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Case Report

Uncommon IgG Lymphoplasmacytic Lymphoma: Case report

Syeda Mah Ali, Naila Raza
Department of Hematology, Liaquat National Hospital & Medical College, Karachi.

Abstract

Lymphoplasmacytic lymphoma is quite rare neoplasm of mature B lymphocytes. It accounts for less than 1% of Non Hodgkin Lymphoma in west. Its incidence is 10 times less in Asian countries.In majority of cases, patients have a circulating monoclonal IgM which is called Waldenström Macroglobulinemia. Less commonly, the tumor cells produce other immunoglobulins like gamma heavy chain or alpha heavy chain or combination of immunoglobulins (i.e. IgM and IgG). These cases are not properly defined and raises diagnostic challenges and often misdiagnosed as multiple myeloma. The purpose of this article is to report the description of an IgG lymphoplasmacytic lymphoma case which was diagnosed recently in the haematology department of Liaquat National Hospital and Medical College, Karachi.
Key words: Non IgM, IgG, lymphoplasmacytic lymphoma.

Introduction

According to the World Health Organization (WHO) classification of 2017, Lymphoplasmacytic lymphoma (LPL) is an uncommon malignant condition in which there is a clonal proliferation of small and mature B lymphocytes having plasmacytic differentiation. The immunophenotype of neoplastic cells is usually similar to normal B lymphocytes that expresses pan B markers (CD 19,CD 20, CD 79a) and plasma cell marker(CD 138). These cells are also different from myeloma cells which abnormally expresses CD56.[1] There is a wide range of variability in the clinical presentations of patients. Most commonly the symptoms are usually related to the cytopenia (mainly anemia and/or thrombocytopenia) because of neoplastic cells infiltrating the bone marrow. Systemic symptoms which include fever, weight loss and night sweats are also frequently encountered.[2]

Majority patients show monoclonal gammopathy on serum protein electrophoresis, however it's not necessary for the diagnosis of LPL. Waldenström Macroglobulinemia is a similar condition in which there is an IgM monoclonal gammopathy.[3,4] It is a rare disorder, more common in white people as compared to other populations.[5] A study from Pakistan shows that this is among the uncommon B cell Non Hodgkin Lymphomas.[6] Lymphoplasmacytic lymphoma (LPL) with non IgM monoclonal gammopathy is more rare neoplasm than Waldenström Macroglobulinemia, comprising less than 1% of Non-Hodgkin Lymphoma in western countries.[7] The incidence is 10 times less in Asian population.[8] Diagnosis of non-IgM LPL is often difficult. Genetic mutation of MYD88 is most of the time helpful in making diagnosis but is not specific for LPL and is also identified in other B-cell Lymphomas.[9] There is no confirmatory test for diagnosis. Moreover it does not fit into any other B cell lymphoid neoplasm. Diagnosis is often made after excluding other related small B-cell lymphoid neoplasmslike multiple myeloma, chronic lymphocytic leukemia, splenic or nodal marginal zone lymphomas and follicular lymphoma. The purpose of this article is to describe an IgG lymphoplamacytic lymphoma case diagnosed recently in the haematology department of Liaquat National Hospital, Karachi, Pakistan.

Corresponding Author:
Syeda Mah Ali
Department of Hematology,
Liaquat National Hospital & Medical College, Karachi.
Email: dr.mah92@gmail.com

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Authors Contribution

SMA & NR conceptualized the project and did literature search, drafting, revision & writing of manuscript.

Case Report

A Fifty years old female patient resident of Sindh in Pakistan presented in clinic with chief complaint of fever for about 1 month. Temperature

