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CASE REPORT

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Amyloid tumours in the soft tissues of the legs

Case report and review of the literature

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Abstract We present a case of multiple amyloidomas occurring in the calves of a 61-year-old woman, without systemic amyloidosis or plasma cell dyscrasia. The disappearance of Congo red positivity after potassium permanganate treatment and immunohistochemical results showed that this was a case of reactive AA amyloidosis. True soft tissue amyloidomas are extremely rare, and this is the first case of AA amyloidoma in the soft tissues of the legs.

Key words Amyloidosis · Amyloidoma · Soft tissue · Amyloid protein AA

Introduction

Localized amyloidosis in tumour-like presentation (amyloidoma) is rarely observed and usually associated with immunocytic dyscrasias [10]. We report a case of reactive AA amyloidomas in the soft tissues of the legs of a 61-year-old woman and discuss the different clinical settings for such amyloidomas and the problems encountered in classifying these particular forms of amyloidosis.

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Clinical history

A 61-year-old nun was admitted for examination of multiple nodules which had appeared on her legs over 3 months. Her past history included Raynaud's phenomenon dating from adolescence and autoimmune thyroiditis with antithyroglobulin and antimicrosomal antibodies. At present she is being treated with L-thyroxine sodium for hypothyroidism and has persistently elevated titers of antinuclear antibodies with no evidence of systemic lupus erythemetosus, rheumatoid arthritis, chronic inflammation, infective disease or occult neoplasm. Laboratory findings, including serum proteins and the immunological profile were normal except for the antinuclear antibodies.

Clinical examination revealed multiple bilateral subcutaneous nonpainful nodules in the legs with no relationship to bones or joints. The overlying skin was slightly atrophic but not infiltrated. Radiography of the legs revealed multiple masses from 1 to 5 cm across in the subcutis and calf muscles (Fig. 1).

The biggest nodule, situated in the left calf, was surgically enucleated. The postoperative course was uneventful, and the patient was discharged without therapy. The patient is alive and well 1 year after surgery. Residual nodules in the legs remain unchanged, and no sign of systemic amyloidosis is present.

