

## CASE REPORT



# Primary systemic amyloidosis associated with multiple myeloma \*

## Amiloidose sistêmica primária associada ao mieloma múltiplo

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**Abstract:** This case report is about a 48-year-old female patient with systemic amyloidosis and multiple myeloma simultaneously. Amyloid cutaneous infiltrative lesions like papules, nodules, or plaques with a serous-hemorrhagic aspect were found in the eyelids, neck and retroauricular region, among others. She had presented intermittent papular lesions on the upper eyelids one year before, which worsened following local trauma. A local skin biopsy showed amorphous and eosinophilic substance in the dermis. Congo red staining confirmed the amyloid deposits. Abnormal exams: proteinuria (570mg/24h), Bence-Jones proteinuria and clonal plasma cells (70%) found in myelogram. Following the diagnosis of multiple myeloma based on amyloid skin lesions, the patient was referred to the Hematology service and died 5 months after the diagnosis.

**Keywords:** Amyloidosis; Eyelids; Multiple myeloma; Skin

**Resumo:** Relatamos um caso de uma paciente de 48 anos com amiloidose sistêmica associada a mieloma múltiplo. Lesões infiltrativas cutâneas como pápulas, nódulos ou placas com aspecto sero-hemorrágico podem ser localizados nas pálpebras, pescoço, região retroauricular dentre outras. No presente caso, as pálpebras foram acometidas por pápulas, há 1 ano, de caráter intermitente e piora após trauma local. Biópsia local evidenciou material amorfo e eosinofílico na derme. A coloração vermelho do Congo confirmou presença de substância amiloide. Exames anormais: proteinúria de 570mg/24 horas, proteinúria de Bence-Jones positiva e mielograma com 70% de plasmócitos atípicos. Assim, realizou-se o diagnóstico de mieloma múltiplo a partir de manifestações cutâneas de amiloidose. Paciente encaminhada ao serviço de hematologia e foi a óbito em 5 meses.

**Palavras-chave:** Amiloidose; Mieloma múltiplo; Pálpebras; Pele

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## INTRODUCTION

Amyloidosis is the term used to describe abnormal deposition of a protein-rich substance (insoluble and proteolysis resistant) in the skin or other organs.<sup>1,2</sup>

The composition of such amyloid substances, in addition to fibrils, although formed by different types of proteins and carbohydrates presents some common aspects: they bind to Congo red dye, having a reddish coloration in normal light or birefringent green coloration under polarized light. They also bind to thioflavin, becoming strongly fluorescent and conferring a peculiar aspect to histological sections.<sup>2,3</sup>

Tissue infiltration by these amyloid deposits occurs in a localized or systemic manner. When localized, there is only cutaneous involvement and when systemic, it may be primary or secondary.<sup>1</sup>

The primary systemic form is related to hidden dyscrasia or multiple myeloma, while the secondary form arises from complications of chronic inflammatory processes like rheumatoid arthritis, osteomyelitis, scleroderma, Hansen's disease and tuberculosis, among others.<sup>2</sup>

We report a case of systemic amyloidosis associated with multiple myeloma, which was diagnosed based on the cutaneous symptom complex.

## CASE REPORT

A white, 48-year-old female patient presented at the dermatology service complaining of papulous lesions with bloody content in the upper eyelids for one year. The first lesions appeared following emotional stress and regressed spontaneously within 15 days. Since then she started presenting new lesions in outbreaks, always in the same places. Such lesions



FIGURE 2: Purpuric papules on upper eyelids triggered by local trauma with blunt object (Sign of Barth)

worsened when there was local trauma. Concerning associated pathologies, arrhythmia (she was using a pacemaker), hypertension and fibromyalgia were informed. During the physical examination confluent papules of varied sizes were observed in the internal half of upper eyelids and more discreet in the internal corner of the lower eyelids (Figure 1). After local trauma with a blunt object, there was onset of local purpuric papules - a Sign of Barth (Figure 2).

