Sjögren's syndrome associated with multiple myeloma

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ABSTRACT

There have been very few reported cases of multiple myeloma (MM) which had Sjögren syndrome (SS) as the first presentation. We report a 63-year-old Moroccan woman with IgA-lambda-type MM presenting as SS and who responded to anti-myeloma treatment. The patient, treated for SS, was admitted to our department for persistent and increasing thoracic pain. Clinical examination was normal. Laboratory investigations showed haemoglobin of 10 g/dL. Erythrocyte sedimentation rate was 80 mm/hr. Monoclonal spike was found in the betaglobuline region of the serum protein electrophoresis. Immunofixation identified it as IgA lambda and the level was 3.7 g/dL. The bone marrow contained 35 percent plasma cells, with atypical features. Radiographs showed diffuse lytic lesions. Treatment with vincristine, adriamycine and dexamethasone (VAD) was started and bisphosphonate was administered regularly. After three cycles of VAD therapy, the MM regressed without any evidence of SS symptoms. The development of MM in the setting of SS is unusual and the aetiopathogenic mechanism still unknown. However, some elements orient toward a common pathway for these two diseases, like the clinical remission of SS after treatment of the MM, such as described in our patient.

Keywords: gammopathy macroglobulinaemia, lymphoma, multiple myeloma, Sjögren's syndrome

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INTRODUCTION

Sjögren's syndrome (SS) is a chronic autoimmune disease associated with the production of auto-antibodies and is characterised by a progressive lymphocytic and plasma cell infiltration of the salivary and lachrymal glands, leading to xerostomia and xerophthalmia. SS is predominantly a disease of middle-aged women, while myeloma is a disease of the elderly, with only 2% of cases occurring in patients less than 40 years of age. There have been very few reported case of multiple myeloma (MM) which had SS as the first presentation.[1] SS has been recognised to have a high incidence of benign monoclonal gammopathy, although MM is very rare. Most of the monoclonal gammapathies in patients with SS involve the IgM class.[2] We report a female patient with IgA-lambda-type MM presenting as SS and who responded to anti-myeloma treatment.

CASE REPORT

A 63-year-old Moroccan woman presented with a history of dry eyes, dry mouth, and polyarthralgia of five years' duration. This led to painful, red and excessive tearing of the eyes, and difficulty in swallowing dry food. Schirmer's test was abnormal. Treatment with tears and saliva substitutes were not effective. She was admitted to our department for persistent and increasing thoracic pain. She also complained of mild shortness of breath and poor appetite. Physical examination revealed that the patient was moderately well-nourished. The temperature was 36.5°C, the pulse was 96/min, the blood pressure was 120/80 mmHg, and respirations were 22/min. No jaundice, skin rashes, or petechiae was present. She had no jugular vein dilation. No superficial lymph nodes were palpated. She had no thoracic malformations or tenderness. She had a normal heart size, with a regular heart rhythm. Her abdomen was soft without tenderness. No hepatosplenomegaly was palpated. The vertebral column and joints of the extremities were normal. No positive nervous system signs were found.

Laboratory investigations showed haemoglobin of 10 (normal range 12–16) g/dL, mean cell volume (MCV) of 83 (80–98) fL, white cell count of 3,700/L (4,000–10,000/L) and platelets of 144,000/L (150,000–300,000/L). The bleeding time and coagulation time were normal. Erythrocyte sedimentation rate was 80 (0–16) mm/hr and C-reactive protein was 13 (0–5) mg/L. Rheumatoid factor was 9.5 (0–15) UI/ml. Monoclonal spike was found in the betaglobuline region of the serum protein electrophoresis. Immunofixation identified it as IgA lambda and the level was 3.7 (0.085–0.45) g/dL. A 24-hour specimen

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of urine revealed a creatinine clearance of 115 (120 ± 20) ml/min/1.73 m^2. Calcium level was normal. The bone marrow contained approximately 35% plasma cells, with atypical features. Radiographs showed a lytic defect in the cranial bone. The skeletal survey showed diffuse lytic lesions. Treatment with vincristine, adriamycine and dexamethasone (VAD) was started and bisphosphonate was administered regularly. After three cycles of VAD therapy, the MM regressed without any evidence of SS symptom. The follow-up duration was 39 months. The last outpatient control revealed no increase in size or number of lytic bone lesions, with serum paraprotein level within the normal range.

DISCUSSION

SS is a chronic autoimmune disease with a well-documented association of lymphoid malignancies during the progress of the disease. Although several types of malignancy have been reported in SS, low-grade non-Hodgkin's lymphomas are the most frequently observed.[3] B-cell lymphoma, which is an occasional complication of SS macroglobulinaemia, develops in some patients.[4] Most of the reported monoclonal gammapathies in patients with SS involve the IgM class.[5] Non-IgM monoclonal gammapathies in patients with SS is infrequent. This report describes a Moroccan patient with SS associated with IgA-lambda-type MM.

SS is characterised by two main autoimmune phenomena: B-cell hyperactivity and lymphocytic infiltration of the exocrine glands. B-cell lymphoma develops in 5% of patients. Hyperimmune reaction has been assumed to play an important role in the lymphoma genesis in SS. SS patients have been recognised to have a high incidence of benign monoclonal gammopathy demonstrated either in the urine or serum,[6,7] although MM is very rare.[8] Osserman and Takatsuki observed that chronic inflammation may represent a stimulus in the development of MM.[9] The exact mechanism remains under speculation. The same immunological disorder may play a role in the pathogenesis of monoclonal gammopathy in SS.

Factors associated with monoclonal or malignant transformation during the course of the disease are not fully understood. However, dysregulation in the mechanisms leading to apoptosis, hyperstimulation of B-1 cells, or an infectious agent may contribute to lymphoproliferation in SS.[10,11] SS associated with MM of the IgA type is extremely rare. To our knowledge, only some cases have been published.[12,13] Previous reports have shown that treatment of the underlying myeloma did not favourably effect the clinical manifestations of SS.[1,8] Chemotherapy with melphalan and prednisolone was not effective in a patient with SS associated with IgG MM. In this patient, rapid recovery of SS was evident following three cycles of VAD. One wonders whether this feature could be explained by the fact that VAD regimen is more effective than the conventional melphalan-prednisone (MP) chemotherapy, or whether SS associated with IgA paraprotein is more responsive to treatment than those associated with non-IgA monoclonal gammopathies.

The development of MM in the setting of SS is unusual and the aetiopathogenic mechanism still unknown. The coexistence of these two relatively uncommon disorders may merely represent a chance association. However, some elements orient toward a common pathway for this two diseases, like the clinical remission of SS after treatment of the MM, as described in our patient.

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