Is Sjögren’s syndrome involved in the formation of localised nodular amyloidosis?

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ABSTRACT

The case of a patient who presented with Sjögren’s syndrome complicated by localised cutaneous nodular amyloidosis is reported. We discuss the possible link between these two diseases.

Introduction

Sustained, high concentrations of serum amyloid A protein, which is a major acute-phase reactant, are found in diseases which predispose to amyloidosis, most commonly rheumatoid arthritis. On the other hand diseases with low or moderately raised acute phase proteins, such as Sjögren’s syndrome (SS), are less likely to be complicated with systemic amyloidosis (1). However, several cases of localised amyloidosis associated with SS have been reported. Nodular amyloid deposits were found in the lung (2,3), skin (4-9) and tongue (10). Is this just a coincidence or could these two different diseases share a common pathogenetic mechanism?

Here we report a case of SS complicated by localised cutaneous nodular amyloidosis (LCNA). In the light of our histologic findings, as well as data from the available literature, we discuss the possible mechanisms of amyloidosis in this clinical setting. We also consider the therapeutic strategy of the presented case.

Case report

A 68-year-old Caucasian woman was referred to our department of rheumatology in 1996; her chief complaint was dryness of the eyes and mouth which had begun 5 years ago. She also noticed skin nodules on her right shin, gradually increasing in size and number (up to 4) over the last 3 years. They were asymptomatic, but had recently become occasionally painful.

Physical examination revealed a dry oral mucosa and tongue and 4 firm, non-fixed, ovoid, shiny, brown-pink nodules on the right shin. The lesions ranged from 2.5 to 5 cm in diameter and were surrounded by healthy skin (Fig. 1). The overlying skin on one of the lesions was ulcerated. Laboratory abnormalities included: slight leucopenia 3.7 x 10⁹/l; elevated erythrocyte sedimentation rate (Westergren) 64 mm/hour; polyclonal increase in gamma globulin; and strongly positive antinuclear, anti-Ro (SS-A) and anti-La (SS-B) antibodies. Immunoelectrophoresis of the serum and concentrated urine did not show monoclonal immunoglobulins or light chains. A Schirmer-I test (right eye 3 mm and left eye 1 mm after 5 minutes) and the Rose Bengal test (right eye 5 and left eye 7 according to the Bijsterveld scoring system) were positive, as was a salivary scintigraphy (class 3 following Schall’s criteria). A minor salivary gland biopsy revealed marked focal mononuclear cell infiltration with a focus score of 7 foci/6.7 mm².

One of the skin nodules was surgically resected and histologically examined. It consisted of abundant hyaline eosinophilic masses on hematoxylin-eosin staining, filling almost the entire dermis. Infiltration with lymphocytes and plasma cells around the sweat glands was prominent (Fig. 2). Sections that stained positive with Congo red and with thioflavine T led to the diagnosis of amyloidosis. The result of immunohistochemical studies revealed that the amyloid proteins were of light-chain origin (Fig. 3). The minor salivary glands were not evaluated for B-cell monoclonality. Subcutaneous abdominal tissue samples and the minor salivary glands were stained with Congo red and no amyloid deposits were found. Bone marrow aspiration was normal.

The patient was diagnosed as having primary SS and LCNA. Two weeks after the surgical excision the wound recovered completely. We recommended surgical excision of all the lesions, but the patient refused. Tear and saliva substitutes were prescribed. The patient presented again in January 2000. There were no new lesions, but the pre-existing lesions appeared to be substantially enlarged, one of them showing a large central ulceration. No signs of internal organ involvement due to SS or amyloidosis developed. The patient underwent surgical procedures for removal of all the skin lesions with good results.

Discussion

LCNA is a rare form of cutaneous amy-
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loidosis, with fewer than 60 reported cases in the international literature. Its pathogenetic features are very similar to the nodular lesions of systemic amyloidosis, in which amyloid fibrils are derived from monoclonal immunoglobulin light chains secreted by bone marrow plasma cells (10, 11). Some authors have demonstrated the presence of a locally expanded monoclonal plasma cell population in the skin lesions of LCNA (12). On the other hand, despite the rareness of LCNA it has been reported with unusual frequency in SS (4-9). In the remainder of the cases of LCNA, a suspicion of SS may be raised in some instances. In 1976 Goerttler et al. (13) summarized the findings of 29 reported cases of nodular cutaneous amyloidosis: several patients had elevated levels of gamma globulins and some of them were positive for antinuclear antibodies.

The major histopathological lesion of SS is a round cell infiltrate which affects the exocrine glands: in the early lesions it begins around the ductal epithelial cells, whereas in advanced lesions the infiltrate extends and replaces the functional tissue (14). We noticed in our patient prominent infiltration with lymphocytes and plasma cells around the sweat glands in the skin lesion. A similar infiltration in the skin appendages was described in other reported cases of localised nodular cutaneous amyloidosis (4-6,9). Nevertheless, some cases of localised nodular amyloidosis of the lung and tongue associated with SS have been reported (2,3,10). Most of them proved to be of light chain origin. When SS affects the lung, it mainly involves the airways.

Initially the mononuclear cell infiltrates start in the large airways around the exocrine glands, and they subsequently extend to the peripheral airways (14). In the case of the primary localised nodular tongue amyloidosis plasma cell infiltration was observed around the minor salivary glands (9).

We can speculate that the primary event in the described cases of localised nodular amyloidosis could be the round...
cell proliferation which affects the exocrine glands, probably due to SS. Local and as yet unknown factors may alter the immunglobulin light chain conformation, leading to aggregation, fibril formation and localised nodular amyloidosis.

The excised lesion in our patient did not recur over a period of 3 years, but the pre-existing ones enlarged considerably and became painful. Therefore, surgical resection of the nodular lesions could represent a good therapeutic strategy.

References