Biopsies of the eyelid, gums and rectal mucosa lesions were performed, with the following results:

Skin: accumulation of amorphous and eosinophilic material, fragmented and globular in the papillary and reticular dermis, replacing collagen fibers; dilated and congested within them.



FIGURE 1: Papulous lesions on upper eyelids

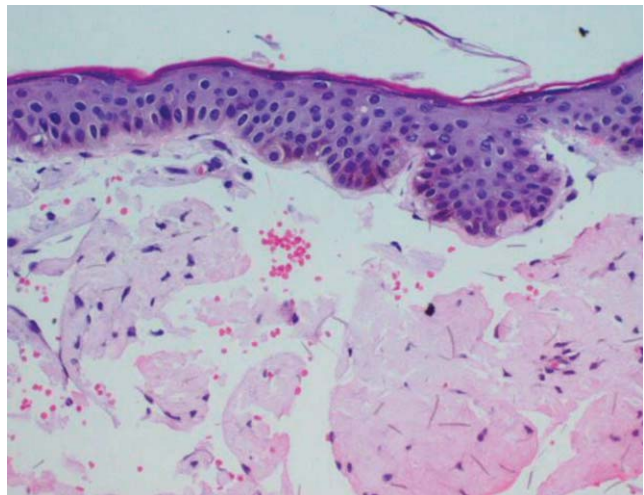


FIGURE 3: Skin fragment demonstrating deposit of amorphous and eosinophilic deposit in the papillary and reticular superficial and reticular dermis, with small caliber blood vessels irregularly dilated and congested within them. (HE, 200x)

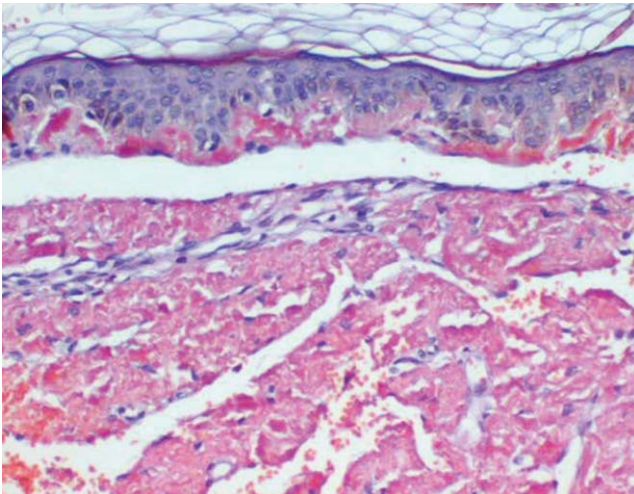


FIGURE 4: Congo red dye revealing pink-orange staining of amyloid substance. (200x)

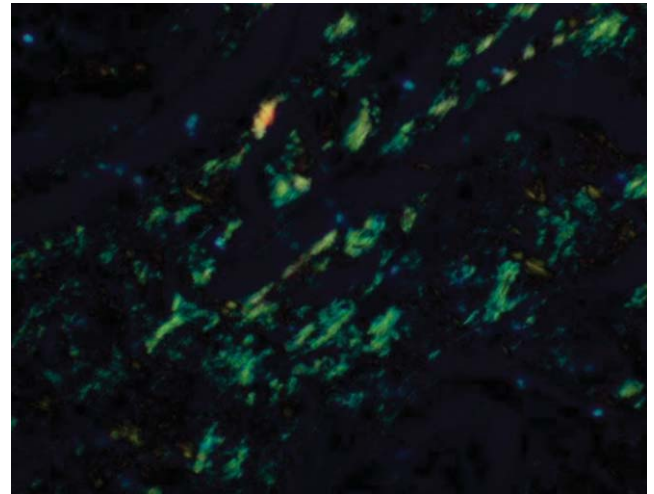


FIGURE 5: Congo red dye subjected to polarized light revealed greenish refringence characteristic of amyloid substance

ted and congested blood vessels (Figure 3). Congo red staining confirmed it was an amyloid substance (Figures 4 and 5).

