Case Report

Retinal detachment as the inaugural manifestation in Waldenstrom's macroglobulinemia

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ABSTRACT

Waldenstrom's macroglobulinemia (WM) is a rare disorder and forms 1–2% of hematological malignancies. Rarely retinal detachment precedes the diagnosis of WM. In this case report, we present 65-year-old man with retinal detachment as the inaugural manifestation in WM. Clinical manifestations in WM are related to direct tumor infiltration, circulating immunoglobulin M (IgM) and deposition into tissues, amyloidogenic properties and autoantibody activity of IgM. Diagnosis is difficult, when a rare disease manifests differently, as in our case. Delay in diagnosis can be prevented by heightened awareness of this rare disease.

Key words: Immunoglobulin M, lympho plasmacytic lymphoma, retinal detachment, Waldenstrom's macrogloublinemia

INTRODUCTION

Waldenstrom's macroglobulinemia (WM) is a malignant lymphoproliferative disorder with monoclonal pentameric immunoglobulin M (IgM) and is a rare disorder, forms 1–2% of hematological malignancies.[1] In 1944 Jan Gorta Waldenstrom first described 2 patients with oronasal bleeding, lymphadenopathy, anemia and thrombocytopenia, high serum viscoscity level, normal bone radiographs and bone marrow demonstrating lymphoid cells.[2] Hyperviscosity occurs in up to 30% of patients. The paraprotein may also have autoantibody or cryogloubulin activity, resulting in autoimmune phenomena or cryoglobulinemia seen in 20% of patients with WM. Neuropathies occur in a minority of patients and may result from reactivity of the IgM paraprotein with myelin sheath antigens, cryogloublinemia or a paraprotein deposition. Deposits of IgM may occur in the skin or the gastrointestinal tract, where they may cause diarrhea. Coagulopathies may be caused by IgM binding to clotting factors, platelets and fibrin.[3] Rarely retinal detachment precedes the diagnosis of WM. In this case report, we present 65-year-old man with retinal detachment as the inaugural manifestation in WM. Delay in diagnosis can be prevented by heightened awareness of this rare disease.

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CASE REPORT

A 65-year-old male presented to a general practitioner for dimness of vision in the right eye and a B scan of the eyes showed incomplete retinal detachment in the right eye and internal echoes in the right vitreous, which was interpreted as vitreous hemorrhage [Figure 1]. Funduscopic examination of the right eye at an ophthalmic center revealed vitreous hemorrhage and rhegmatogenous retinal detachment for which he underwent vitrectomy, belt buckling, endolaser and silicone injection. Furthermore, he gave a history of easy fatigability for the last 6 months for which, was referred to an hematologist. He was a known diabetic for which he was on oral antidiabetics for the past 11 years and was hypothyroid for which was on thyroxine for the last 8 months. Clinically significant anemia was detected, and a bone marrow aspiration was done. This showed an infiltrate of lymphoid cells for which he was referred to our center, which is a tertiary care oncology center. The pale patient with a congested right eye did not show any other significant findings.

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Computed tomography scan of the abdomen detected a mild hepatosplenomegaly. The hemogram showed a hemoglobin of 82 g/L (N-150 ± 20 g/L), total white cell count of 3.1 × 10^9/L (N-7 ± 3 × 10^9/L), with a differential count of 38% lymphocytes and 62% neutrophils and platelet count was 186 × 10^9/L (N-150–400 × 10^9/L). The peripheral smear revealed rouleaux formation. The patient was investigated for a possible myeloma. Skeletal survey including plain X-ray of the skull, pelvis, vertebrae, ribs, clavicles and scapulae showed no lytic lesions.

