or systemic involvement associated with multiple myeloma or chronic inflammatory diseases, and can mimic various rheumatic syndromes. We report the case of a patient with amyloidosis associated with multiple myeloma, showing clinical characteristics of pseudomyopathy

Keywords: multiple myeloma, myositis, amyloidosis.

INTRODUCTION

Amyloidosis is a generic term that refers to the deposition of amyloid fibrils in bodily tissues. In light chain amyloidosis (AL amyloidosis), whether primary or associated with multiple myeloma (MM), there is an excessive production and deposition of light chain monoclonal immunoglobulin fragments or fragments containing the light chain's variable region.[1] This deposition constitutes the amyloid fibrils, which can be identified by Congo red staining.

The classification of amyloidosis is based on different fibrillar proteins, as well as their different precursors.[2] In primary amyloidosis, the fibrillar protein is termed AL and its precursors are light chain immunoglobulins, kappa (κ) and lambda (λ).[3]

AL amyloidosis usually develops after the age of 40 years, with multisystemic involvement and characteristics of rapid progression and reduced survival.[4] Although multisystemic involvement of organs such as heart and kidneys is determinant to prognosis and survival of patients, AL amyloidosis draws the attention of rheumatologists when its signs and symptoms mimic a series of rheumatologic conditions: amyloid infiltration of the skin, which mimics scleroderma with skin thickening;[5] amyloid infiltration of synovial and periarticular tissues, leading to stiffness and polyarthritis suggestive of rheumatoid arthritis;[6] and amyloid deposition in the salivary glands causing xerostomia and mimicking Sjögren's syndrome,[7–9] which may lead to diagnosis of muscular pseudohypertrophy[10] or pseudomyopathy, as in the patient described below.

CASE REPORT

MCC, a 35 year-old woman who was in good health condition until three months earlier, when she started to feel pain in the upper and lower limbs. The pain was constant and prevalent in the proximal segments of the lower limbs, including the gluteal region bilaterally. The patient was referred to orthopedics and diagnosed with bilateral trochanteric bursitis.

Approximately one month later, she noticed the appearance of tongue swelling, numbness in the hands, and nodules in arms and legs. After consultation with a neurologist, she was diagnosed with carpal tunnel syndrome (CTS), which motivated bilateral surgical decompression. However, the symptoms did

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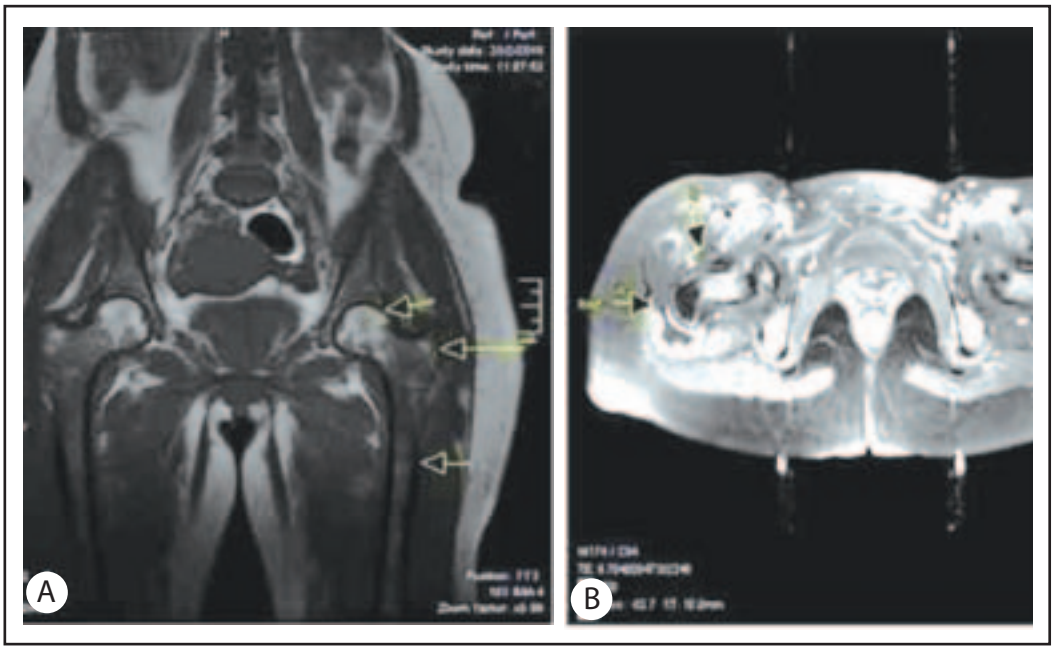

