

Case report

Waldenstroms Macroglobulinemia- Diagnostic difficulties- a rare case report

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Abstract:

Waldenstrom's macroglobulinemia(WM) is a B-cell neoplasm characterized by infiltration of the bone marrow by a lymphoplasmacytic infiltrate and an IgM monoclonal gammopathy. We report a rare case of a 72 year-old male who presented with fever, shortness of breath for one month. Examination revealed cervical and axillary lymphadenopathy with mild hepatomegaly. On evaluation, peripheral smear show significant rouleaux formation & bone marrow aspiration showed lymphoplasmacytic infiltration. Flow cytometry on bone marrow aspirate suggestive of B cell neoplasm and serum protein electrophoresis & Immunofixation study confirms diagnosis of Waldenstroms macroglobulinemia. We report this case to emphasize diagnostic difficulties in diagnosis of Waldenstroms macroglobulinemia and application of flow cytometry and immunofixation study for further confirmation and treatment.

Keywords: Waldenstroms Macroglobulinemia; PS/BM morphology; Flow cytometry; Immunofixation study.

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Introduction:

Waldenstrom's macroglobulinemia (WM) is a pleomorphic lymphoproliferative disorder characterized by production of a monoclonal immunoglobulin (IgM) protein and a lymphoplasmacytic infiltrate in the bone marrow. WM was named after the Swedish oncologist Jan G. Waldenstrom in 1944¹.

The pathologic designation of Waldenstroms macroglobulinemia is lymphoplasmacytic lymphoma because of its morphologic and immunophenotypic features. Clinically, symptoms can be attributed either to tissue infiltration with malignant B cells or IgM dependent changes in serum (hyperviscosity syndrome) and /or various tissue sites (immunoglobulin deposition disease, autoimmunity)².

The diagnosis of Waldenstroms macroglobulinemia rest on the identification and quantitation of M protein by immunoelectrophoresis and bone marrow flow cytometry. In this case report, initially there is marked overlap in clinical features, hematological

finding and immunologic profile with plasma cell dyscrasia.

Case Report:

A 72-year-old man presented with shortness of breath and fatigue for 25 days. Fever on and off for three days. On general examination patient was pallor with fever 100.7 F, pulse rate was 98 /min, respiratory rate 20 /min. Systemic examination reveal hepatomegaly. Right cervical and right deep axillary lymph node was palpable.

At the initial examination, laboratory results were as follows: hemoglobin 8.0g/dl (12–15 g/dl); white blood cells 4700/cumm (4000–11000/cumm); platelets, 1.8 lakhs/cumm (1.5-4.5laks/cumm); Peripheral blood leishman stained smear show normocytic normochromic RBCs with significant rouleaux formation (Fig 1) and erythrocyte sedimentation rate (ESR) 150mm/h (10–20 mm/h). Coagulation study were normal. Biochemical examination revealed Total serum protein 13.8 (6.3-8.5gms/dl); albumin 3.8 (3.5-5.1gms/dl); 10.4 globulin (2.3-3.5gms/dl); A/G ratio reversal, Total bilirubin 0.3 (0.2-1.3mg/

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dl), alkaline phosphatase 97 (38-126U/L), SGOT 32(14-60U/L) & SGPT 60(9-69U/L) were normal. Electrolytes , sodium 138(137-145mmol/L), Potassium 4.0(4.0to 5.1 mmol/L) & Chlorides 102 (98-107mmol/L) , Random plasma glucose 122mg/dl, serum creatinine 1.8 mg/dl (0.8-1.5mg/dl), Blood urea 22 mg/dl (19-43mg/dl) were normal. Serum calcium elevated 11.8(8.4-10.2 mg/dl) ,elevated level uric acid 11.1 (2.5-6.2 mg/dl) Serum LDH (lactate dehydrogenase)394 U/L . Urine examination show mild proteinuria. Bence-jones protein was negative.

