Case Report

Lymphoplasmacytic Lymphoma with IgA Hypergammaglobulinemia and Liver Involvement

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Background: *Lymphoplasmacytic lymphoma (LPL) is a low grade lymphoma. Most cases are Waldenstorm macroglobulinemia which has IgM hypergammaglobulinemia. Lymphoplasmacytic lymphoma with IgA hypergammaglobulinemia is less than 5%. Liver involvement was reported in 20%. However this disease has been found to be mostly presented with lymphadenopathy and hypergammaglobulinemia.*
Case Report: *We present a forty-year-old woman with anemia, renal insufficiency and abnormal liver function test. Liver biopsy showed atypical clonal B-cell lymphoproliferation, small cells with prominent plasmacytic differentiation. Serum protein electrophoresis showed monoclonal gammopathy which was IgA. Rituximab, fludarabine and cyclophosphamide were given and resulting in partial response.*
Conclusion: *The presentation of LPL can mimic multiple myeloma (anemia, renal failure and monoclonal gammopathy). Definite histological and immunological technique should be done to confirm the diagnosis.*

Keywords: *Hypergammaglobulinemia, Immunoglobulin A, Liver diseases, Waldenstrom macroglobulinemia*

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Lymphoplasmacytic lymphoma is a neoplasm of small B lymphocytes, plasmacytoid lymphocytes, and plasma cells[1] which usually presents with monoclonal paraprotein, hyperviscosity syndrome, lymphadenopathy and cytopenia. The majority of patients have a monoclonal IgM serum paraprotein which is called Waldenström macroglobulinemia, but IgA paraprotein was reported in less than 5%[2]. Lymphoplasmacytic lymphoma is one of the indolent lymphomas in which tumor commonly involves the bone marrow, lymph nodes and spleen. Liver involvement is not a common site for this entity[3].

In this report, we present a lymphoplasmacytic lymphoma in a middle-age female patient with IgA paraproteinemia and liver involvement (proved by liver biopsy) in which clinical presentation mimics multiple myeloma.

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Case Report

A forty-year-old female Thai patient came to the hospital for check-up. Her physical examination was found to be unremarkable, and a routine blood examination was done. Her hemoglobin was 9.3 mg/dl, Hct 28.3%, MCV 94.3 fL, WBC 5,400/mm^3, N 55.1%, L23.4%, M 9.3%, E 9.2%, B 0.3% and platelet 455,000/mm^3. Her creatinine was 4.7 mg/dL. Liver function test showed abnormality in which the AST was 210 U/L (15-37), ALT was 171 U/L (30-65), ALP was 584 U/L (50-136) and serum globulin was 8.1 g/dL (1.5-3.5). Serum protein electrophoresis was done and showed monoclonal gammopathy. Serum immunoelectrophoresis was IgA, kappa type. Serum IgA level was 19.05 g/L (0.7-4) whereas serum IgM and IgG were within normal limit. Bone marrow aspiration was showed increased lymphoplasmacytoid lymphocytes, accounting for 40% of all nucleated cells in bone marrow and 10% mature plasma cells. Bone marrow biopsy and immunohistochemistry showed hypocellular trilineage marrow and no evidence of malignancy.

Ultrasonography of the whole abdomen showed no intra-abdominal lymphadenopathy, but there was chronic parenchyma lesion of both kidneys. Liver biopsy and complete immunohistochemistry examinations showed atypical clonal B-cell lymphoproliferation, small cells, with prominent plasmacytic differentiation. CD20 was focally positive where as CD5, CD10, Bcl-6, Cyclin D1 and CD23 were negative (Fig. 1). The overall clinical information of this patient is consistent with lymphoplasmacytic lymphoma. Rituximab, combined with fludarabine and cyclophosphamide, was given and the patient showed some response after 2 cycles.

