International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 03 Issue 06 June 2023

Page No: 1114-1118

DOI: https://doi.org/10.47191/ijmscrs/v3-i6-15, Impact Factor: 6.597

Waldenstrom Macroglobulinemia, a Rare Hematological Malignancy: A Case Report

Dr. Ancy Mathew[1], Dr. Priya V.S.[2]

[1]Junior Resident, Department of Pathology, Govt. Medical College, Thiruvananthapuram

[2]Assistant Professor, Department of Pathology, Govt. Medical College, Thiruvananthapuram

ABSTRACT

Waldenstrom macroglobulinemia is a rare hematological malignancy which accounts for only about 1% of the diagnosis. It is unique among B cell malignancies that usually produce a large amount of immunoglobulin M(IgM). Some patients may be symptomatic commonly fatigued due to anemia, bleeding or neurologic complaints, while others may be asymptomatic. There is a greater proportion of men and are diagnosed in their mid-60s. Here we report a case of a 58-year-old male who presented with increased fatigability. Routine blood investigation showed anemia with raised ESR and reversal of albumin globulin ratio.Bone marrow study was done to rule out multiple myeloma,which showed hypercellular marrow predominantly composed of atypical mononuclear cells with variable morphology from lymphocytes to plasma cells.Serum electrophoresis was adviced which revealed elevated serum **β**2 microglobulin and IgM levels.Immunohistochemical studies were done and we confirmed our case of waldenstorm macroglobulinemia.

KEYWORDS: Waldenstrom macroglobulinemia, lymphoplasmacytic lymphoma, IgM, lympho-plasmacytes

ARTICLE DETAILS

Published On:
15 June 2023

Available on:
https://ijmscr.org/

INTRODUCTION

Waldenstrom macroglobulinemia is a subset of lymphoplasmacytic lymphoma, which is an indolent slow growing mature B cell neoplasm of lymphocytes, plasmacytoid lymphocytes and plasma cells involving bone marrow, lymphnode and spleen with increased serum IgM, which accounts for only 1% of diagnosis [1]. Patients may be asymptomatic or symptomatic and the symptoms are in response to the infiltration of cells and increased immunoglobulin levels.Infiltrating population characterized by lymphocytic, lymphoplasmacytic and plasma cell morphology.The key genetic mutation is L256P in MYD88.Increased IgM levels results in symptoms due to hyperviscosity.Though it has an indolent course , disease remains incurable for many patients.

CASE REPORT

Here we describe a case of waldenstrom macroglobulinemia. A 58-year-old male with no relevant personal or family history presented with increased fatigability and there were no other symptoms of bleeding or neurologic complaints or visual disturbances. On physical examination patient was afebrile and mild anemic

Table 1: laboratory studies at the time of presentation

CBC: Hb-8.9gm%, WBC- 6000/mm3, DC-N28 L63 E8 Platelet-2.3 lakhs/mm3 ESR- 93mm/hr
Total protein-10.7, Albumin-3.7gm/dl Globulin 7gm/dl Ca/P -8.9/3.4
RFT: Urea-17gm/dl Creatinine- 1 mg/dl Uric acid 34 gm/dl

Ultrasonography of abdomen done which showed fatty liver and prostatomegaly, no splenomegaly.
HRCT Thorax done which showed features of bronchitis
Peripheral Smear

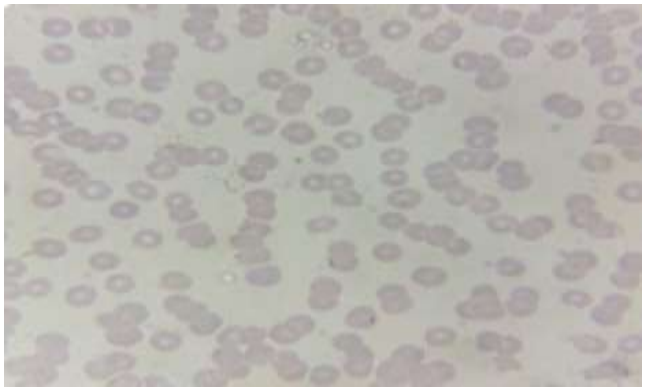

Figure 1: Normocytic normochromic anemia with rouleaux formation. Other parameters within normal limits