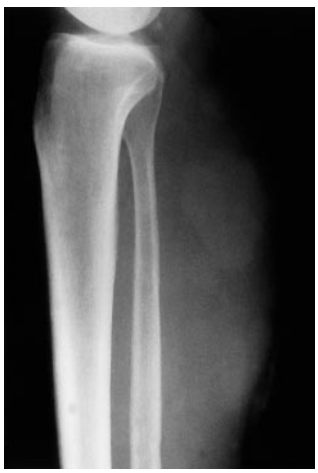
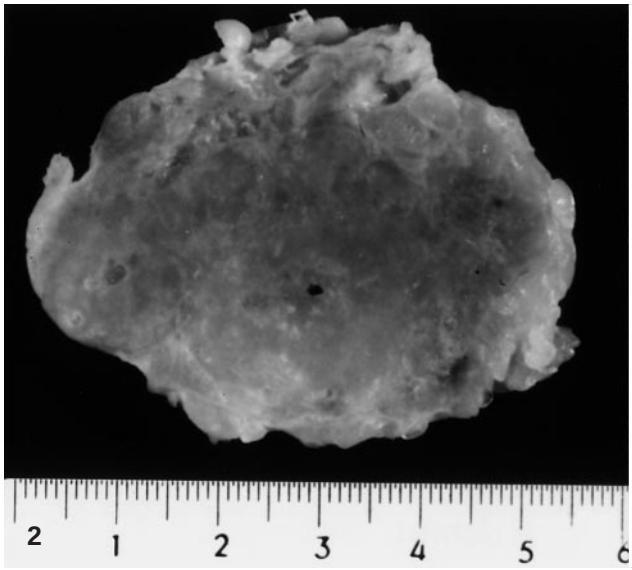
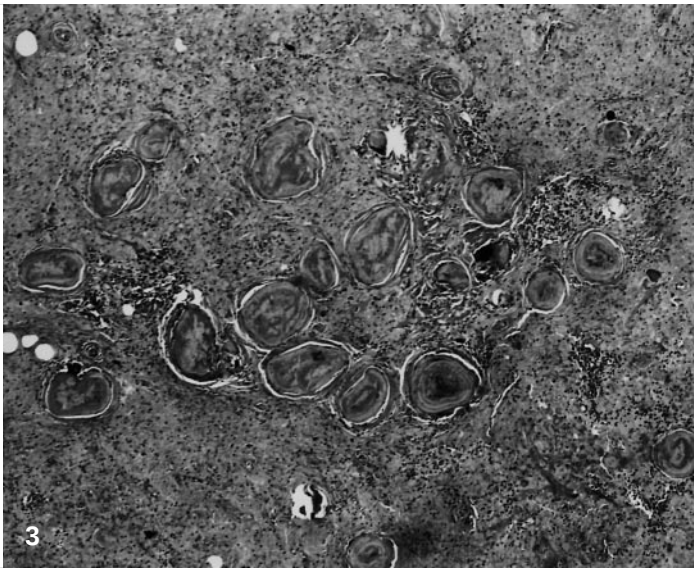
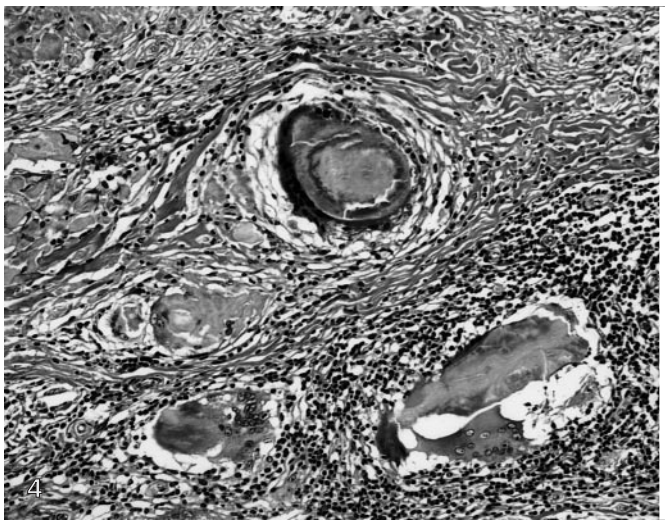


Fig. 1 Radiologic appearance of left leg showing multiple nodules in subcutis and calf muscles







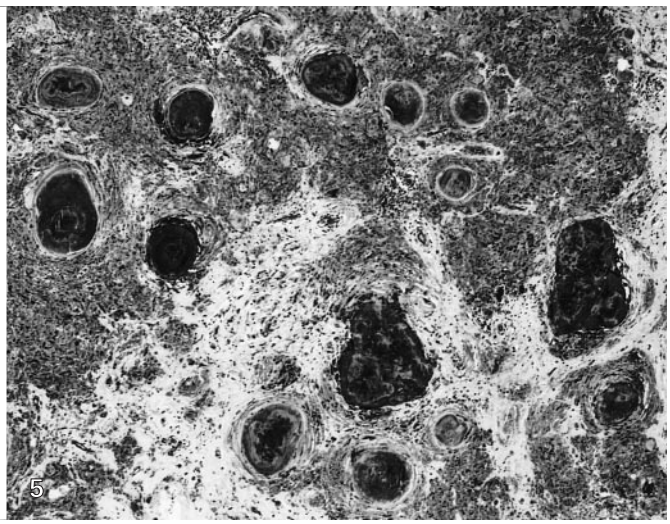


Fig. 2 Cut surface of the biggest nodule revealing a waxy appearance

Fig. 3 Round masses of amyloid in a fibrous stroma. Haematoxylin & eosin, ×40

Fig. 4 Foreign-body giant cells sourrounding amyloid deposits with associated chronic inflammatory infiltrate. Haematoxylin & eosin, ×150

Fig. 5 Diffuse immunostaining of amyloid deposits for anti-human amyloid component. Immunoperoxidase, ×40

Fig. 6 Electron micrograph showing an intracellular felt of rigid, nonbranching fibrils 10–15 nm in diameter. ×30,000