Serum protein electrophoresis revealed an "M" spike in the gamma region. An elevated IgM level of 64.14 g/L (N 4–23 g/L) was detected on heavy chain assay. Beta 2 microglobulin level was 6.52 mg/L (N-0.7–2 mg/L). Serum levels of blood urea nitrogen, creatinine, blood glucose, calcium, and liver function tests were all within normal limits. Serology for HIV and hepatitis B were negative. Bone marrow biopsy showed a hypercellular marrow with an extensive infiltrate of lymphocytes, lymphoplasmacytoid cells and mature plasma cells [Figures 2 and 3]. A morphological diagnosis of lymphoplasmacytic lymphoma was offered. Conventional cytogenetics showed a normal karyotype. The marrow was sent for fluorescence *in situ* hybridization at the time of aspiration to look for the following translocations t (11:14), t (4:14), t (4:16), and for del 17p13.1 and del 13q14.3. None of these were found. Immunohistochemistry on the bone marrow biopsy was positive for CD20 and CD79a in the lymphocytes, plasma cells showed positivity for CD138 and lambda restriction [Figure 4]. CD5, CD23, CD10 and CD3 were negative. Correlating the clinical features, the presence of an IgM monoclonal gammopathy, bone marrow morphology and immunohistochemistry, a diagnosis of WM was made. Combination chemotherapy with vincristine, endoxon and wysolone was instituted, to which he responded well.

DISCUSSION

Waldenstrom's macroglobulinemia is a rare disorder and forms 1–2% of hematological malignancies.[1] Second International workshop on WM, defined it as lymphoplasmacytic lymphoma with bone marrow involvement and an IgM monoclonal gammopathy of any concentration and the same has been adopted by the World Health Organisation.[2,3] Lymphoplasmacytic lymphoma shows infiltration of bone marrow by small B lymphocytes, plasmacytoid lymphocytes and plasma cells, and sometimes the lymph nodes and spleen are also involved.[3] Clinical manifestations in WM are related to direct tumor infiltration, circulating IgM, IgM deposition into tissues, amyloidogenic properties, and autoantibody activity of IgM.[4] Serum hyperviscosity is observed in <15% of patients at diagnosis and symptoms of hyperviscosity usually appear when serum IgM level is 30 g/L.[1,5] In our patient, the predominant

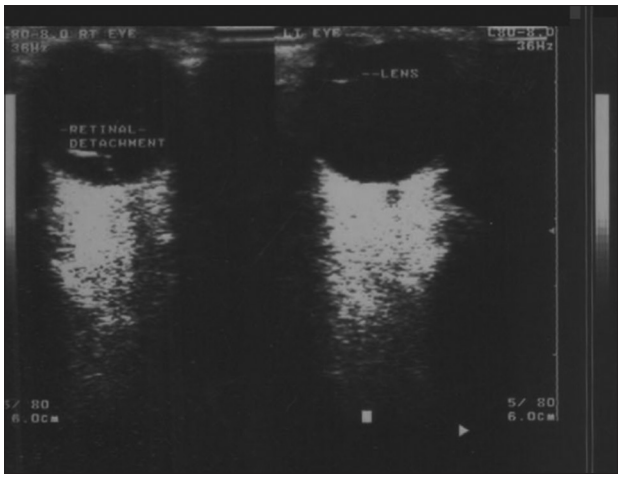

Figure 1: Internal echoes seen in the right vitreous was interpreted as vitreous hemorrhage

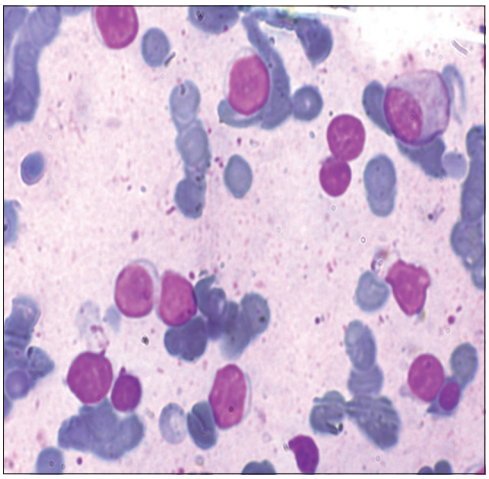

Figure 2: Bone marrow aspiration showing hypercellular marrow with an extensive infiltrate of lymphocytes, lymphoplasmacytoid cells and mature plasma cells

