CASE REPORT

Pulmonary MALT Lymphoma with Amyloid Production in a Patient with Primary Sjögren’s Syndrome

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Abstract

A 53-year-old woman was admitted to our hospital complaining of cough, low grade fever, chest pain and sicca symptoms. A chest radiograph showed an abnormal shadow and chest computed tomography revealed a tumor in left S6. She was diagnosed as Sjögren’s syndrome by sialography and histological findings of labial biopsy. The surgically resected tumor specimen showed proliferation of lymphoid cells with lymphoepithelial lesions, which were positive for CD20 and kappa light chain. Kappa light chain-positive amyloid was found within the tumor. The tumor showed rearranged kappa light chain genes. The diagnosis was pulmonary mucosa associated lymphoid tissue lymphoma with amyloid production.

Key words: maltoma, lung, amyloidosis

Case Report

A 53-year-old woman was admitted to our hospital complaining of cough, low grade fever, chest pain and sicca symptoms. She smoked one package of cigarettes a day for 32 years. Her prior history showed no evidence of pulmonary diseases. The physical examination was normal. The results of common blood cell counts and blood chemistry were within normal limits. ESR was 126 mm (1 hour) and CRP was 1.18 mg/dl. The serum level of RF rose to 33 IU/ml. The serum levels of IgG (3,060 mg/dl) and IgA (696 mg/dl) were elevated. A high titer of anti-SS-A antibody was disclosed (>256x). The titer of anti-SS-B antibody was 1x. The serum level of IL-2 receptor was 711 U/ml. The results of pulmonary function studies were within normal limits. Cytological examination of sputum revealed atypical lymphocytes. Saxon test, Schirmer’s test and the rose bengal test were positive. A chest radiograph showed abnormal shadows in left middle lung field and right lower lung field. A chest computed tomography (CT) revealed a tumor shadow in left S6 (Fig. 1) and an irregular shadow in the right lower lobe without mediastinal lymph node swelling. The sialography showed an apple tree appearance and the labial biopsy revealed atrophy and fibrosis of acinus with infiltration of lymphocytes, consistent with Sjögren’s syndrome.

A transbronchial lung biopsy specimen of the tumor showed infiltration of lymphocytes in the peribronchiolar area. Because of a gradual increase of the tumor size in left S6, video-assisted thoracic surgery was performed. The surgically resected tumor was yellowish in color and the size was 38x38x20 mm. Microscopic findings of the biopsy specimen showed diffuse infiltration of small to medium-sized lymphoid cells without formation of a germinal center, which infiltrated around the bronchiole and presented the features of a lymphoepithelial lesion (Fig. 2A). In addition, deposits of eosinophilic amorphous material were found in the tumor. Congo red staining (Fig. 2B) was performed and a diagnosis of amyloid protein was confirmed by apple green birefringence under polarized light examination. The lymphoid cells were positive for CD20 (L26) and kappa light chain, and negative for CD45RO (UCHL-1)

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Figure 1. Chest CT showing a tumor in right S6.

and lambda light chain. The amyloid deposits were also positive for kappa light chain and negative for AA amyloid, indicating that deposits were AL amyloid component of immunoglobulin kappa light chains. Southern blot hybridization of the tumor showed clonal rearrangement of J region of the immunoglobulin kappa light chain (Fig. 3). The patient was diagnosed as pulmonary MALT lymphoma (stage I) with amyloid production. The lymphocyte infiltration without atypia was seen in the lung tissue around the tumor, which is due to Sjögren's syndrome.

The tumor of pulmonary MALT lymphoma was surgically resected. In addition, combination chemotherapy was selected; cyclophosphamide 1,100 mg/body, hydroxydaunomycin 75 mg/body, and oncovin 2 mg/body were administered on day 1 and prednisolone 100 mg/body was administered on days 1 to 5. After four courses of combination chemotherapy, the irregular shadow in the right lower lobe did not change. No evidence of recurrence was found for 16 months after tumor resection.

Discussion

Primary Sjögren's syndrome, a chronic organ-specific autoimmune disease characterized by dysfunction of exocrine glands, presents various manifestations including involvement of the extraglandular organs. The less common but crucial disorders of Sjögren's syndrome include lymphoproliferative disorders. Monoclonal non-malignant and malignant lymphoproliferative disorders have been reported to develop

Figure 2. Lung biopsy specimen obtained by video-assisted thoracic surgery showing proliferation of small to medium-sized lymphoid cells, in conjunction with lymphoepithelial lesions (arrowhead) (A: HE stain, ×200) and the deposits of amorphous amyloid protein in the tumor. (B: Congo red stain, ×100)

Figure 3. Southern blot hybridization with the immunoglobulin light chain gene J kappa probe from surgically resected tumor. Restricted enzymes BamH I and Hind III were used. Arrowheads show rearrangement bands in the lane 1 (BamH I) and the lane 2 (Hind III).
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in 25% and 5% of patients with Sjögren’s syndrome, respectively (2). The risk of development of lymphoma of patients with Sjögren’s syndrome is 43.8 times higher than that of the general population (3). As for malignant lymphoma in Sjögren’s syndrome, a high incidence of B cell lymphoma as well as monoclonal gammopathy has been recognized. Low grade B cell lymphomas in Sjögren’s syndrome are frequently observed, including follicular lymphoma and MALT lymphoma (4).

Recently the association between antecedent autoimmune diseases and lymphoproliferative disorders has been reported (2). It has been speculated that some background stimuli leads to local or diffuse lymphoid hyperplasia, which is then followed by neoplastic transformation. Accumulation of many genetic abnormalities including bcl-2 overexpression and mutations of p53 genes by chronic stimulation of T cells and B cells at the site of the autoimmune reaction may be important in the high occurrence of lymphoproliferative disorders in autoimmune diseases (2, 5). There is a complex process in the occurrence of malignant lymphomas in Sjögren’s syndrome from chronic autoimmune reactions.

Malignant lymphomas arising in the lung are rare tumors that comprise 0.34% of all lymphomas (6). The tumors have been estimated to comprise only 3% to 4% of all extranodal lymphomas (6). Primary extranodal lymphomas are thought to be derived from MALT, as well as the most common type, low grade B cell lymphomas. In 1983 Isaacson and Wright (7) described a distinctive type of B cell lymphoma which arises from MALT of the gastrointestinal tract and they subsequently reported in 1984 an extranodal lymphoma arising from the lung, thyroid, salivary gland and gastrointestinal tract (8).

The etiology and pathogenesis of MALT lymphoma are unclear. MALT lymphomas are low grade B cell lymphomas and tend to remain localized for a prolonged period (9). However, MALT lymphomas can transform into high grade lymphomas after up to 18 years; diffuse lymphomas can be a result of the transformation from low grade B cell lymphomas (5). The majority of MALT lymphomas may be a progressive state to high grade malignancy. Further study on the long-term prognosis of MALT lymphomas is necessary.

In the present case, amyloid deposits were present within the stroma of the MALT lymphoma but were not present in the other discrete sites. A few reports have described nodular amyloidosis in association with pulmonary lymphoma (10). Amyloidosis associated with MALT lymphoma is thought to occur in less than 1% of cases (11). In some instances, amyloid deposits may be related to preexisting chronic inflammation or autoimmune diseases. However, in the present case the positive staining of monoclonal kappa light chain in both the MALT lymphoma and the amyloid deposits indicated their association. We concluded that amyloid components were produced from a local monoclonal proliferation of MALT lymphoma cells.

References