Pathological findings

The gross specimen was a lobulated nodule, five cm at maximum diameter, with a white-yellow waxy surface (Fig. 2) and focal calcification. After formalin fixation and paraffin embedding, routine haematoxylin-eosin staining revealed a fibrous stroma with numerous interspersed roundish accumulations of concentrically lami-

nated, eosinophilic material reminiscent of the corpora amylacea of the prostate (Fig. 3). Most of these micronodules were surrounded by multinucleated giant cells associated with focal collections of mature lymphocytes and rare typical plasma cells (Fig. 4). Foci of metaplastic bone and entrapped peripheral nerves were also present. Congo red staining showed diffuse positivity of the eosinophilic material, which disappeared after treatment with potassium permanganate. Fluorescent staining with thioflavin T was also positive. Immunohistochemical staining for anti-human amyloid A component (Dakopatts, dilution 1:100) gave strong positivity (Fig. 5). Immunohistochemical stains using polyclonal antisera for light kappa and lambda chains (Dakopatts, dilution 1:3,000 and 1:5,000, respectively) were negative in amyloid deposits. The ultrastructural study performed on formalin fixed tissue revealed a felt of nonbranching fibrils 10–15 nm in diameter (Fig. 6).

The final histopathological diagnosis was amyloid tumour (AA amyloidosis).

Discussion

Amyloidosis is a well known complication of chronic inflammation, haemodialysis, plasmacytic dyscrasias and malignant neoplasms [20]. Based on the deposit patterns, amyloidosis can be divided into systemic or localized forms.

Localized "tumour-like" deposits of amyloid (amyloidomas) are unusual and mainly described in visceral locations, such as the lung [7], urinary system [1], and gastrointestinal tract [8], and in organs such as the breast [12]. Soft tissue amyloidomas, as in our case, are even more rare, and because of the nonuniform criteria and terminology adopted there are controversies about true locations in soft tissues. In fact, in the largest reported series [10] the authors describe 14 cases and cite only 5 previously reported cases. However, 13 of their 14 cases were in the retroperitoneum, mediastinum and mesentery, and only 1 was in the soft tissues of the right flank. On the basis of the anatomical location and the frequent presence of concomitant lymphoplasmacytoid lymphomas (8/13) with neoplastic cells intermingled with the amyloid deposit, it is likely that the true location of amyloidosis was in the lymph nodes and not in the adipose tissue. Similar considerations may be applied to other cases of amyloidoma reported in the mediastinum [6, 13, 15, 19] or in other lymph-node-rich regions such as the groin [4, 12] and the neck [3, 4, 14].

It is not clear whether the so-called tumefactive forms of cutaneous amyloidosis [2, 16] are variants of localized skin amyloidosis or true soft tissue amyloidomas. From the nosological point of view the simple distinction of primary and secondary forms is no longer reliable, since amyloidosis is currently classified by the identification of fibril proteins constituting amyloid deposits, and 16 fibril protein precursors have been identified [17]. When the clinical, histochemical and immunohistochemical criteria are integrated the principal forms that emerge are those associated with immunocytic dyscrasias, in which the amyloid is derived from the immunoglobulin light chains (AL amyloid), those associated with inflammatory disease (AA amyloid), the familial forms, those associated with solid tumours (such as medullary carcinomas of the thyroid) and those arising in long-term haemodialysis patients (beta-2 microglobulin amyloid).

It is surprising that despite the well-known high incidence of amyloidosis in long-term haemodialysis patients, tumours in soft tissue are very rare with only three reported cases [5, 18, 21].

Similar considerations can be applied to connective tissue disease. In fact, in spite of the high incidence of systemic amyloidosis in rheumatoid arthritis no cases of amyloidomas have been described in this condition. The only connective tissue disease in which amyloidomas, mainly visceral, have been sporadically described is Sjøgren syndrome, in which AL amyloid has been demonstrated in 2 cases [9, 14].

Our patient had undifferentiated connective tissue disease [11] but no signs of "sicca syndrome", and the amyloid fibrils were of AA type.

No other case with similar clinico-pathological features has been reported in the literature, and it seems that soft tissues are particularly refractory to massive deposits of amyloid in all the known amyloidogenetic conditions.

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