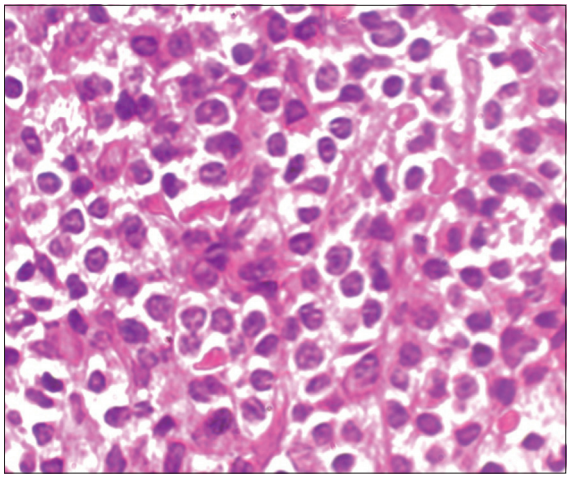

Figure 3: Bone marrow biopsy showing hypercellular marrow with an extensive infiltrate of lymphocytes, lymphoplasmacytoid cells and mature plasma cells

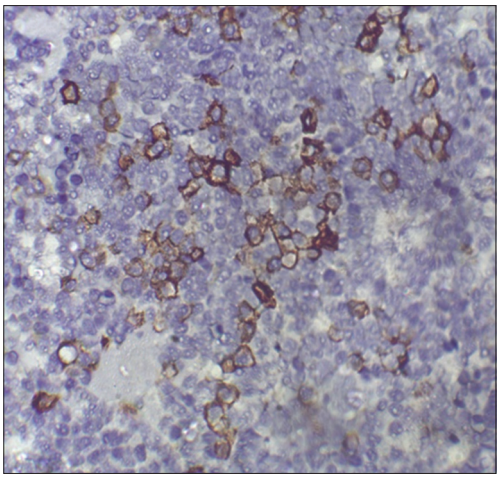

Figure 4: Plasma cells showed positivity for CD138

clinical manifestation was visual disturbances due to retinal detachment and the presence of the monoclonal IgM was detected after the surgery for retinal detachment. Patients with hypervicosity syndrome have constitutional symptoms, skin and mucosal bleeding, cardiovascular, neurologic disorders and ocular symptoms such as retinopathy with visual disturbances, as in our case.[1,4,5] The reasons for hyperviscosity are increased protein content and large size and abnormal shape of the IgM molecules.[1,5] Funduscopic examination may reveal retinal vein engorgement and hemorrhage[4] and with more marked hyperviscosity sausage like segmentation of distended retinal veins and retinal hemorrhage develops.[4,6] Our patient showed the flame shamed hemorrhages in left fundus and B scan showed vitreous hemorrhage in the right eye. The unusually shaped high molecular weight IgM, increases osmotic pressure in the vasculature and contraction of fibrin in extravasated plasma causes tear in the retina, further leading to accumulation of subretinal fluid with high concentration of IgM, this further contributes to retinal detachment.[7] Plasmapheresis is an effective method for immediately reducing the circulating IgM and systemic cytoreductive therapy is indicated for the underlying lymphoma in order to inhibit the IgM production.[4,5] As part of the fourth international workshop on WM a consensus panel updated its recommendations on both first line and salvage therapy[8] with first line combinations such as rituximab with nucleoside analogs with or without alkylating agents or with cyclophosphamide based therapies. In conclusion, we describe a 65-year-old man who was surgically treated for retinal detachment, but there was an inordinate delay of 2 months in the diagnosis of the underlying malignancy, WM. It is obvious that such a delay in treatment puts the other eye at risk as well as the risk of coagulopathy, neurological and cardiovascular complications. In our patient, retinal detachment preceded the diagnosis of WM. Such delays in diagnosis can be prevented by heightened awareness of this rare malignancy.

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