Discussion

Lymphoplasmacytic lymphoma with IgA paraproteinemia was reported by Basu D. and colleagues[4] who described a patient presented with a clinical and hematological picture mimicking Waldenström's macroglobulinemia as in our patient. There is another lymphoplasmacytic lymphoma

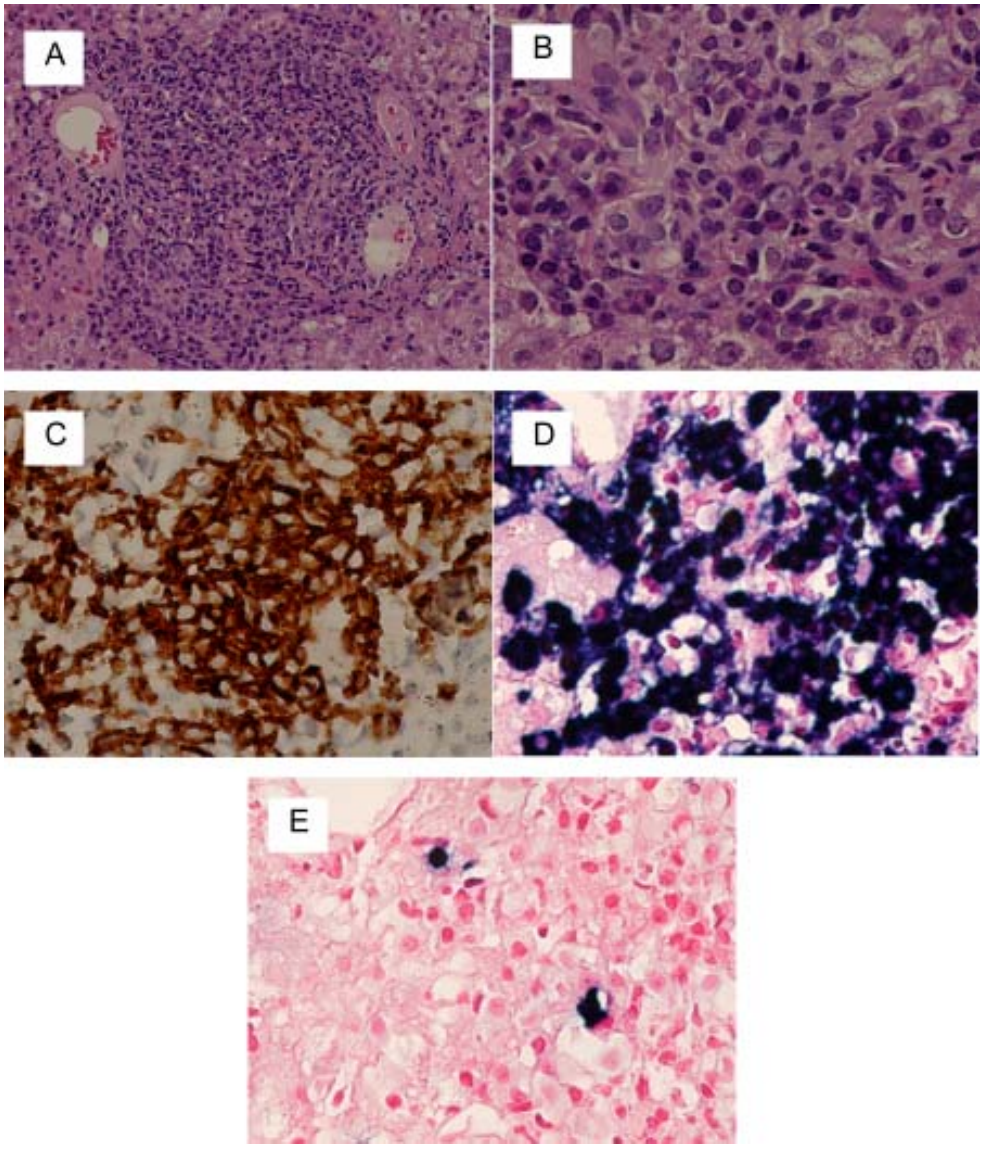

Fig. 1 Liver biopsy showed abnormal aggregation of clonal lymphoid cells. (A and B) Which were positive for CD 20 (C), kappa staining (D) and negative for lambda staining (E)

producing IgA paraproteinemia reported by Alan R. Burg and colleagues[5]. But in their case, the patient was diagnosed as lymphoplasmacytic lymphoma with various autoimmune phenomena and developed the production of three monoclonal proteins (IgM, IgA and IgG). Our patient supported the existence of lymphoplasmacytic lymphoma producing IgA paraproteinemia whose presentation was similar to Waldenström's macroglobulinemia.