Figure 1
Nuclear magnetic resonance **(A)** Change in T1 and T2 signal involving the heads/necks and greater trochanters metaphyses/diaphyses of the proximal femoral region. **(B)** Distension of the bursa of the gluteus medius E.

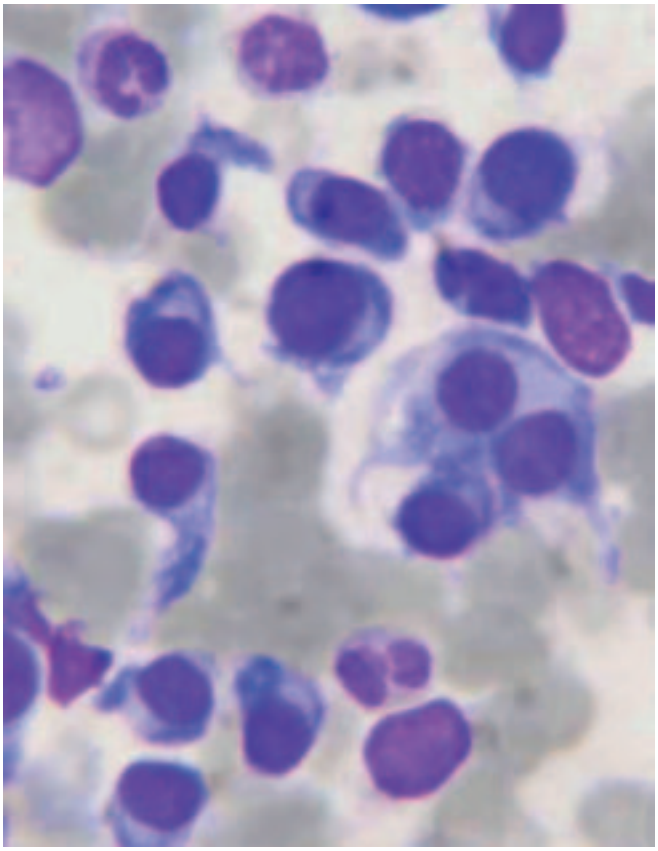

Figure 2
Myelograma showing excess of plasma cells: cells with rounded and eccentric nuclei; blue cytoplasm with irregular borders; large nucleus relative to the cytoplasm.

not improve; the painful symptoms became more intense and spread throughout the body, followed by bilateral ear pain and difficulty in walking. The patient was experiencing limitations in daily activities, such as bathing, combing hair, dressing, sitting down and standing up from a chair. She also reported having lost 5 kg since the onset of disease.

Physical examination showed blood pressure of 100/70 mmHg, pulse of 86 pbm, clear lungs to auscultation, macroglossia, edema and periorbital bilateral echimosis, edema of the lower limbs+/4+, and positive Mingazzini maneuver for lower extremities.

In laboratory tests, blood count, ESR, glucose, transaminases, CPK, ANA, serum protein electrophoresis, kidney, liver and thyroidal function tests, urinalysis, and chest X-ray did not show abnormalities. PPD was nonreactive. Nuclear magnetic resonance (NMR) of pelvic girdle showed bilateral trochanteric bursitis, with lipomatous swelling in supra-adjacent intermuscular planes; bilateral ischial bursitis; medius-left subgluteal bursitis; and nonspecific diffuse signal changes in bone marrow of femoral necks, metaphysis/diaphysis of the proximal femur, hip, and sacrum bones (Figure 1).

Biopsied tissue collected from the right trochanteric bursa showed positive birefringence under polarized light after Congo red staining. Bone marrow aspirate showed 73% of plasma cells (Figure 2). Serum immunofixation revealed a biclonal pattern IgG κ/IgA κ. X-ray of the cranial cavity showed diffused lytic lesion. Renal function and calcium levels were normal. After evaluation, we conclude that the diagnosis was amyloidosis associated with multiple myeloma.

