

Nodular primary localized cutaneous amyloidosis: presentation of 2 case reports and literature review

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Abstract

The nodular primary localized cutaneous amyloidosis is rare and characterized by skin deposition of amyloid substance. There are cases of progression to invasive disease. The type of amyloid substance is not specific to this disease, also being found in primary systemic amyloidosis or systemic amyloidosis associated with multiple myeloma.

The authors describe two cases of nodular primary localized cutaneous amyloidosis. A 70-year-old man underwent excision of papule on the mouth left commissure, and a 39-year-old woman with a vulva's labia majora swelling that was excised, in which the histology revealed a nodular amyloidosis, both without systemic involvement.

Although the prognosis is benign, the follow-up of the patient is required for early detection of a possible evolution to systemic disease, or exclusion of an underlying systemic amyloidosis.

Key words: Primary cutaneous amyloidosis. Amyloidosis. Amyloid substance

Palabras clave: Amiloidosis cutánea primaria. Amiloidosis. Sustancia amiloide.

Introduction

Amyloidosis is a common term used to describe a collection of diseases that are characterized by extracellular deposition of insoluble fibrillar protein amyloid substance.^{1,2,3,4,5} It can be divided into systemic and localized forms.^{1,2,4,5} In the former, there is widespread deposition of amyloid substance in various organs and tissues, while in the latter the deposition of this material is restricted to a single organ or tissue.² Both can be further subdivided into primary or secondary.¹

The primary localized cutaneous amyloidosis is a rare disorder characterized by three clinically and histologically distinct variants: macular, lichenoid and nodular, the last variant being the rarest.^{6,7} The type of amyloid substance found in this variant is not unique to the localized form, being also found in primary systemic amyloidosis or amyloidosis associated with multiple myeloma.⁸ The risk of progression for the systemic amyloidosis ranges from 7 to 50%.^{1,3,5,6,8}

In this work, we present two cases of nodular localized cutaneous amyloidosis.

Case 1

70-year-old Caucasian man, with hypertension, type 2 diabetes and hypercholesterolemia, with a 2-year history of a non pruriginous erythematous papule on left commissure of his mouth (**Figure 1**). The patient had no other systemic complaints. The skin lesion biopsy showed amorphous eosinophilic material in the dermis, with a tendency to confluence and positivity for the Congo Red staining, compatible with histological diagnosis of nodular amyloidosis (**Figure 2**). A total excision of the lesion was conducted, to exclude systemic disease. Laboratory testing showed normal complete blood count, erythro-

cyte sedimentation rate, C-reactive protein, renal and liver function, serum and urine protein electrophoresis, immunoglobulins, serum and urine light chains, β_2 -microglobulin and 24-hour urine protein. In addition, antinuclear antibodies and serology for syphilis, human immunodeficiency virus and hepatitis B and C virus, were all negative. A chest X-ray, abdominal ultrasound and electrocardiogram were normal. An echocardiogram showed normal left ventricular systolic function, left atrium slightly enlarged and left ventricular diastolic dysfunction.

One year after the excision, a new papular lesion on left commissure of his mouth appeared, and it was excised. Histology revealed a recurrence of nodular amyloidosis.

Currently, the patient remains in follow-up, with no evidence of systemic disease.

Case 2

39-year-old woman, with asthma and hypertension, was assessed due to hyper-pigmented swelling of her vulva labia majora, which had appeared since one year before. She referred painful bouts. Excision of this vulva lesion was performed, and histological examination showed nodular deposits of amorphous eosinophilic material in the dermis, without signs of malignancy. Staining with Congo Red was positive for amyloid substance. Other skin lesions and systemic disease were searched and excluded.

Laboratory testing included complete blood count, erythrocyte sedimentation rate, C-reactive protein and coagulation study, which were all normal; kidney and liver function were unremarkable, as well as angiotensin converting enzyme, serum protein electrophoresis, immunoglobulins, light chains, β_2 -microglobulin and antinuclear antibodies. Serology for syphilis, human immunodeficiency virus and hepatitis C virus were negative, and the patient was immune to hepatitis B. Normal 24-hour urine protein. An abdominal computed tomography (CT) scan, electrocardiogram and echocardiogram were normal. A biopsy of periumbilical subcutaneous tissue did not reveal histopathologic findings suggested of amyloid substance.

Currently, the patient remains in follow-up, with no evidence of systemic disease.

