CASE REPORTS

Immunoglobulin Light Chain Amyloidosis Associated with Multiple Myeloma in a Young Patient: A Case Report

OO Morais[1], LO Costa[2], DH Shinzato[3],G Hans-Filho[4]

ABSTRACT

The authors present an uncommon case of systemic amyloidosis associated with multiple myeloma in a 35-year old woman. Systemic amyloidosis commonly presents in association with clonal plasma cell proliferative disorders, and less frequently as secondary or of a hereditary origin. Amyloidosis is usually associated with multiple myeloma in older patients and frequently has an unfavourable prognosis.

Keywords: Amyloidosis, multiple myeloma

Amiloidosis de Cadenas Ligeras de Asociada con Mieloma Múltiple en un Paciente Joven: Reporte de un Caso

OO Morais[1], LO Costa[2], DH Shinzato[3],G Hans-Filho[4]

RESUMEN

Los autores presentan aquí un caso raro de amiloidosis sistémica asociado con mieloma múltiple en una mujer de 35 años de edad. La amiloidosis sistémica normalmente se presenta asociada con desórdenes proliferativos de las células plasmáticas clonales, y con menor frecuencia con origen secundario o hereditario. Amiloidosis se asocia normalmente con el mieloma múltiple en pacientes de mayor edad y frecuentemente tiene una prognosis desfavorable.

Palabras claves: Amiloidosis, mieloma múltiple

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INTRODUCTION

Amyloidosis may present as a localized or systemic disorder, with diverse aetiologies. Immunoglobulin light chain amyloidosis (AL) is a disorder characterized by extracellular deposition of insoluble monoclonal immunoglobulin light chain fragments in various tissues, leading to tissue dysfunction. The pathogenesis of AL seems to involve aberrant *de novo* synthesis and abnormal proteolytic processing of light chains and do occur as a result of clonal plasma cell proliferative disorder (1). Among lymphoproliferative disorders, multiple myeloma (MM) is most commonly associated with AL, and approximately 10–15% of patients with MM are diagnosed with AL either at initial presentation or subsequently.

CASE REPORT

A 35-year old female patient presented with a 5-month history of yellow papular-nodular lesions, at times ecchymotic, involving eyelids, external ears and nasal vestibules (Figs. 1, A–B). The palms had a diffuse soft tissue infiltration associated with yellow nodular lesions, accompanied by symptoms of carpal tunnel syndrome (Fig. 2). Nodular

From: [1]Médico Residente em Dermatologia da Universidade de Brasília (UnB), Ex-aluno da Faculdade de Medicina da Universidade Federal de Mato Grosso do Sul (UFMS), [2]Médica Dermatologista, Ex-aluna do Programa de Residência Médica em Dermatologia da Universidade Federal de Mato Grosso do Sul (UFMS), [3]Médica, Ex-aluna da Faculdade de Medicina da Universidade Federal de Mato Grosso do Sul (UFMS), [4]Médico Dermatologista, PhD, Chefe do Programa de Residência Médica em Dermatologia da Universidade Federal de Mato Grosso do Sul (UFMS).

Correspondence: Dr OO Morais, Rua Utiariti, 197. Vila Rica, Campo Grande, Mato Grosso do sul, Brasil, Postal Code 790 22-240. Tel: +55(61) 9916-2339. E-mail: orlando.unb@gmail.com

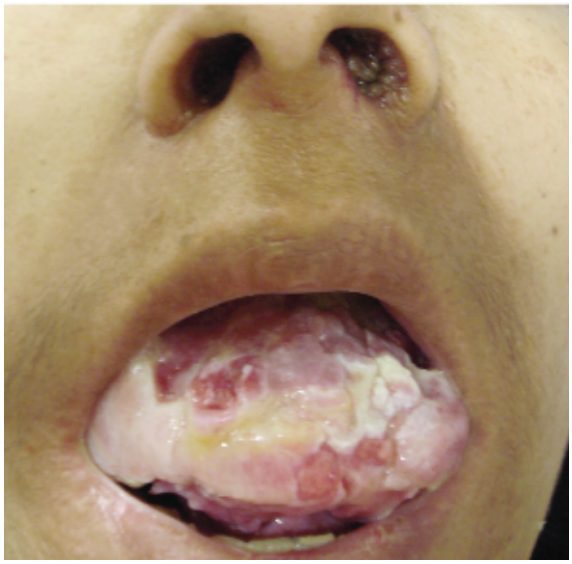

Fig. 1(A): Extensive macroglossia showing vegetant aspect;

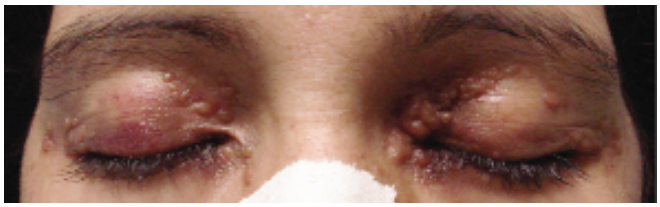

Fig. 1 (B): Typical yellow papular-nodular lesions in the eyelids.

