

Waldenstroms Macroglobulinemia

P Baburaj^a, Edwin J George^a, Harikrishnan BL^a

a. Department of Medicine, Jubilee Mission Medical College & Research Institute, East Fort, Thrissur, Kerala*

ABSTRACT

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The authors report the case of a COPD patient who presented in OPD with repeated episodes of headache, transient blurring of vision and numbness of lower limbs. O/E he had pallor, hepatosplenomegaly and features in favour of CCF. Bone marrow study revealed lymphocytic plasma cells suggestive of Waldenstrom's Macroglobulinemia. The cytological features, clinical findings, hyperviscosity and treatment strategies are discussed here.

Keywords: Hyperviscosity, Waldenstroms Macroglobulinemia, Lymphoplasmacytoid lymphoma

*See End Note for complete author details

INTRODUCTION

Approximately 2% of the lymphomas are Waldenstroms Macroglobulinemia. It is characterized by an uncontrolled clonal proliferation of terminally differentiated B lymphocytes. The underlying etiology is not yet known but a number of risk factors have been identified. WM was first described by Jan G. Waldenstrom (1906–1996) in 1944 in two patients with bleeding from the nose and mouth, anemia with hypofibrinogenemia, swollen lymph nodes, neoplastic plasma cells in bone marrow and increased viscosity of the blood due to increased levels of heavy proteins called macroglobulins.

For a time, WM was considered to be related to multiple myeloma due to the presence of monoclonal gammopathy and infiltration of the bone marrow and other organs by plasmacytoid lymphocytes. The new WHO classification, however, places WM under the category of lymphoplasmacytic lymphomas, itself a subcategory of the indolent (low-grade) non-Hodgkin lymphomas

CASE REPORT

Noorudheen, 64 year old manual labourer from Palakkad, who is a diagnosed case of COPD presented to us with gradually progressive dyspnoea on exertion and non-productive cough. He also experienced repeated attacks of headache and occasional transient blurring of vision. No history of chest pain, symptoms to suggest PND.

General examination showed moderately built and nourished body, pallor, no evidence of icterus, cyanosis, clubbing, pedal edema and lymphadenopathy. He was having moderate breathlessness in sitting position. His PR was 78/?, BP was 138/90. No evidence of thyromegaly or bone tenderness was there. Systemic examination revealed elevated JVP, cardiomegaly and S3 gallop rhythm. B/L basal crackles were heard. He had moderate tender hepatomegaly. Neurological examination neither showed fundus changes or focal neurological deficits.

Investigating him, we found (Table 1).

Table 1. Biochemical values

• Hb-6.7	• AVG Ratio-0.2
• ESR-164	• SGOT-19
• Platelets-50000	• SGPT-39
• Serum Protein -11.8	• Serum Bilirubin (total) -1.0
• Albumin-2.0	• Direct Bilirubin -0.6
• Globulin-9.8	
• S.Urea- 37	BT - 3MT CT- 12MT
• Creatinine- 1.7	Urine Bence Jones Proteins -VE
• S.Iron- 94	

- Xray skeletal survey revealed no osteolytic lesions.
- USG abdomen- Hepatosplenomegaly, Hypochoic liver parenchyma, features of CCF, Grade1 prostatomegaly, Normal renal echotexture.
- ECG- Normal sinus rhythm, No chamber hypertrophy.
- ECHO- Concentric LVH, Grade 1 diastolic dysfunction, Moderate TR, Moderate PAH, No sparkling of myocardium.

Corresponding Author:

Dr. Harikrishnan B L, Assistant Professor, Department of Medicine, Jubilee Mission Medical College & Research Institute, East Fort, Thrissur, Kerala. Email: drpbaburaj@yahoo.co.in

- PBS- Normocytic normochromic anemia with plasmacytoid cells and thrombocytopenia.
- SERUM PROTEIN ELECTROPHORESIS - Reversal of AG ratio, a thick monoclonal 'M'band seen in gamma globulin region (church spire appearance).
- Serum IgM – 4.5g/dl (immunoelectrophoresis).