Bone Marrow Aspiration

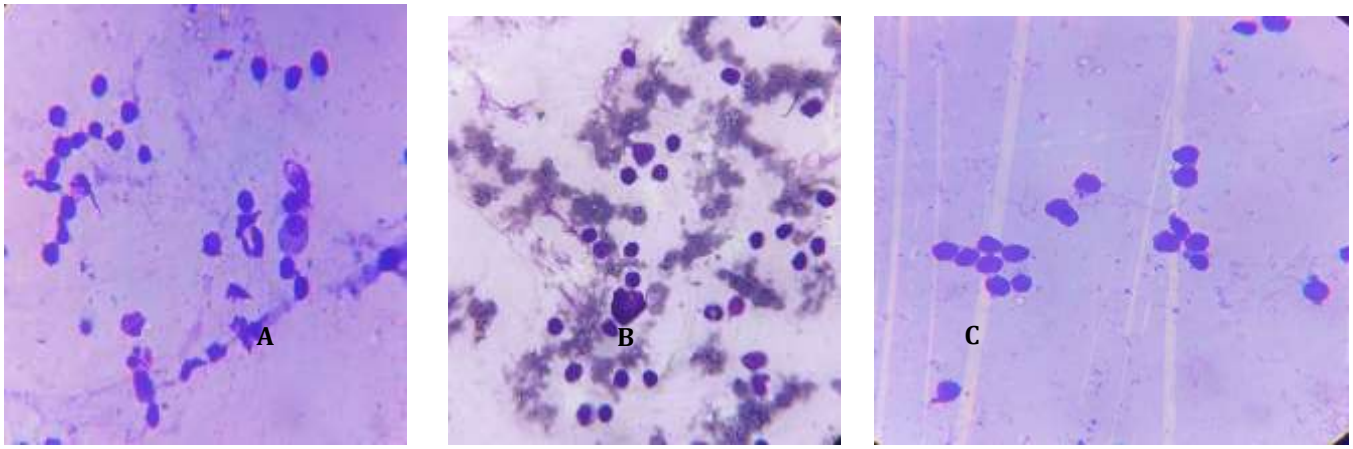

Figure 2A, B&C: Particulate cellular marrow aspirate showed predominantly atypical mononuclear cells (80%) admixed with few scattered hematopoietic elements. Individual cells are small to medium- sized with scant cytoplasm, high N: C ratio, open chromatin and inconspicuous nucleoli. Some cells show distinct nucleoli. Also seen are plasmacytoid lymphocytes and plasma cells. Few scattered mast cells seen

Bone Marrow Trephine & Immunohistochemistry

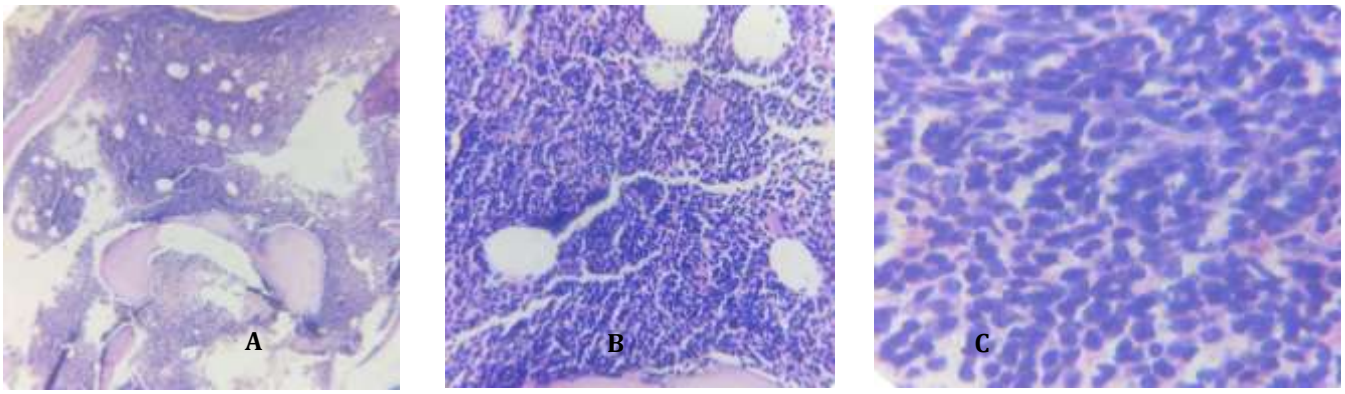

Figure 3 A, B&C: Cellular bone marrow spaces showed diffuse infiltration by monomorphous population of small to medium sized atypical mononuclear cells with scant cytoplasm, round to oval nucleus with coarse clumped chromatin and inconspicuous nucleoli. Also seen clusters of plasma cells with scattered erythroid and myeloid cells. Megakaryocytes seen mildly proliferated