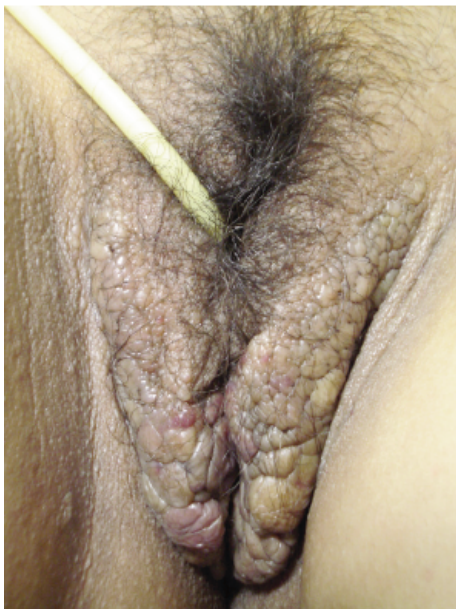

Fig. 2: Confluent nodular lesions at the vulva with characteristics resembling condyloma acuminatum with ecchymotic points.

lesions were also observed in the vulval area with characteristics similar to condyloma acuminatum (Fig. 3). During the same period in which the lesions had evolved, the patient

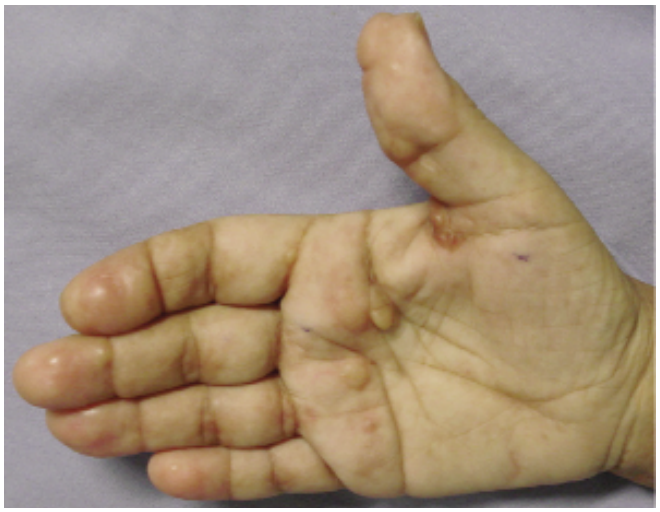

Fig. 3: Diffuse infiltration of palms associated with yellow papular-nodular lesions.

lost 33 pounds, primarily due to mastication and deglutition difficulties caused by significant macroglossia (Fig. 1B). The patient also experienced ambulatory impairment due to lumbago that was not responsive to symptomatic drug treatment.

Testing procedures involved cutaneous biopsies of the eyelid, vulval and palmar regions. These biopsies showed widespread deposition of eosinophilic material that stained positive for crystal violet (Figs. 4, A–B) and was birefringent

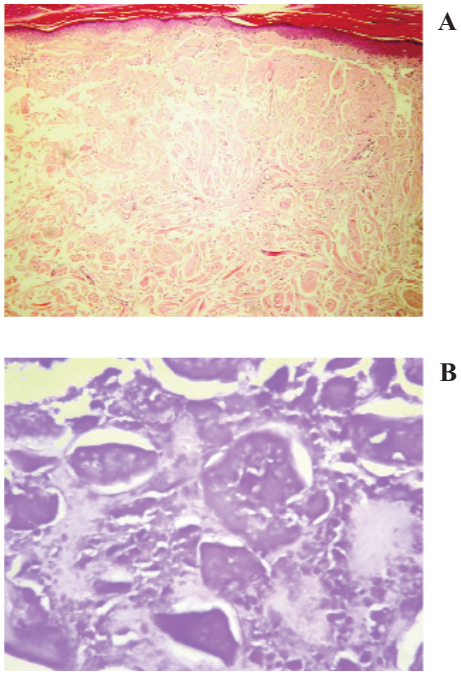

Fig. 4 (A): Biopsy of vulval nodules showing extensive dermal deposition of amorphic eosinophilic material (H&E, x 20) enhanced by crystal-violet stain (B) (x40).