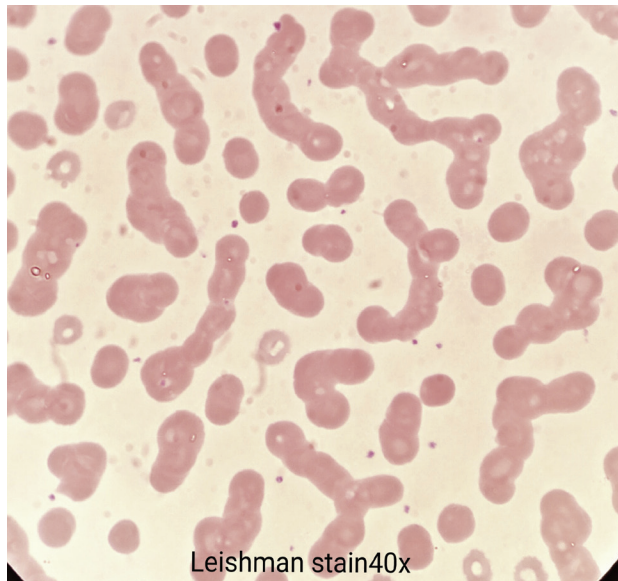


Figure:1: RBCs show significant rouleaux formation (blue arrow).

Chest X- ray show normal study. Ultrasound abdomen reveal Hepatomegaly with altered renal parenchymal echotexture.

Fine needle aspiration cytology from right axillary lymph node reveal monomorphic small to intermediate size lymphoid cells with in sheets with round nuclei with clumped chromatin, cytoplasm is scanty. Few plasmacytoid cells seen (Fig 2)

Bone marrow aspirate flow cytometry immunophenotyping for these lymphocytes positive for CD20, HLA-DR, lambda (strong) and weak positivity for CD23, CD38 and FMC7. These lymphoid cells negative for kappa , CD5, CD10, CD34, CD103 and ZAP 70. Overall suggestive of B cell neoplastic population.

Serum protein electrophoresis performed show presence of M band. Serum immunofixation positive for Ig M band and marked increased in lambda light chain & Beta 2 microglobulin (Table 1)

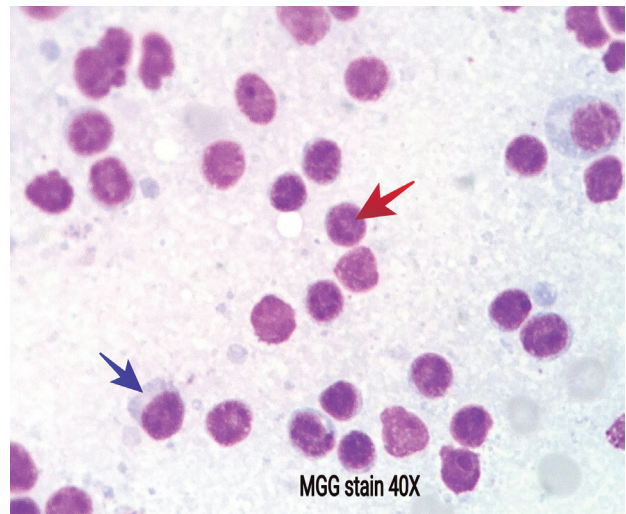


Figure:2 FNAC Right axillary lymph node cytospin show monomorphic cells (red arrow) plasmacytoid cells (blue arrow)

Bone marrow aspiration performed and bone marrow aspirate sample processed for flow cytometry. Bone marrow aspirate cytospins show lympho-plasmacytosis with few large atypical plasmacytoid lymphocytes.

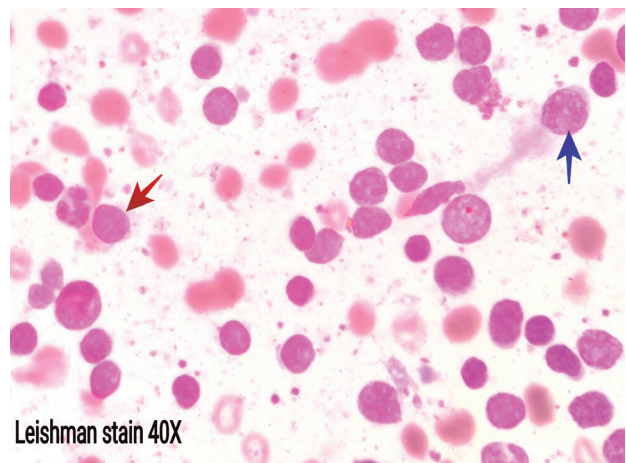


Figure :3: Bone marrow aspirate with lymphocytic infiltrate (red arrow) with few plasmacytoid cells (blue arrow)

Based on the history, the blood film and bone marrow findings, serum protein electrophoresis, flow cytometry, and other investigations, Final diagnosis of WM made and treated.