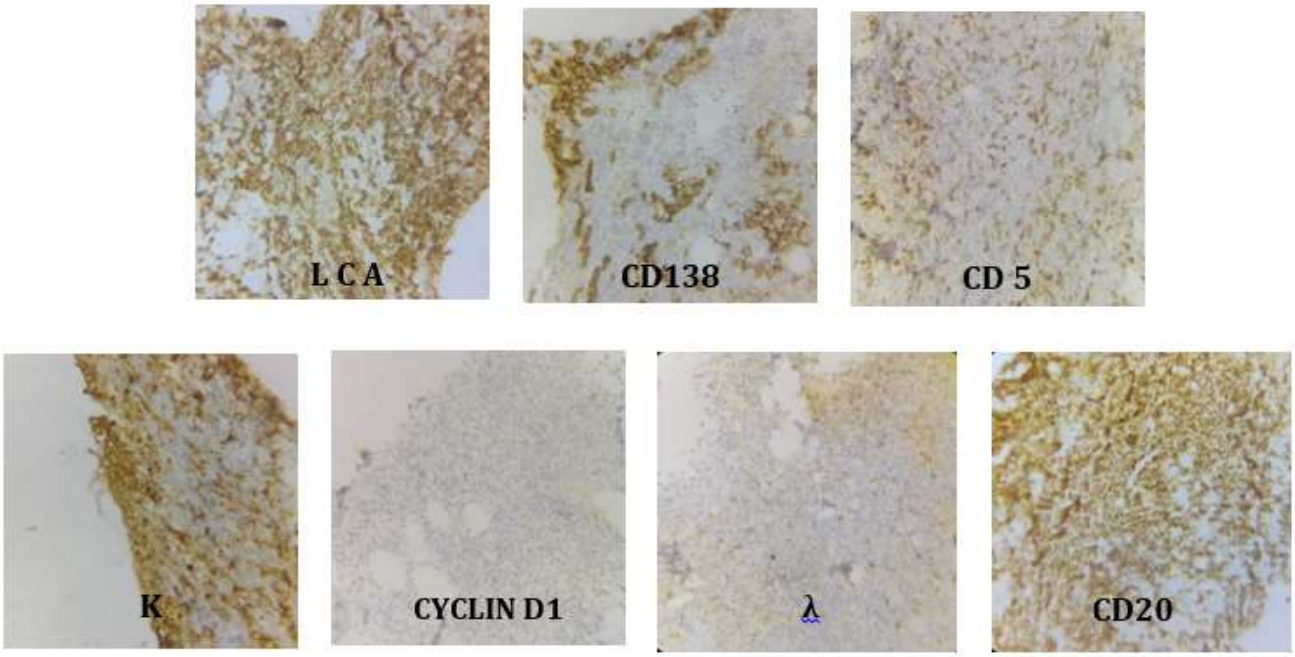

Figure 4: CD20 and LCA shows diffuse positivity.CD138 shows scattered and focal clustered positivity. κ restricted. CD5 and Cyclin D1 negative

Serum protein electrophoresis done. Table 2 and Table 3 shows the results.

Table 2: Serum electrophoresis Gamma markedly increased with an M spike of approximate concentration of 3.50 gm/dl at mid gamma region

Albumin	3.75gm/dl
Alpha 1	0.35 gm/dl
Alpha 2	0.7 gm/dl
Beta 1	4.7gm/dl
Beta 2	0.34gm/dl
Gamma	3.48gm/dl(0.8-1.35)
Total protein	9.05gm/dl
A/G ratio	0.71

Table 3: Serum Electrophoresis- Elevated IgM levels, Kappa free light chain and β2 microglobulin

Total IgA	2.58 gm/L
Total IgG λ	13.30 gm/L
Total IgM	47.86 gm/L(0.4-2.3)
Kappa free light chain	1490 mg/L (3.3-19.40)
Lambda free light chain	23.70 mg/L

Kappa Lambda ratio	62.87
β2 microglobulin	2371 ng/ml(609-2366)

Urine Bence Jones protein: Absent

FINAL DIAGNOSIS

Correlating all the findings we arrived at our diagnosis of Waldenstrom Macroglobulinemia

DISCUSSION

Lymphoplasmacytic lymphoma is a slow growing indolent B cell non-Hodgkin lymphoma, a neoplasm of small B lymphocytes, plasmacytoid lymphocytes and plasma cells usually involving bone marrow and sometimes lymph nodes and spleen, which does not fulfill the criteria of any the other small B cell lymphoid neoplasms that can also have plasmacytic differentiation. Waldenstrom macroglobulinemia is defined as lymphoplasmacytic lymphoma with bone marrow involvement and an IgM monoclonal gammopathy.Jan G. Waldenstrom described Waldenstrom macroglobulinemia in 1944. He reported an unusual presentation of lymphadenopathy, bleeding, anemia, elevated sedimentation rate, hyperviscosity and hyper-gammaglobulinemia in two patients [3]

Waldenstrom macroglobulinemia is rare forms 1% of the diagnosis with an annual incidence of about 5 cases per 1 million people leading to a total of about 1500 cases per year, occurs in adults with a median age in the sixth to seventh decade of life and a slight male predominance [2].

