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A Case of Reactive Plasmacytosis Mimicking Multiple Myeloma in A Patient with Primary Sjögren's Syndrome

Primary Sjögren's syndrome (pSS) is a chronic autoimmune disease with well-documented association of lymphoid malignancies during the progress of the disease. Although several types of malignancy and pseudomalignancy have been reported in pSS, low-grade non-Hodgkin's lymphomas are the most frequently observed. Reactive plasmacytosis mimicking myeloma is a very rare condition in association with pSS. We describe a 72-yr-old woman with pSS who presented with hypergammaglobulinemia, and extensive bone marrow and lymph node plasmacytosis, which mimicked multiple myeloma. In this patient, there was an abnormal differentiation of memory B cells to plasma cells in the peripheral blood suggesting underlying pathogenetic mechanism for this condition.

Key Words : *Sjogren's Syndrome; Plasma Cells; Plasmacytosis; B Cell Differentiation*

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INTRODUCTION

In primary Sjögren's syndrome (pSS), there is a well-documented association of lymphoid malignancies during the progress of the disease (1). Low-grade non-Hodgkin's lymphomas of B cell origin are the dominant type observed in association with pSS (2). Reactive plasmacytosis is an extremely rare condition in association with pSS with only one previous case report (3). This report describes a patient with pSS who presented with hypergammaglobulinemia, and extensive bone marrow (BM) and lymph node (LN) plasmacytosis, which mimicked lymphoproliferative malignancy. Also, in this patient, abnormal differentiation of memory B cells to plasma cells was observed in the active phase of the disease, suggesting that abnormal B cell differentiation may play a role in the pathogenesis of this condition.

CASE REPORT

A 72-yr-old Korean woman presented in February 2003 with recent enlargement of inguinal LNs in association with fatigue and weight loss of 2 kg in 3 months. She had a previous history of microscopic hematuria 20 yr ago, and hyperthyroidism 15 yr ago. In February 2001, an iron deficiency anemia refractory to iron supplementation and polyclonal gammopathy was found during the preoperative workup for a cataract operation. In October 2001, she was referred to the rheumatology outpatient clinic for evaluation of autoantibody positivity, and a diagnosis of pSS was made based on ocular and oral sicca symptoms for 30 yr, positive Schirmer test, salivary gland involvement on salivary scintigraphy, and FANA (1:160+, speckled pattern), and rheumatoid factor (26.7 IU/mL) positivity. Anti-SSA/SSB were negative. Salivary gland biopsy was not performed.

Physical examination revealed cachexic woman with pale conjunctiva and multiple inguinal LN enlargement. Laboratory investigations showed a hemoglobin of 7.9 g/dL, white cell count of 6,800/μL, platelet of 399,000/μL, and MCV of 73.3 fL. ESR was 56 mm/hr and C-reactive protein was 13.0 mg/dL. She had a total protein of 10 g/dL with 7.1 g/dL of globulin. β2-microglobulin was elevated to 3,490 ng/dL. Serum electrophoresis demonstrated a polyclonal pattern with increased amount of IgG (4,610 mg/dL) and IgA (681 mg/dL). In the BM aspirate, plasma cells were 18.2% of the nucleated cells. BM biopsy revealed normocellular marrow with multifocal increase of plasma cells that were normal in morphology and maturation (Fig. 1A). LN biopsy revealed extensive infiltration of plasma cells (Fig. 1B). The LN plasma cells were also normal in morphology and maturation, and immunostaining stained equally for both kappa and lambda light chains. Expression of CD27 on $CD19^+$ peripheral blood B cells enables the grouping of B cells into 3 populations; $CD27^-$ naïve B cells, $CD27^+$ memory B cells, and $CD27^{high}$ plasma cells (4). Immunofluorescence staining of the peripheral B cells revealed marked increase of $CD19^+/CD27^{high}$ plasma cells and significant reduction of $CD19^+/CD27^+$ memory B cells (Fig. 2A).