used to fluctuate between 99 -101°F with rigors and chills. It was also associated with nausea, headache and decreased appetite. It was intermittent, relieved by taking antipyretics. She also complained of significant weight loss of approximately 8-10 kg in last 1 month and developed rashes for last 15 days which had gradually increased and covered most of her trunk. The rash surfaces were slightly raised. They were red coloured and non-itchy in nature. These were seen on abdomen, on back and on external surfaces of bilateral arms and legs. Baseline physical examination revealed bilateral cervical lymphadenopathy, moderate hepatomegaly and splenomegaly. CBC showed hemoglobin of 8.4 g/dl, white blood cells count: $19.1x10^9$/L (neutrophils 42%; lymphocytes 37%) and platelet count was $95x10^9$/L. Peripheral smear showed atypical plasmacytoid lymphocytes as well as marked rouleaux formation (Figure-1). She had with her right cervical lymph node Fine needle aspiration cytology report, which was done in outside hospital and showed reactive changes. Our differential diagnosis included Lymphoma, multiple myeloma and autoimmune disorder. To reach at conclusive diagnosis we went for further laboratory investigation which included antinuclear antibody (ANA) profile which was negative. Serum Protein electrophoresis showed polyclonal gammopathy with increase fraction of immunoglobulin at gamma region i.e. 4.9g/dl with broad based peak. Immunoquantification showed significantly raised IgG of 4974 mg/dl (normal range: 700-1600 mg/dl), but IgM and IgA were in the normal limits. Serum light chain assay shows Kappa Light Chain of 34.7 mg/dl (normal range: 6-14mg/dl) and Lambda Light of Chain 32.1 mg/dl (normal range: 3.1-7.2mg/dl). Serum Albumin was 3.0 g/dl, ionized calcium was 1.21 mM/L (normal range: 1.15 – 1.32mM/L), Serum LDH was 128U/L and beta-2 microglobulin was significantly elevated i.e 5.9 mg/L (normal range: <2.4mg/L) andother test showed raised Serum Uric Acid of 11mg/dl. Antibody against HCV infection was also detected.

Computed tomography scans showed moderate hepato-splenomegaly with multiple splenic and hepatic deposits along with extensive supraclavicular, axillary, mediastinal, hilar, abdominopelvic and inguinal Lymphadenopathy. No bony lytic lesion was seen. We performed bone marrow biopsy to see the marrow infiltration, it showed a hypercellular marrow with 40% infiltration of small to medium sized lymphoplasmacytoid lymphocytes with 4% of plasma cells (Figure-2).

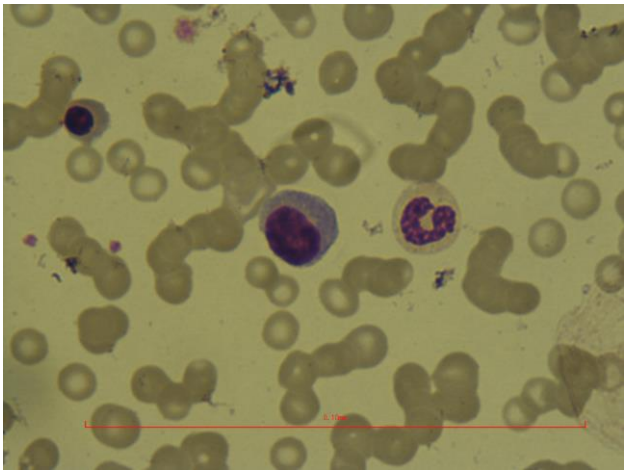

Figure 1: Peripherel smear.

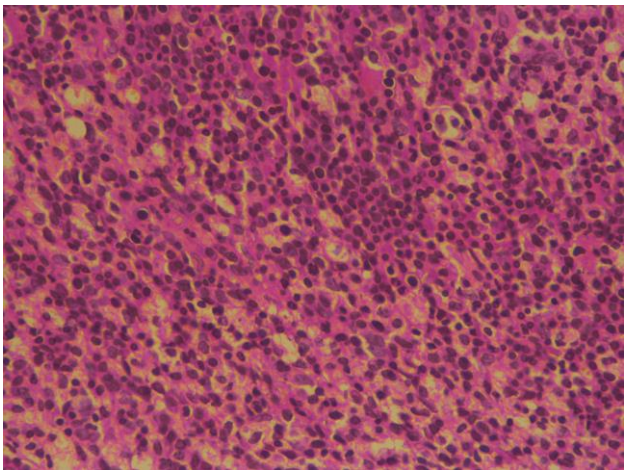

Figure 1: Bone marrow trephine biopsy.