Genetic susceptibility linkage has been identified for loci in chromosomes 1q,3q and 4q.17. Most common cytogenetic finding in WM are deletions of chromosome 6q. The key finding now identified as universal in waldenstrom macroglobulinemia is a mutation in the gene MYD88.In the eminent study by the group of Treon and Colleagues, MYD88 was detected in 90% of cases [1].

The extent of clonal growth and rapidity of the expansion of these clonal cells result in a spectrum of clinical presentations.Some patients will present with extensive organ involvement and are highly symptomatic, whereas others are only incidentally discovered.The infiltrative nature of these cells, causes enlargement of tissues including hepatomegaly and splenomegaly or displacement of the normal bone marrow function, leading to impaired hematopoiesis. Monoclonal IgM protein can also lead to characteristic symptoms including hyperviscosity, immune deposits or any other antibody mediated disorders.

Lymphoplasmacytic lymphoma morphology is that it is quite pleomorphic with some cases having a small lymphocytic morphology with condensed chromatin at one end of the spectrum to cells that have plasma cell morphology at the other end with intermediate lymphoplasmacytic morphology. The lymphoplasmacytic cells display high levels of surface CD19, CD20 and immunoglobulin light chain expression and lack the expression of CD10 and CD5 to differentiate from follicular lymphoma and chronic lymphocytic leukemia and mantle cell lymphoma respectively.Plasmacytic cells have the same immuno- globulin light chain restriction and are also positive for CD138 and lose expression of PAX5, CD19 and CD20. Lympho- plasmacytic cells can also express CD25, CD27, FMC7 and Bcl2 and lack expression of Bcl6 and CD79[1].

Diagnosis is based on the combination of clinical and pathological features.IgM lymphoplasmacytic neoplasms can be categorized as IgM monoclonal gammopathy of undetermined significance, smoldering waldenstrom macroglobulinemia and active waldenstrom macroglobulinemia based on serum IgM monoclonal protein, bone marrow infiltration and end-organ damage indicated by anemia, constitutional symptoms, hyperviscosity, lymphadenopathy or hepatosplenomegaly. Waldenstrom macroglobulinemia is said when serum IgM of any size and > 10% bone marrow infiltrate, and when end organ damage is present attributable to the lymphoplasmacytic disorder. Smoldering waldenstrom macroglobulinemia when serum IgM is ≥3g/dl and /or bone marrow infiltration ≥10% and no evidence of end-organ damage. IgM MGUS is considered when IgM protein <3% and bone marrow infiltration < 10% and no end organ damage [5].

The International Prognostic Scoring Systems for Waldenstrom macroglobulinemia (IPSSWM) has defined five prognostic markers associated with short survival and that can segregate patients into three groups.The negative prognostic markers are age>65 years, hemoglobin <11.5g/dl, platelet count <100000/ml,**β**2 microglobulin> 3 mg/L and a monoclonal IgM >7g/dl[6]. Patients are divided according to the presence of these five variables into those that have scores 0-1, 2, >2 factors and have a 5-year survival probability of 87%,68% and 37% [2]

Even though Waldenstrom macroglobulinemia has an indolent course, for most patients the disease remains incurable and depending on the age of diagnosis, the disease remains a likely life-ending diagnosis. The median survival for newly diagnosed symptomatic patients is approximately 8 years

CONCLUSION

Waldenstrom macroglobulinemia is a hematological malignancy offers challenging in diagnosis in terms of its rare occurance, variable presentation and need of immunohistochemistry

REFERENCES

I. WHO hematolymphoid neoplasm, 4th edition
II. Wintrobes clinical hematology, 14th edition
III. Hatem Kaseb;Luis F. Gonzalez Mosquera; Meghana Parsi, Prerna Mewawalla Lymphoplasmacytic lymphoma.
IV. 4.Kudo N, Usui M, Nakabo Y, Yoshida KI, Miki K, Osafune T, Nishimura K, Imashuku S. Waldenstrom's Macroglobulinemia: A Report of Two Cases, One with Severe Retinopathy and One with Renal Failure. Case Rep Hematol. 2017; 2017:3732902. doi: 10.1155/2017/3732902. Epub 2017 Oct 31. PMID: 29225979; PMCID: PMC5684595.
V. Gertz MA. Waldenström macroglobulinemia: 2017 update on diagnosis, risk stratification, and management. Am J Hematol. 2017 Feb;92(2):209-217. doi: 10.1002/ajh.24557. PMID: 28094456.
VI. 6.Merlini G, Baldini L, Broglia C, Comelli M, Goldaniga M, Palladini G, Deliliers GL, Gobbi PG, Prognostic factors in symptomatic Waldenstrom's macroglobulinemia. Semin Oncol. 2003 Apr,30(2):211-5. doi:10.1053/sonc2003.50064. PMID: 12720138.