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Waldenstrom macroglobulinemia presenting as plasma cell leukemia associated with hyperviscosity syndrome

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Abstract

Objective: Waldenstrom macroglobulinemia (WM) is a rare indolent neoplastic disease characterized by a wide range of clinical presentations related to the direct tumor infiltration. The disease is characterized by monoclonal immunoglobulin M protein in the serum and infiltration of bone marrow with lymphoplasmacytic cells.

Case report: We, herein, present an unusual case of WM. A 77-year-old woman admitted to the hospital with fatigue, anorexia, and fever. She had white blood cell elevation and splenomegaly. The patient had no peripheral lymphadenopathy. A large number of plasmablast-like cells were seen in the peripheral blood smear. Laboratory studies revealed a white blood cell count of 54.8 × 103/µl, hemoglobin level of 8.2 g/dl and platelet count was 120 × 103/µl. The diagnosis of WM was established after immunohistochemical analysis of the patient's bone marrow that revealed the presence of a lymphoid/lymphoplasmacytoid-like bone marrow infiltrate along with an elevated serum IgM level. The patient responded to the chemotherapy both clinically and serologically. This case is unusual since numerous plasmablast like cells were seen in peripheral blood smear like plasma cell leukemia at the admission to the hospital.

Conclusion: This is the case report of a patient with Waldenstrom macroglobulinemia presenting like plasma cell leukemia in the first admission adding to the spectrum of clinical presentations seen in this disease. This adds to the wide variety of clinical presentations of Waldenstrom macroglobulinemia.

Keywords: Monoclonal gammopathy, Plasma cell leukemia, waldenstrom Waldenstrom macroglobulinemia

Introduction

Waldenstrom macroglobulinemia (WM) is an unusual lymphoplasmacytic lymphoma characterized by an extensive range of clinical presentations related to direct tumor infiltration. The disease is characterized by monoclonal immunoglobulin M protein in the serum and infiltration of bone marrow with lymphoplasmacytic cells (1).

Most commonly it presents with cytopenias, hepatosplenomegaly, lymphadenopathy, constitutional symptoms and hyperviscosity syndrome. The highest incidence of WM occurs among older individuals, with a median age at diagnosis in the 60s (2). The etiology of WM is unknown. No obvious causative or predisposing factor has been identified. Both somatic mutations and chromosomal abnormalities have been identified in the malignant B cells of WM.

A recurrent mutation of the MYD88 gene (MYD88 L265P) is present in the most majority of patients with WM (3, 4). There is no standard therapy for the treatment of WM.

While various drugs and combinations have demonstrated clinical benefit in prospective trials, these have not been compared directly in randomized trials. For patients who are symptomatic therapeutic strategies for WM should be based on individual patient and disease characteristics, including the age, suitability as a candidate for autologous stem cell transplantation, hyperviscosity, and comorbidities.

Case report

A 77-year-old woman admitted to the hospital with the symptoms of fatigue, anorexia, fever, and blurred vision. She could not walk for 2 weeks because of weakness and neuropathy. She had white blood cell elevation and splenomegaly (20 cm). A large number of plasmablast-like cells were seen in the peripheral blood smear (figure 1). Laboratory studies revealed a white blood cell count of 54.8 × 103 /µl, hemoglobin level of 8.2 g/dl and platelet count was 120 × 103/µl. Serum creatinine was 0.9 mg/dl and calcium was 9 mg/dl.