Therapy was initiated with high doses of dexamethasone (40 mg/day on days 1–4, 9–12 and 17–20), associated with an inhibitor of osteolysis (pamidronate 90 mg/monthly). Painful symptoms disappeared and there was an improvement of dysphagia and postprandial plenitude. Two weeks later, the patient developed cough, shortness of breath, and worsening of lower limbs edema. Chest x-ray revealed bilateral pleural effusion. Electrocardiogram was consistent with left bundle brunch block. Echocardiogram showed moderate left ventricular hypertrophy, with diastolic relaxing alteration. Furosemide was started and cardiac decompensation symptoms improved. The patient is being prepared for autologous stem cell transplantation

DISCUSSION

Two atypical aspects are noteworthy in this uncommon presentation of amyloidosis associated with multiple myeloma: the patient's age, 35 years, and the presentation as pseudomyopathy of the proximal girdles. NMR of pelvic girdle with multifocal tissue infiltration in addition to normal muscular enzymes and electroneuromyography made the diagnosis of myopathy less likely. The bilateral CTS, for which the patient underwent surgery two months earlier, could be attributed to amyloid deposition, although histopathological study was not performed. Systemic evaluation showed cardiac involvement, but not kidney or other organs involvement, except perhaps the peripheral nervous system in the form of CTS. The association with MM was confirmed based on studies of bone marrow with 73% of plasma cells, serum immunofixation with biclonal pattern IgG κ/IgA κ, and X-ray of the cranial cavity with diffused lytic lesions.[11]

AL amyloidosis is always associated with plasma cell dyscrasia. Insidious onset, vague symptoms, and diversity of clinical manifestations make diagnosis more difficult. Amyloid infiltration into joints, periarticular structures, soft tissues, and bones have been gaining more attention, sometimes appearing as early forms of presentation.[5–10] This explains the need for the presence of a rheumatologist during disease investigation, as well as in clinical care offered to such patients. One must be aware of the fact that these patents usually have evidence of acute phase, ESR and CRP within normality, aside from the absence of rheumatoid factor and anti-CCP. Rheumatoid arthritis,[6] scleroderma,[5] Sjögren's syndrome,[8,9] and polymyalgia rheumatica[12] may appear as diagnosis, before being defined as AL amyloidosis. In a series of 191 AL amyloidosis patients, 82 (42,9%) presented evidence of bone and soft tissue involvement. Such involvement tends to occur in the context of multiple organs involvement.[1] In the group of patients with AL amyloidosis associated with MM, soft tissue involvement have appeared more frequently in the form of CTS,[13] macroglossia,[13] arthropathy,[14] and myopathy.[7]

The organs most frequently affected by amyloidosis are the kidneys and the heart. Nephrotic proteinuria and kidney failure are well documented events. Cardiac involvement was present in 83% of the patients.[15] Our patient presented various of the classical findings of cardiac amyloidosis, such as left bundle branch block, left ventricular hypertrophy with impaired diastolic relaxing, and congestive heart failure.

The diagnosis of amyloidosis is made by a tissue biopsy. Abdominal fat aspiration is a less invasive method and presents 80% sensitivity in a single aspiration. The specificity of the method is 98% and the negative predictive value is 76%.[15] Imaging tests may be useful. The NMR of our patient was able to exclude intrinsic muscular disease, identifying multifocal involvement of the pelvis, aside from allowing adequate selection of the tissue to be biopsied, while a simple cranial X-ray allowed visualization of the lytic lesions in the cranial cavity.

The patient was treated with dexamethasone and furosemide, in addition to pamidronate, an inhibitor of osteolysis. Painful symptoms disappeared and there was regression of signs and symptoms of cardiac decompensation. The patient is being prepared to autologous stem cell transplantation.

CONCLUSION

In conclusion, AL amyloidosis clinical presentation can mimic different rheumatologic syndromes. Therefore, patients presenting clinical signs and symptoms resulting from infiltrative processes of soft tissues, joints, periarticular tissues, and bones should be submitted to an investigation of AL amyloidosis after excluding rheumatic disease.

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