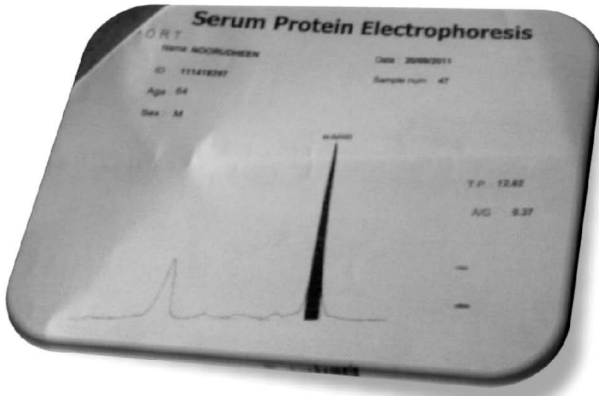


Figure 1. Serum Electrophoresis

BONE MARROW STUDY showed plenty of lymphoplasmacytic cells consistent with LYMPHOPLASMACYTIC LYMPHOMA.

Diagnostic features in this Patient

- Anemia with high ESR
- Hyper gamma globulinemia
- M band in S. Electrophoresis
- Absence of osteolytic lesions
- PBS-lymphocytic plasma cells
- BM-sheets of lymphocytic plasma cells
- High serum IgM – 4.5g/dl

DISCUSSION

Waldenstrom Macroglobulinemia is a rare, indolent NHL also called lymphoplasmocytic lymphoma as defined by REAL and WHO.¹ It starts in B lymphocytes which forms an important part of the body's immune system. They form in the lymph nodes, spleen, and other lymphoid tissues, including bone marrow. Some B cells become plasma cells, which make, store, and release antibodies. Antibodies help the body fight against viruses, bacteria, and other foreign organisms.²

In 1944, a Swedish physician, Jan Gosta Waldenstrom identified malignancy of lymphoplasma-cytoid cells that secretes IgM which is an uncommon monoclonal disorder. This disorder is characterized by features of

anemia, hyper viscosity and pathological presence of lymphocytic plasma cell in bone marrow. The incidence of WM is higher in males and higher in whites. Incidence increases sharply with age. The median age at diagnosis is 63.

Immunophenotyping

Immunophenotyping is important for diagnosis and differential diagnosis of WM. WM cell express pan B cell antigen CD19, CD20, CD22, CD79, CD45 (RA+/RO-) is present in all cases.³

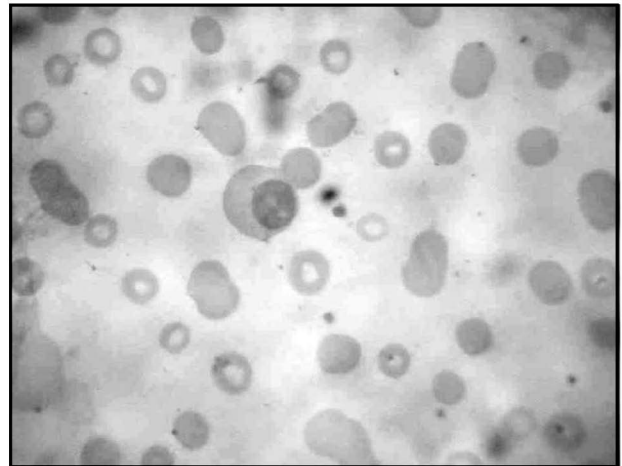


Figure 2. Patient's blood smear showing lymphoplasmacytoid cell

Secondary Amyloidosis of organs like heart and produce a restrictive type of cardiomyopathy. Osteolytic lesions are rare. Patient may present with features of hyperviscosity syndrome like –headache, stroke / visual blurring.