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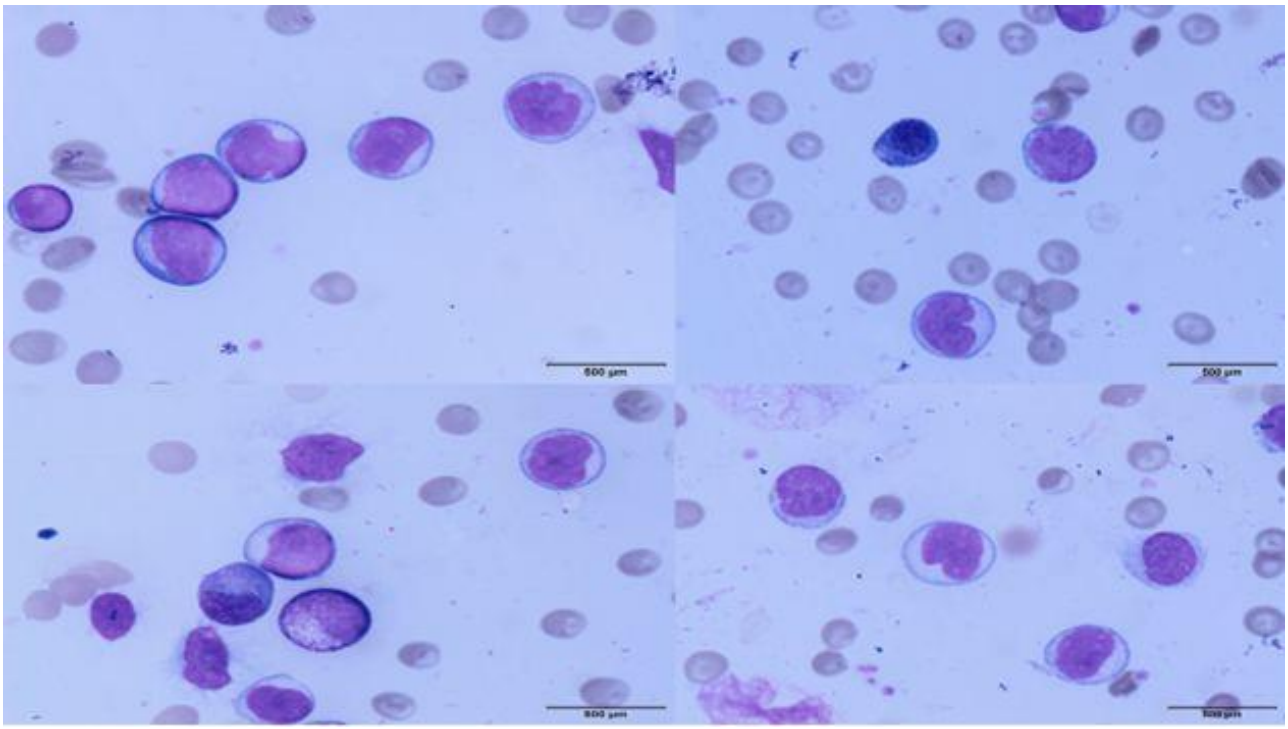

Figure 1. Peripheral blood smear was suggestive of normocytic anemia and numerous plasmablasts like cells (when evaluating peripheral smear at the time of admission hospital)