A diagnosis of reactive plasmacytosis in associated with

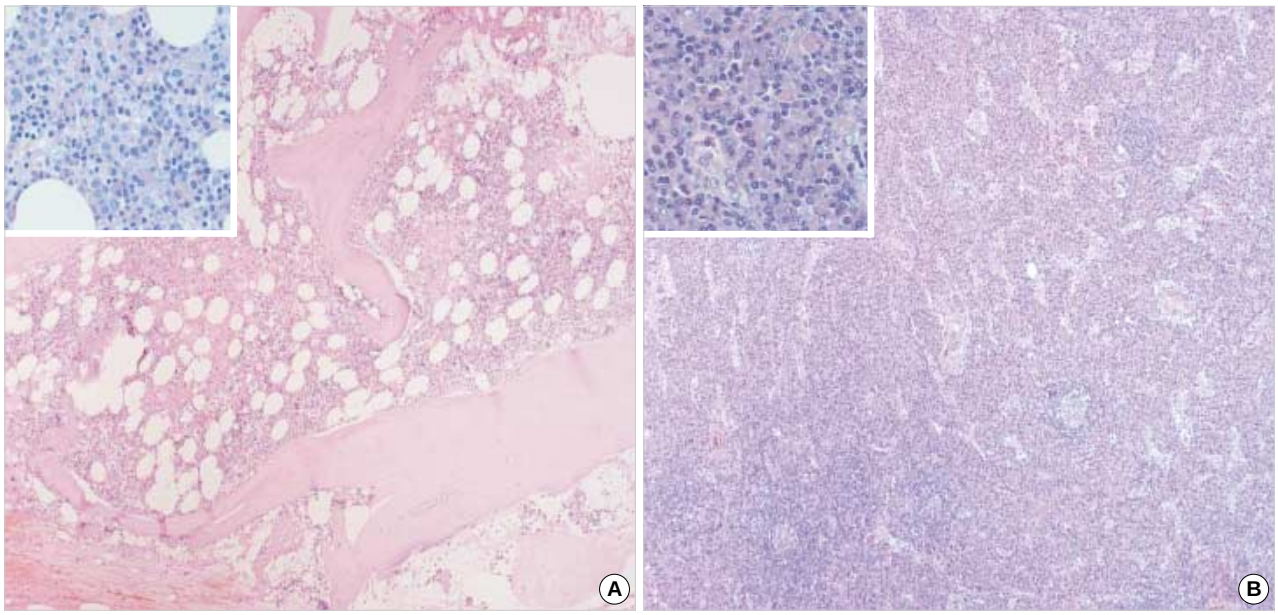

Fig. 1. Bone marrow biopsy (A) and lymph node biopsy (B) specimens. BM biopsy revealed normocellular marrow with multifocal increase of plasma cells. Lymph node biopsy shows profound germinal center reaction with infiltration of plasma cells (H&E stain, ×400).

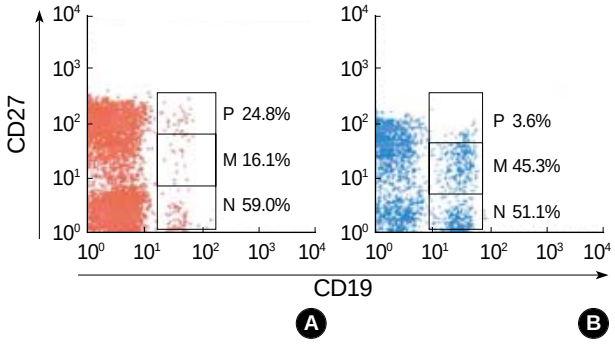

Fig. 2. Immunofluorescence staining of CD27 on $CD19^+$ peripheral blood B cells at baseline (A) and 3 months after treatment (B). At baseline, there was marked increase of $CD19^+/CD27^{high}$ plasma cells and significant reduction of $CD19^+/CD27^+$ memory B cells. After treatment, reduction of mermory B cells with abnormal plasmacytosis was no longer observed. P, plasma cell; M, memory B cell; N, naive B cell.

pSS was made. Immunosuppressive therapy with high-dose glucocorticoid and cyclophosphamide 500 mg IV pulse fortnightly was initiated with concerns for malignant transformation. After completion of 6 cycles of cyclophosphamide pulse therapy, constitutional symptoms improved and lymphadenopathy regressed. Her hemoglobin level improved to 10.9 g/dL and MCV was 84.8 fL. Total protein and globulin decreased to 8.2 g/dL and 4.9 g/dL, respectively. IgG, IgA, β-2 microglobulin also decreased in significant amount with IgG 2,350 mg/dL, IgA of 573 mg/dL, and β2 microglobulin 2,630 ng/mL. Upon follow up immunofluorescence staining of the peripheral B cells, reduction of memory B cells with abnormal plasmacytosis was no longer observed (Fig. 2B). The patient is doing clinically well on methylprednisolone 4 mg/day and azathioprine 100 mg/day without any evidence of lymph node enlargement and malignant transformation up to present.

DISCUSSION

Our patient manifested with severe anemia, enlarged LNs, and high serum β2-microglobulin in the course of pSS that warranted search for malignancy. Although clinical features mimicked multiple myeloma, the biopsies of LN and BM revealed benign, polyclonal plasma cell infiltration, compatible with reactive plasmacytosis. Although there are reports of plasmacytosis at unusual sites such as skin and lung (5, 6), plasma cell infiltration in the BM in association with pSS is extremely rare (3).

This case is unique in that plasma cell infiltration was not only found in the BM, but also in the LN with abnormal expansion of plasma cells in the peripheral blood. Recent studies involving pSS patients have shown that reduction in the circulating memory B cell compartment is associated with an increase in serum IgG levels suggesting plasmacytosis and overactive differentiation of memory B cells to plasma cells (7, 8). Such abnormal immune reaction has been suggested to play an important role in lymphomagenesis in pSS (9). We also observed in this case, an abnormal differentiation of memory B cells to plasma cells in the peripheral blood, which was corrected with immunosuppressive therapy. The factors that might be responsible for directing a patient with pSS to develop lymphoproliferative malignancy are still obs-

cure. Also therapeutic intervention that can possibly modulate lymphomagenesis is unknown. However, accumulation of cases like ours might enable us to answer these questions.

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