Lymphoplasmacytic lymphoma usually associates with tumor involving the bone marrow. Extramedullary involvement can also occur but is infrequently notable. Tumor can infiltrate liver (20%) and spleen (15%) which causes hepatomegaly and spleno-megaly[6]. Another report from Lin P. and colleagues described the autopsy of 44 Waldenström's macroglobulinemia patients in which 40 of them were lymphoplasmacytic lymphoma, and revealed the extramedullary sites of involvement: lymph node 70%, soft tissue 7.8%, spleen 5.9%, skin 3.9%, lung 3.9%, tonsil 2%, colon 2%, liver 2% and gall bladder 2%[7]. By histology and immunohistochemistry technique, our patient proved to have liver involvement which defined her diagnosis.

In this case report, we presented a lymphoplasmacytic lymphoma patient with anemia, renal failure and hypergammaglobulinemia with mimicked multiple myeloma. After thorough investigation and histological examination, lymphoplasmacytic lymphoma was the compatible diagnosis according to WHO classification. This patient had IgA paraproteinemia and also liver involvement which were both uncommon in lymphoplasmacytic lymphoma.

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มะเร็งต่อมน้ำเหลืองชนิด lymphoplasmacytic lymphoma ที่สร้างโปรตีนชนิด IgA และมีการลุกลามที่ตับ

จันทนา ผลประเสริฐ, กานดิษฐ์ ประยงค์รัตน์

ภูมิหลัง: *มะเร็งต่อมน้ำเหลืองชนิด lymphoplasmacytic lymphoma เป็นมะเร็งต่อมน้ำเหลืองชนิดโตช้า ส่วนใหญ่เป็น Waldenstorm macroglobulinemia ซึ่งมีการผลิตโปรตีนชนิด IgM มะเร็งต่อมน้ำเหลืองชนิด lymphoplasmacytic lymphoma ที่ผลิตโปรตีนชนิด IgA พบได้น้อยกว่า 5% และการที่พบมะเร็งต่อมน้ำเหลืองลุกลามที่ตับ 20% อย่างไรก็ตามส่วนใหญ่โรคนี้มักจะพบว่าผู้ป่วยมาด้วยอาการมีต่อมเหลืองโตและมีระดับของโปรตีนสูง*

รายงานผู้ป่วย: *ผู้เขียนนำเสนอผู้ป่วยหญิงอายุ 40 ปีมาตรวจด้วยพบว่าซีด, ไตวายและมีการทำงานของตับผิดปกติ ภายหลังจากที่ทำการตัดชิ้นเนื้อที่ตับ ผลการอ่านทางพยาธิวิทยาพบว่า มีลักษณะของเม็ดเลือดขาวผิดปกติเข้าได้กับชนิด lymphoplasmacytic lymphoma การตรวจ protein electrophoresis พบว่ามีโคลนของโปรตีนที่ผิดปกติ (Monoclonal gammopathy) ชนิด IgA ผู้ป่วยได้รับยา rituximab, fludarabine และ cyclophosphamide ซึ่งพบว่าผู้ป่วยมีการตอบสนองต่อการรักษา*

สรุป: *ผู้ป่วยมะเร็งต่อมน้ำเหลืองชนิด lymphoplasmacytic lymphoma สามารถมาพบแพทย์ด้วยอาการที่คล้ายโรคมะเร็งไขกระดูกได้ (multiple myeloma) ซึ่งมีอาการซีด, ไตวาย และตรวจพบระดับของโปรตีนที่ผิดปกติชนิดเดียว ซึ่งผู้ป่วยควรได้รับการตรวจทางพยาธิวิทยาอย่างละเอียดเพื่อการวินิจฉัยที่แน่ชัดและนำไปสู่การรักษาที่เหมาะสมต่อไป*