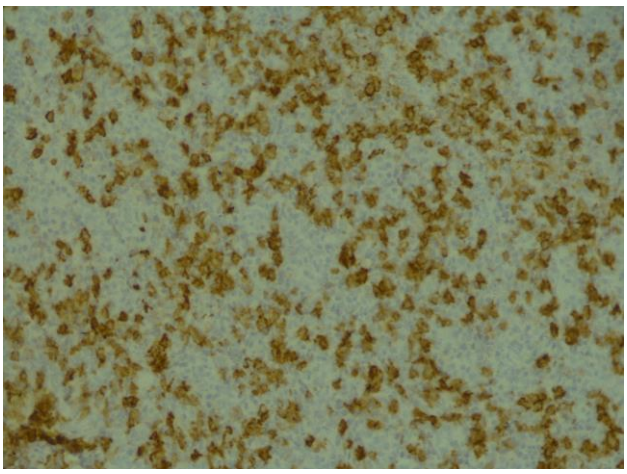

Figure 2: (CD 20 positive) Immunohistochemistry.

Immunohistochemical studies on trephine biopsy showed that atypical lymphoplasmacytes

which expressed CD20, CD138,PAX 5 and were negative for CD3, CD5, CD10, CD56, CYCLIN D1and BCL2, Ki67 showed 60-65% proliferative index (Figure-3). Her final diagnosis was lymphoplasmacytic lymphoma-IgG with Ann Arbor stage IV and IPI risk group was low-intermediate risk.

MYD88 mutation analysis was not done because of financial constraint. Patient was given 6 cycles of Rituximab-Bendamustine, after which she went into disease remission clinically. Three-monthly follow-up showed persistence of remission. Bone marrow biopsy was done after giving treatment which showed reduction of lymphoplasmcytoid lymphocytes from baseline 40% to 17%.

The Ethical approval was obtained from Ethical Review Committee of Liaquat National Hospital, Karachi.

Discussion

Literature review shows that LPL is often associated with IgM paraprotein, the disease is called Waldenstorm Macroglubulienmia.[3,4] Very few cases of LPL are associated with IgA and IgG proteins.[2,10,11] Most of these cases are reported from Europe and East Asia.[12] None of the case report from Pakistan have been published so far and this is due to two main reasons; first is that the disease is rare and second is that there is a lot of ambiguity in making diagnosis because of overlapping clinical and diagnostic features of small B cell lymphomas and non-availability of a confirmatory test. Our case is unique in way that patient has IgG secreting disease.

The previous studies from Asia showed that LPL was more common in elderly patients with an average age of about 62 years with male predilection.[12,13] Also it was found in previous studies that the patients with non-IgM LPL tends to have extramedullary involvement more commonly than LPL/WM group, lymph node involvement and lytic bone lesion are more common than pleural involvement and skin lesion which are quite rare.[14] These findings are consistent with the clinical presentation of our patient who has lymphadenopathies along with suspected skin manifestations. Association of HCV infection with LPL has been noted. It was observed in an Italian multicenter study that 30.8% of LPL patients were positive for HCV infection.[15] We observed this in our patient also.

Different case reports reveal that the diagnosis of non-IgM LPL is quite challenging and many times it is misdiagnosed as multiple myeloma.[12,16] Combination of the clinical presentation, lymph node biopsy, bone marrow examination and molecular/cytogenetic findings are crucial in reaching at the right diagnosis.

No prospective studies have been done so far regarding standard treatment regimens for patients with LPL. According to the National Comprehensive Cancer Network guidelines, treatment options for symptomatic patients with LPL/WM include alkylating agents, nucleoside analogs, Bortezomib, and Rituximab.[17] These guidelines are being followed for non IgM LPL patients and proved to be equally effective and safe.[12,18] In practice, Rituximab based regimens like R-CHOP and BR are commonly used. Previous randomized trials supports their treatment efficacy i.e. 90% overall response rates,[18] it was found to be effective in our case also.

We report a case of Lymphoplasmacytic lymphoma with paraprotein IgG, which is indeed a rare entity. The diagnosis of LPL with paraprotein other than IgM remains a challenge because the conventional practice of distinguishing LPL from other lymphomas by raised IgM level is no longer helpful. More studies are needed to have better understanding of diagnosis and management.

Conflict of interest: None declared.

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