

Persistent Polyclonal B Lymphocytosis With Low IgM

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Citation

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Abstract

INTRODUCTION

Persistent polyclonal B lymphocytosis (PPBL) has been described in many patients^(1,2). These patients typically are female smokers with elevated IgM levels. Other conditions have also reported associations with PPBL, including nodular lymphocyte predominance Hodgkin's disease⁽³⁾, and hairy cell leukemia Japanese variant⁽⁴⁾. In this report, a male patient with a history of splenectomy is described. His features included a B lymphocytosis accompanied by low IgM levels. This association has not been previously reported.

CASE REPORT

A 39 year old male presented on 4/16/2002 with a 3 month history of intermittent recurrent abdominal pain and arthralgias. He had recently been treated for a respiratory infection with antibiotics. His abdominal and joint symptoms would typically last 4-5 days. The joint pains often involved the elbow and the abdominal pain was described as being superficial in location. He had a splenectomy at age 21 after a sports related injury, and he had seasonal rhinitis and asthma during the past 12 years. He used albuterol spray when necessary. He admitted to smoking approximately 10 cigarettes a day for many years.

On physical examination, he had a well healed-midline abdominal scar. No lymphadenopathy, or hepatomegaly was observed. Some tenderness of the medial epicondylar areas was also noted. Laboratory examinations revealed a normal rheumatoid factor (<20 IU/mL) and a negative anti-nuclear antibody. The complete blood count revealed an absolute lymphocytosis of 4978/cu mm. The erythrocyte sedimentation rate was 4 mm/h and the C reactive protein level was <5 mg/L. Allergen specific IgE to dust mite and ragweed was found. The total IgE level was 96 IU/mL. He was given fexofenadine orally and budesonide nasal spray

for allergic symptoms.

He was seen again on 4/30/2002 for continuing joint and abdominal pains sometimes accompanied with neck pains. Laboratory testing at that time showed normal AST, ALT, and CK levels. The C4 was normal 24 mg/dL. A Monospot test was negative. The white blood count however elevated at 11,700/cu mm with an absolute lymphocyte count of 5792/cu mm. On 6/11/2002, the patient had peripheral blood flow cytometric analysis. Increased absolute numbers of CD19 cells (2121/cu mm) were observed in the standard lymphocyte gate. The normal number of CD19 cells is 110-660/cu mm. CD8 and CD4 cell absolute numbers were normal. On 7/12/02 laboratory testing showed a normal serum protein electrophoresis pattern, normal levels of IgG and IgA (1260 and 307 mg/dL respectively) but low levels of IgM 34 mg/dL (normal range 46-194 mg/dL). Immunofixation did not reveal a monoclonal band and the kappa/lambda ratio was 2.3. On 7/22/2002 the patient reported improved abdominal pain but continued arthralgia. Rofecoxib was prescribed. At that time the CD19 count was 5617 with a CD4/8 ratio of 4.1. Epstein Barr antibody titers showed a pattern of past infection only. On 11/12/2002 the patient had no current complaints but reported a recent respiratory infection for which he was prescribed an antibiotic. At that time the CD19 count was 2299/cu mm, and the absolute lymphocyte count was 5748/cu mm. Kappa light chain staining was observed in 20% of the lymphocyte gated cells. Lambda light chain staining was observed in 9% of the lymphocyte gated cells. The IgM level at that time was again decreased at 28 mg/dL and the IgA and IgG levels were within normal range at 334 and 1199 mg/dL respectively. A test for Lyme disease by Western blot was negative. On 1/23/2003 the leukocyte count was 9100/cu mm with an absolute lymphocyte count of 4600/cu mm. No Howell-Jolly bodies were seen. Repeat flow cytometric

lymphocyte subset determination on 2/14/2003 showed 38% of gated lymphocytes having CD19 phenotype (normal percentage 6-29%). The physical examination at that time was unremarkable.

DISCUSSION

Persistent lymphocytosis can be due to lymphocyte clonal expansion in lymphoproliferative diseases and is monoclonal in type. However, the etiology of persistent polyclonal B lymphocytosis is often unclear and has been attributed to tobacco smoking and Epstein Barr infection⁽⁵⁾ as reactive or infectious phenomenon. It has also been stated⁽⁶⁾ that rheumatoid arthritis and HIV may be associated with B lymphocytosis, presumably related to inflammation and infection. Several patients with benign PPBL have been shown to have multiple bcl-2 rearrangements⁽⁷⁾, a typical finding of follicular lymphomas. However, the clinical course of patients with PPBL does not usually involve malignant or clonal transformation. The patient described in this report had presumptive polyclonal B lymphocytosis as evidenced by the expression of both light chains in serum and in flow cytometry. PPBL has been invariably associated with elevated immunoglobulin levels, usually IgM⁽¹⁾. The patient herein described had repeated diminished levels of IgM. While this patient had a history of splenectomy, which may be associated with lymphocytosis⁽⁸⁾, the finding of a diminished IgM level would not be expected in the context of polyclonal B lymphocyte expansion. Indeed Durig and colleagues⁽⁹⁾ found that serum IgM levels highly correlated with absolute B lymphocyte counts post splenectomy. Lymphocytosis due to T lymphocytes and natural killer cells have been described in patients with hyposplenism^(2,10,11). And it has been stated that hyposplenism may be associated with B lymphocytosis⁽⁶⁾. In a study of otherwise healthy patients who had undergone post-traumatic splenectomy⁽¹⁰⁾, CD20 B cells were reported to be decreased in the face of increased CD3 cells. This would seem to imply that B lymphocyte elevations are not the predominant leukocyte alteration in splenectomized patients.

The association between immunoglobulin elevations usually described in PPBL suggests that some of these increased B cells differentiate into antibody secreting plasma cells. In the patient described in this report, it is difficult to explain why IgM levels were diminished. Wolf and colleagues⁽¹²⁾ described decreases in CD4+CD45RA+ lymphocytes in post-traumatic splenectomy patients. The T-cell lymphoproliferative responses to neoantigens were diminished in the patients, suggesting a decrease in primary

immune responses in these patients. It is conceivable that a cumulative diminution in on-going immune responses to neo-antigens could result in low IgM levels. Another possibility is that splenosis, which is common after post-traumatic splenectomy, related to the IgM decreases. Cohen and Ferrante⁽¹³⁾ reported low IgM levels in 3 of 8 children who had undergone post-traumatic splenectomy. All three of these patients were documented to have splenosis. In the patient described in this report, no Howell-Jolly bodies were observed, suggesting that splenosis may be present. Transient decreases in IgM levels seen post-splenectomy return to pre-splenectomy levels by 4 years⁽¹⁴⁾. This phenomenon would not explain the low IgM seen in the patient described here in, as the splenectomy was more than a decade prior.

In conclusion, this case appears to be the first patient in which both diminished IgM levels and B lymphocytosis is described. Unlike the typical asymptomatic PPBL cases described in smoking females, the patient described herein had intermittent abdominal, respiratory infections, and joint pains. Future follow up on this patient will hopefully determine if these symptoms relate to yet undiscovered internal pathology related to the PPBL. More information is needed on the natural history of PPBL.

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