Gums: No alterations. Absence of amyloid material.

Rectal mucosa: unspecific chronic retinitis. Absence of amyloid material.

The hemogram showed that creatinine, protein electrophoresis, VHS, iron and ferritin were within normal values. Cranium and long bones X-rays did not reveal lytic lesions. The echocardiogram was normal, from an anatomic viewpoint.

Among the abnormal tests, we found: proteinuria 570mg/24 hours; positive Bence-Jones proteinuria; and myelogram with 70% atypical plasmocytes.

Thus it was possible to make the diagnosis of multiple myeloma in the initial phase in a patient that presented only cutaneous manifestations of amyloidosis.

The patient was referred to a hematology service for multiple myeloma treatment. She died 5 months after the diagnosis.

## DISCUSSION

The prevalence of amyloidosis associated with multiple myeloma varies from 13% to 26%.<sup>4</sup>

Among the patients with multiple myeloma, 15% may develop some form of amyloidosis.<sup>1,4</sup>

The sequential analysis of aminoacids demonstrated that in systemic amyloidosis associated with multiple myeloma, fibrils are composed of an AL protein (light chain amyloidosis protein), which in turn is composed of variable immunoglobulin light chain (aminoterminal), intact light chain, or both.<sup>1</sup>

The most common cutaneous signs include: petechiae, purpuras and ecchymoses. Such signs

occur spontaneously following trauma and are due to amyloid infiltration in the vascular walls.<sup>5</sup> Other lesions may be seen, such as: plaques, papules and nodules; serous, smooth and shiny, amber or skin colored, non pruriginous, and they may be hemorrhagic. They affect mainly the eyelids, lips, tongue, oral mucosa, neck, axillae, umbilical scar and retroauricular, inguinal and anogenital regions.<sup>1</sup> Bullous lesions are rare.<sup>6</sup>

Some less frequent cutaneous alterations are: jaundice, paleness, hyperpigmentation, infiltrate similar to sclerodermia, alopecia areata or universal, nail dystrophies, cutis laxa and lesions similar to *cutis verticis girata* in the scalp.<sup>1</sup>

Actually, the amyloid material may be deposited in any tissue and/or organ, with specific manifestations.

In primary systemic amyloidosis, the deposit occurs predominantly in tissues such as in the gastrointestinal tract, smooth and skeletal muscles, carpal connection, nerves and skin. In contrast, in the secondary systemic form the amyloid deposition takes place above all in parenchymatous organs: liver, spleen, kidneys and adrenal glans.<sup>1</sup>

The amyloid deposits in the gastrointestinal tract may result in a variety of manifestations: abdominal pain, dysphagia, altered movements. Spleen and liver are present in 10% and 25% of cases, respectively.<sup>4</sup>

The tongue may be affected with macroglossia in 20% of cases, and there may be ulcerations, fissures, hemorrhages and teeth marks laterally.<sup>4</sup>

The heart may be involved in 25% to 40% of cases and the kidneys in 30 to 50%, which are determinants of prognosis.<sup>4</sup>

Multiple myeloma is a bone marrow plasmocyte dyscrasia diagnosed when there is more than 10% plasmocytes in the bone marrow or a plasmocytoma and at least one of the following findings: 1) monoclonal serum protein; 2) monoclonal urine protein; 3) lytic bone lesions<sup>7-8</sup>. The presence of anemia, kidney insufficiency, hypercalcemia e amyloidosis were found.<sup>7</sup>

The prognosis of amyloidosis associated with multiple myeloma is unfavorable, with between 12 and 15 months mean survival rate.<sup>4</sup> It depends on patient response to therapy and the extension of the disease. It is very important to make the earliest possible diagnosis, and always investigate multiple myeloma, especially in cases of systemic amyloidosis in patients considered suspect after the anatomic-pathological test used in this case. □

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