Primary Amyloidosis with Dry Eyes and Dry Mouth—A Case Report

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We report a rare case of dry eyes and dry mouth caused by primary amyloidosis. A 66-year-old woman with keratoconjunctivitis sicca and xerostomia died of acute respiratory failure. Shirmer's test, gum test, and sialography indicated Sjögren's syndrome. Bence-Jones protein was noted in the urine. At autopsy, amyloid deposition was identified histochemically in many organs, mainly on the vessel walls. Primary amyloidosis should be considered as a differential diagnosis of Sjögren's syndrome.

Key words: Sjögren's syndrome, Cutaneous amyloidosis, Primary amyloidosis

Sjögren’s syndrome is a chronic inflammatory disease characterized by keratoconjunctivitis sicca and xerostomia resulting from destructive lymphocytic infiltration into exocrine glands such as the salivary and lacrimal glands. Although the causative mechanism of this syndrome is still unknown, the autoimmune process is believed to be a major part of the lymphocytic destruction of these exocrine glands (1). Some diseases such as sarcoidosis and myeloproliferative disorders are reported to cause destruction of the exocrine glands.

In this report, we describe a patient who suffered from dry eyes and dry mouth caused by primary amyloidosis.

CASE REPORT

The patient was a 66-year-old woman who presented purpura, epidermal desquamation, edema, palpitations, general malaise and xerostomia from 1983. In 1985, she was admitted to our hospital because of blisters on the chest. In January 1986, she experienced chest oppression and was admitted to our hospital for evaluation of cardiac function. Blood pressure was 120/70 mmHg. The skin was edematous. Many purpura, bleeding spots and blisters were noted in the intertriginous regions subject to external stimuli. Her chest had rapidly developing macular skin lesions (Fig. 1). The oral cavity was dry with many decayed teeth. Elevated nodules were present on the lingual surface. Anemia and jaundice were not noted. A superficial keratoconjunctival erosion was noted on the left eye. Thyroid gland was not enlarged and superficial lymph nodes were not palpable. There was no hepatosplenomegaly. No abnormality was present in the neurological findings.

In the laboratory tests at the time of admission, urinary protein excretion was about 1 g/day. The red blood cell count was 389 x 10^6/μl, hemoglobin was 12.5 g/dl, the white blood cell count was 7,600/μl, with 53% neutrophils, 42% lymphocytes and 5% monocytes. The platelet count was 21.6 x 10^5/μl. Liver function tests were normal, BUN 16 mg/dl and creatinine 1.8 mg/dl. The total protein was 6.8 g/dl, with albumin 4.0 g/dl; α1-globulin 5.3%, α2-globulin 13.3%, β-globulin 7.6%, and γ-globulin 11.9%. Monoclonal protein was not noted. CRP was negative. IgG, IgA, and
IgM were 1,110 mg/dl, 145 mg/dl and 212 mg/dl, respectively. Various autoantibodies were negative, including antinuclear antibody. The gum and Schirmer’s tests to check excretory function of the salivary and lacrimal glands both showed decreasing tendencies. Sialography demonstrated scattered, minute and granular shadows (Fig. 2). Lip biopsy demonstrated amyloid deposition around the salivary ducts, and atrophy of the salivary duct by both Congo red stain and Dylon’s stain (Fig. 3). The deposited amyloid proteins were resistant to treatment by potassium permanganate prior to Congo red stain, Dylon’s stain, and green birefringence under polarized light. There was no pathological lymphocytic infiltration. The electrocardiogram was of low voltage with arrhythmia. In the echocardiogram, thickening of the ventricular septum was marked. Technetium pyrophosphate scintigraphy showed no accumulation in the thyroid, liver and heart. By immuno-electrophoresis, \( \lambda \) type Bence-Jones protein was noted in the urine. In the sternal bone marrow, there were 11% plasma cells, showing a slight increase but no atypism.

From the above findings, primary amyloidosis associated with dry eyes and dry mouth was diagnosed. From September 1986, treatment with dimethyl sulfoxide, prednisolone and melpharan was started. Although cyclophosphamide was also added, there was no change in the quantity of protein excreted in the urine. The skin lesions progressed slowly, and blister formation became marked with an increased loss of protein. The patient eventually died of sudden asphyxia. At

Fig. 1. Rapidly developing macular skin lesions on the anterior thorax.

Fig. 2. Sialography showing scattered, minute and granular shadows.

Fig. 3. Microscopic feature of lip biopsy, showing amyloid deposition around the duct, and atrophy of the duct (Dylon’s stain ×100).

Fig. 4. Microscopic findings of skin autopsy
A) Amyloid deposition on the vessel walls under the epidermis (Congo red stain ×200).
B) Amyloid deposition on the vessel walls under the epidermis confirmed by birefringence under polarized light (×200).
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autopsy deposition of amyloid was noted in many organs (heart, lung, G.I. tract from tongue to rectum, liver, pancreas, kidneys, adrenals, and thyroid), mainly on the vessel walls. In the skin, amyloid was noted on the vessel walls under the epidermis (Fig. 4).

**DISCUSSION**

A diagnosis of Sjögren's syndrome is strongly indicated when any two of the three clinical criteria, keratoconjunctivitis sicca, xerostomia or abnormal findings of sialography are present and is confirmed by abnormal findings of the salivary gland biopsy (1). In this case, keratoconjunctivitis sicca and xerostomia were noted. Sialography also showed abnormalities, and the presence of Sjögren's syndrome was suspected. Lip biopsy in typical cases of Sjögren's syndrome usually reveals focal lymphoplasmocytic infiltration often with acinar atrophy and fibrosis. Dry eyes and dry mouth caused by primary amyloidosis presents no pathological lymphocyte infiltration with destruction and atrophy of the exocrine glands caused by amyloid deposition. Dry eyes and dry mouth caused by primary or secondary amyloidosis with deposition of amyloid in the salivary and lacrimal glands has been reported in only a few cases in the literature (2–10). In these reports, the patients were usually quite elderly and no difference was noted between the sexes in incidence, although Sjögren’s syndrome has a well established higher prevalence rate in females. A case has been reported which also involved autoantibodies, making differentiation from Sjögren’s syndrome difficult (6).

The present case was diagnosed as primary amyloidosis based on the histological evidence of the lip biopsy plus the positive Bence-Jonc proteinuria, the absence of a marked increase of atypical plasma cells in the bone marrow, and the lack of evidence of bone destruction. Lip biopsy revealed amyloid deposition around the salivary ducts, there was no indication of chronic sialoadenitis. Based on the above findings, primary amyloidosis associated with dry eyes and dry mouth was diagnosed. The skin lesions, impaired renal function, cardiac hypertrophy, arrhythmia and edema seem to be explainable by the primary amyloidosis.

It is known that AL amyloidosis (primary amyloidosis and amyloidosis complicated by multiple myeloma) is associated with eruptions caused by amyloid deposits. The eruptions vary in type, such as purpura, papulae, small nodules, erythema, tumors and subcutaneous nodules. However, rapidly developing macular skin lesions such as in the present case, are rarely encountered, thus this case is most interesting.

In summary, primary amyloidosis should be considered as a differential diagnosis of Sjögren’s syndrome.

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