Discussion:

Waldenstrom's macroglobulinemia defined as a mature B-cell lymphoid neoplasm composed of small B lymphocytes, plasmacytoid lymphocytes, and plasma cells, usually involving bone marrow and sometimes lymph nodes. It is a diagnosis of exclusion and when associated with IgM monoclonal gammopathy, it is termed as WM. The overall incidence of WM is approximately five cases per

Table : Serum immunofixation

Test Report Status	Results	Biological Reference Interval
MYELOMA BAND	DETECTED	NOT DETECTED
IGG BAND	NOT DETECTED	NOT DETECTED
IGM BAND	DETECTED	NOT DETECTED
IGA BAND	NOT DETECTED	NOT DETECTED
KAPPA BAND	NOT DETECTED	NOT DETECTED
LAMBDA BAND	DETECTED	NOT DETECTED
TOTAL IGA	0.87	0.52 - 4.68 g/L
TOTAL IGG	5.5	6.5 - 16.4 g/L
TOTAL IGM	94	0.39 - 3.38 g/L
SERUM LIGHT CHAINS (KAPPA & LAMBDA)		
KAPPA LIGHT CHAIN	9.02	.30 - 19.40 mg/L
LAMBDA LIGHT CHAIN	951	5.71 - 26.30 mg/L
KAPPA LAMBDA RATIO	0.01	0.26 - 1.65
B2-MICROGLOBULIN	6371	609.0 - 2366.0 ng/mL

Based on the history, the blood film and bone marrow findings, serum proteinelectrophoresis, flow cytometry, and other investigations, Final diagnosis of WM made and treated.

one million persons per year. It accounts for ~1–2% of haematologic malignancies. The median age at diagnosis varies between 63 and 68 years, and has a preponderance for men³.

The etiology is unclear, and no specific environmental or occupational exposure including smoking has been linked to this entity. Onset is insidious and nonspecific. Weakness, anorexia and weight loss are the most common symptoms. The clonal proliferation in the bone marrow leading to anemia and the paraproteinemia is responsible for the development of the hyperviscosity syndrome, difficulty in making peripheral smear and gives bluish hue in microscopic background. The degree of rouleaux depend on level of M protein. WM develop hepatosplenomegaly and lymphadenopathy during the course of their disease⁴. The laboratory diagnosis of Waldenström macroglobulinemia is contingent on demonstrating a significant monoclonal IgM spike and identifying malignant cells in bone marrow aspirate, flow cytometry or bone marrow biopsy immunohistochemistry. Both manifestations in this case could make the diagnosis. However, differential diagnoses includes chronic lymphocytic leukemia, splenic marginal zone lymphoma (SMZL), Non-

Hodgkins lymphoma, monoclonal gammopathies of uncertain origin, and also Multiple Myeloma⁵.

The typical immunophenotype of WM consists of expression of pan B-cell surface markers (CD19, CD20, CD22), cytoplasmic Igs, CD38, and CD79a; CD10 and CD23 are mostly absent, and CD5 is expressed in 5% to 20% of cases [6]. immunoelectrophoresis included in diagnostic work up⁶.

The WM is an incurable disease but may have a longer median age of survival if diagnose early. Treatment recommendations based on individual patient and disease characteristics. Combinations of bortezomib/dexamethasone or provide durable responses and are indicated for most patients. Other rituximab with cyclophosphamide/dexamethasone/bendamustine⁷. Our patient responded very well with Combinations of bortezomib/dexamethasone. Rituximab could not be used in our patient as he had financial constraints. It is mandatory to carry out plasmapheresis before starting chemotherapy for those patients who present with symptoms of hyperviscosity. In young patients with chemosensitive disease and in newly diagnosed patients with very-high-risk features, autologous stem cell transplantation may be considered.

Conclusion:

This case report concluded that patient with Waldenström macroglobulinemia present as overlapping features of plasma cell dyscrasia and other common lymphoproliferative disorder which create diagnostic difficulties.. However, Through clinical examination, haemogram with peripheral blood smear morphology, bone marrow morphology immunophenotyping and immunoelectrophoresis studies are necessary and required for the correct diagnosis.

Ethical clearance: this case report was ethically approved.

Declaration of interest

The authors declare that they have no significant competing financial, professional or personal interests that might have influenced the performance or presentation of the work described in this manuscript.

Author's contribution:

Data gathering and idea owner of this study: Majed Momin, Anamika Aluri

Study design: Majed Momin, Anamika Aluri

Data gathering: Majed Momin, Anamika Aluri

Writing and submitting manuscript: Majed Momin, Anamika Aluri

Editing and approval of final draft: Majed Momin, Anamika Aluri

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