under polarized light with Congo red staining. Laboratory analysis indicated anaemia, hypoalbuminaemia, increased

lactic dehydrogenase, proteinuria but normal levels of serum urea and creatinine. Serum protein electrophoresis did not detect hypergammaglobulinaemia and the patient was negative for Bence Jones proteinuria. Serum immunofixation electrophoresis, however, showed the presence of monoclonal lambda light chains, and a serum nephelometric free light chain assay revealed decreased κ values and increased λ values. Echocardiography did not demonstrate alterations consistent with restrictive cardiomyopathy or myocardial thickening. Hepatic and renal ultrasonographs were also normal. The diagnosis of MM was confirmed by a myelogram showing an infiltration of 20% plasma cell in the bone marrow. Osteolytic lesions in a cranial radiograph and anaemia were also found.

Due to conditions favourable for Autologous Stem Cell Transplantation (ASCT), the patient was subjected to induction therapy with dexamethasone in weekly cycles.

DISCUSSION

This case of AL associated with MM in a 35-year old patient is uncommon because the median presentation age of these pathologies is in the seventh decade of life, and only two per cent of MM cases are diagnosed in patients younger than 40 years (1, 2). The clinical manifestations of AL vary depending on the main organs involved. Soft tissue involvement can cause macroglossia, carpal tunnel syndrome, amyloid lymphadenopathy, vascular infiltration leading to jaw or limb claudication, skeletal muscle pseudohypertrophy and periarticular amyloid deposition (3). Macroglossia is present in about 12–40% of cases, commonly associated with purpura, papules, nodules and oral ulcers. Infiltration of the salivary and lachrymal glands can cause xerostomy and dry-eye symptoms (4).

Cutaneous manifestations are also present in 10–44% of cases and can be the key to diagnosis. Petechiae and ecchymoses involving the periorbital and flexure areas of the skin result from vascular amyloid infiltration and are the most frequent cutaneous signals of AL. Skin lesions most typical of AL, however, include papules, plaques and non-pruriginous flat translucent nodules of yellow or purpuric tones (4). These lesions histopathologically lack significant inflammatory infiltration and usually involve the periorbital area, centre of the face, lips, oral mucosa, neck, armpits and perianal and vulval regions [where they resemble condyloma acuminatum] (5).

Laboratory diagnosis of AL is made by evidence of amyloid deposits originating from an immunoglobulin light chain. Serum and urine immunofixation electrophoresis show better sensitivity and specificity than serum electrophoresis in identifying the presence of a monoclonal immunoglobulin light chain. Furthermore, quantification of free light chains obtained by immunonephelometric assays can be useful as a complement to immunofixation, because an abnormal κ: λ ratio is seen in 92% of patients (6). The diagnosis of MM requires the infiltration of 10% or more plasma cells in the bone marrow, monoclonal protein in the serum or urine and evidence of end-organ damage believed to be secondary to the underlying plasma cell disorder. The most frequent MM manifestations are bone pain, weariness and recurrent infections. Anaemia, elevated serum creatinine and hypercalcaemia are present at the time of diagnosis in approximately 70%, 50% and 25% of patients, respectively, and nearly 80% of cases show lytic bone lesions on radiographs (7).

Current AL and MM treatments are based on the patient's eligibility for ASCT and aim to reduce monoclonal protein, decrease tumour mass in the bone marrow and stabilize or reverse organ dysfunction caused by amyloid deposition (3). Such criteria as age, performance status, number of damaged organs and extent of cardiac involvement allow the physician to determine risk benefits of ASCT. Recent studies of patients treated with ASCT have shown prolonged and impressive organ remissions in approximately 50% of patients, although it can be difficult to assess the response to anti-AL therapy, with cardiac involvement most adversely impacting outcome (1, 7).

We present this case to reinforce that prompt diagnosis of AL is critical to enable patients to obtain timely access to therapeutic interventions and to potentially improve their prognosis. It is necessary that medical practitioners identify the clinical presentations of AL and consider AL as a differential diagnosis during evaluations of patients presenting with yellow to ecchymotic nodular lesions involving the eyelids, macroglossia, peripheral neuropathy, nephrotic range proteinuria and also, unexplained hepatomegaly, unexplained congestive heart failure or atypical multiple myeloma. Despite improvements in the treatment and diagnosis of AL amyloidosis, continued basic and clinical research is needed to help improve the outcome for patients with this recognized fatal disease.

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