Fundus shows venous dilatation and sausage shaped retinal veins and renal involvement is minimal. The eye manifestations of Macroglobulinemia can include mid-peripheral hemorrhages, sludging of blood in the conjunctival vessels, blurred disc margins, exudates in the fundus and serous retinal detachment.

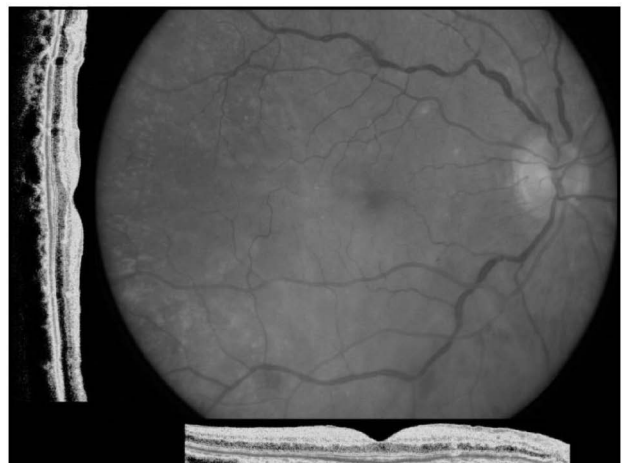


Figure 3. Optic fundus showing dilated and sausage shaped retinal Vein

Viscosity

The diagnosis is established by measuring serum viscosity, frequently done with Ostwald viscosimeter. Normal serum viscosity is around 1.8. Patients with values between 2 and 4 are only rarely symptomatic, while symptoms occur in most patients with values between 5 and 8.⁴

Normal serum viscosity–1.8 (double of water)

Hyperviscosity– 5 and above

Hyperviscosity and M protein

IgM> 4g/dl

IgG> 5g/dl

IgA > 7g/dl

FEATURES

Hyperviscosity can lead to impairment in the micro-circulation of the central nervous system, possibly resulting in headache, dizziness, vertigo, nystagmus, hearing loss, visual impairment, somnolence, coma, and seizures. Other possible findings include mucosal hemorrhage due to reduced platelet function, heart failure, which has been attributed to an expanded plasma volume.

	IgM MYELOMA	WALDENSTROM
Incidence	0.01 % of myeloma	2 % of Lymphoma
Bone	Present	Absent
HSM	+ve	++
LN E	-ve	+ve
Cytology	Myeloma Cell	Lymphoplasmacytoid cell

TREATMENT

In 2002, a panel at the International Workshop on WM agreed on criteria for the initiation of therapy. They recommended starting therapy in patients with constitutional symptoms such as recurrent fever, night sweats, fatigue due to anemia, weight loss, progressive symptomatic lymphadenopathy or splenomegaly, and anemia due to marrow infiltration. Complications such as hyperviscosity syndrome, neuropathy, amyloidosis, renal insufficiency were also suggested as indications

for therapy. Therapy is postponed for asymptomatic patients. Currently, there is no specific agent/regimen that reigns superior in WM. Choice of therapy therefore must consider toxicity, mode of administration and cost to the individual patient. In WM, as with other indolent diseases, single-agent alkylators or nucleoside analogs are standard choices for first-line therapy.⁵

Options include

- Plasmapheresis to reduce hyper viscosity.
- Alkylating agents such as chlorambucil.
- Fludarabine
- Monoclonal CD20 antibody Rituximab
- Median survival - 5 yrs

END NOTE

Author Information

1. Dr. P Baburaj, Professor & Unit Head, Department of Medicine, Jubilee Mission Medical College & Research Institute, EastFort, Thrissur, Kerala
2. Dr. Edwin J George, Senior Resident, Department of Medicine, Jubilee Mission Medical College & Research Institute, East Fort, Thrissur, Kerala.
3. Dr. Harikrishnan B L, Assistant Professor, Department of Medicine, Jubilee Mission Medical College & Research Institute, East Fort, Thrissur, Kerala

Conflict of Interest: None declared

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