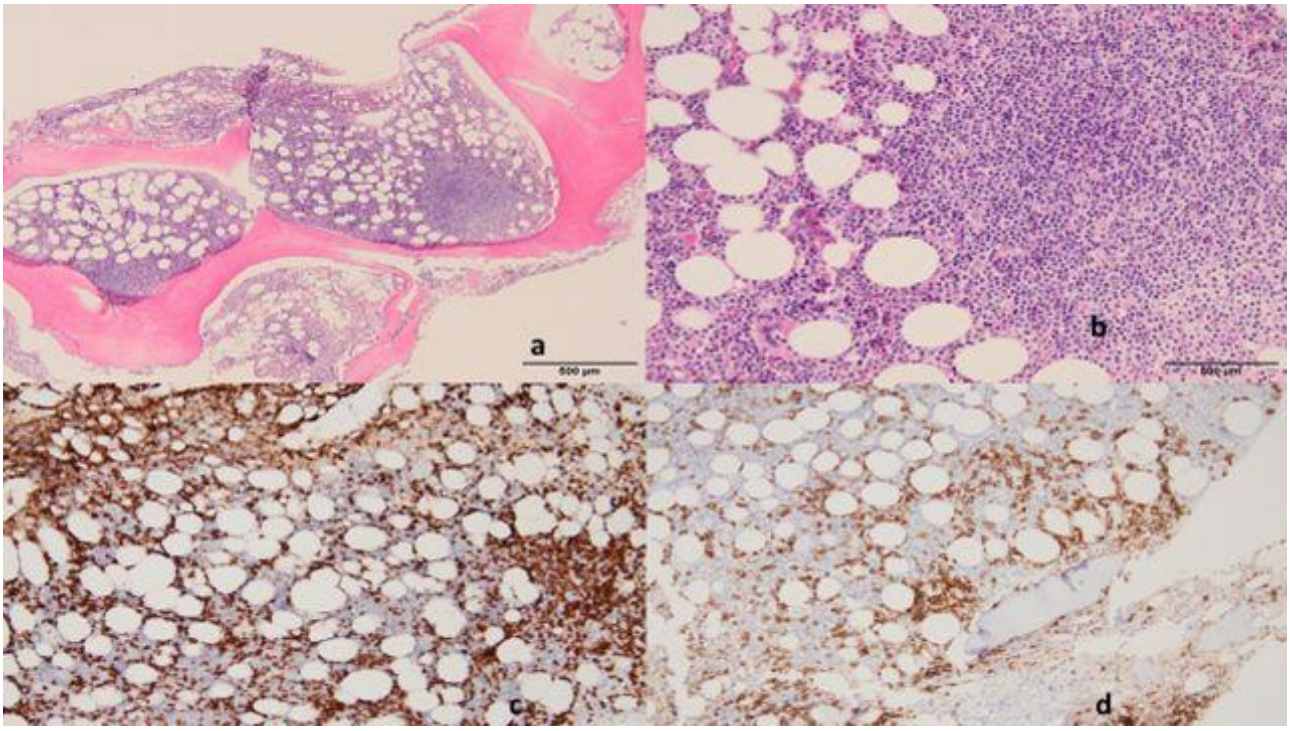

Figure 2. Marrow was infiltrated by lymphoplasmacytoid cells on bone marrow biopsy. Her bone marrow biopsy showed a massive proliferation of small lymphocytes (of all nucleated cells), admixed with plasmacytoid lymphocytes and plasma cells. (Figure 2a and 2b) Small lymphocytes were highlighted with CD20 (Figure 2c), and plasma cells with CD138 stains (Figure 2d.)

The serum protein electrophoresis revealed a homogeneous band in the gamma globulin area, which on immunoelectrohoretic studies corresponding to an IgM-kappa immunoglobulin. Plasma immunoglobulin concentrations: IgG 457 mg/dl (normal range:700-1600), IgA 66 mg/dl (normal range:70-450), IgM 15000 mg/dl (normal range:40-230).

The neoplastic lymphoplasmacytoid cells express CD19, CD20, CD22 and FMC7 in the flow cytometry. CD5, CD10, CD11c, CD56 and CD23 were negative. Chromosomal analysis showed a karyotype of 47, XX+12(40)/46, XX (10).

Axonal polyneuropathic involvement was found in sensory and motor fibers in EMG to assess neuropathy. Papilla edema was observed on ophthalmoscopic examination. Due to hyperviscosity syndrome of patients plasma exchange was performed. Bone marrow examination showed diffuse infiltration by small lymphoid cells. These cells were identified as plasma cells or lymphoplasmacytoid cells.

The diagnosis of WM was established after immunohistochemical analysis of the patient's bone marrow that revealed the presence of a lymphoid/lymphoplasmacytoid like bone marrow infiltrate along with an elevated serum IgM level. In the patient's follow-up rituximab, bortezomib and dexamethasone were administered by 3 courses. A cycle of therapy consisted of bortezomib 1.3 mg/m2 on days 1, 4, 8, 11 subcutanous; dexamethasone 40 mg on days 1, 4, 8, and 11 peroral; and rituximab 375 mg/m2 on day 1 intravenously (5).

The patient responded both clinically and serologically to the chemotherapy. Total IgM in the serum decreased from11500 mg/dl to 5210 mg/dl. Her white blood cell was decreased 54.8 × 103/µl to 5.8 × 103/µl. With the proper therapy she could walk, her neuropathy was decreased. The patient's vision improved and papilla edema disappeared on ophthalmoscopic examination. The patient received 6 courses of chemotherapy.

Discussion

Dao et al. presented four cases of sarcomatous or leukemic types of WM. They are characterized by tumoral and compressive localizations of lymph node or spleen, or by a hyper-leukocytosis with many circulating abnormal cells. These cells are different from the lympho-plasma cells regularly observed in WM, and can be assimilated to malignant immunoblasts (6). In this case, the cells seen in peripheral smear were different lympho-plasma cells. A large number of plasmablast-like cells were seen in peripheral smear. The reported case here described WM presenting with hyperleukocytosis and its response to chemotherapy. This case was presented as plasma cell leukemia at the time of admission to the hospital. Because a large number of plasmablast-like cells were seen in the peripheral blood smear.

The diagnosis of WM was made based on the presence of inter- trabecular bone marrow infiltration by atypical lymphocytes showing plasma cell and plasmacytoid differentiation along with elevated serum IgM. With chemotherapy, the white cell was decreased from 54.8 × 103 /µl to 5.8 × 103 /µl and patient's complaints regressed.

Conclusion

This is the case report of a patient with Waldenstrom macroglobulinemia presenting like plasma cell leukemia in the first admission adding to the spectrum of clinical presentations seen in this disease. This adds to the wide variety of clinical presentations of Waldenstrom macroglobulinemia.

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Ethical issues: All Authors declare, Originality and ethical approval of research. Responsibilities of research, responsibilities against local ethics commission are under the Authors responsibilities.

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