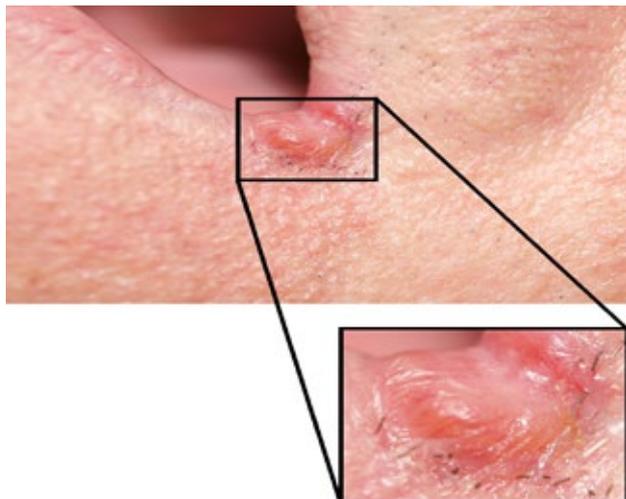
Discussion

The localized cutaneous amyloidosis is a rare type of amyloidosis in which extracellular amyloid substance deposits are located only in the skin, and includes three variants: lichenoid, macular and nodular amyloidosis.^{6,8,9,10}

The lichenoid and the macular amyloidosis are often grouped together, since both have constituents derived from keratin on amyloid deposits, that do not invade the blood vessels and do not extend below the papillary dermis.^{6,8}

The nodular amyloidosis is the rarest variant,^{5,6,8,9} its amyloid deposits are formed by immunoglobulin light chains (AL amyloid

Figure 1. Photograph of the papular lesion located at the left corner of the mouth.



substance type)^{6,8,9} produced by local plasma cells,^{6,11} infiltrating the entire dermis, the subcutaneous layer and the blood vessel wall.^{6,8} The AL protein is not specific for the nodular cutaneous amyloidosis, it also exists in the primary systemic amyloidosis or the amyloidosis associated with multiple myeloma.

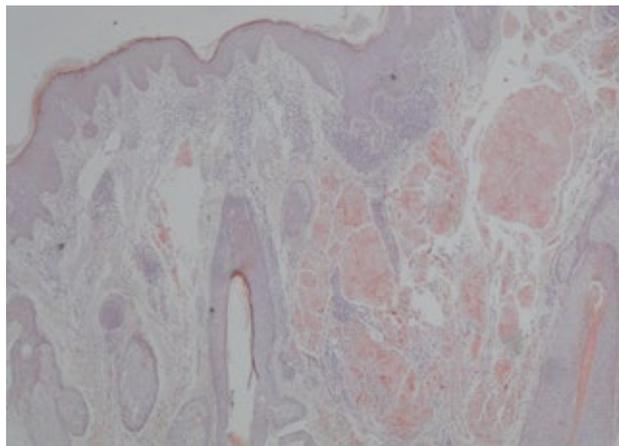
There are reports of nodular cutaneous amyloidosis associated with systemic diseases like diabetes,⁴ and autoimmune diseases, such as Sjögren's syndrome,^{2,8,12} CREST syndrome, primary biliary cirrhosis, rheumatoid arthritis and systemic lupus erythematosus.^{5,6,13} Other rare associations described in the literature include alcoholic cirrhosis,¹¹ atopic dermatitis^{14,15} and sarcoidosis⁷. In one of the case reports presented here the patient was diabetic.

The nodular localized cutaneous amyloidosis may manifest itself as a pinkish, or brownish, single or multiple nodes or plates, which appear most frequently in the legs, followed by the head, trunk, arms and genitals.⁵ The disease is most prevalent between the 4th and 6th decades of life without gender predominance.^{3,4,5}

There are reports of progression from nodular cutaneous amyloidosis to primary systemic amyloidosis.⁶ The risk of progression varies from 7 to 50%.^{1,3,5,6,8} Consequently, it is important to exclude underlying systemic disease and long-term clinical monitoring is recommended. There are no formal guidelines to monitor these patients.⁶ Searching for possible systemic disease is advisable and it should include: complete blood count, serum and urine protein electrophoresis, antinuclear antibodies, renal and liver function tests, 24-hour urine protein, chest radiograph, electrocardiogram, abdominal ultrasound and echocardiogram. An abdominal wall fat biopsy with Congo Red staining may also be performed.⁶ The radiolabelled serum amyloid P component scintigraphy allows multiple organ detection of amyloid deposits in vivo.⁵ In our case reports there is no current evidence of systemic disease.

There are many treatments recommended for nodular cutaneous amyloidosis (cryotherapy, dermabrasion, laser therapy and surgical excision). However, none of them proved to be consistently effective, and recurrence is frequent,^{5,6} which

Figure 2. Deposits of amyloid substance in the dermis (Congo Red staining; x40).



happened in one of the case reports presented here, one year after the complete surgical excision of the lesion.

Nodular primary localized cutaneous amyloidosis is a rare disease that can cause aesthetic and functional changes that lead patients to seek treatment, but with a benign prognosis. However, understanding how to properly diagnose and treat this condition, as well as the need for surveillance and monitoring of the patient for early detection of a possible evolution to systemic disease, or the exclusion of an underlying systemic amyloidosis, are critical in patient's prognosis.

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