International Journal of Biomedical Research

ISSN: 0976-9633 (Online)
Journal DOI:10.7439/ijbr
CODEN:IJBRFA

Case Report

Waldenstrom's Macroglobulinemia - A coincidental finding in a case of carcinoma of buccal mucosa

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Abstract

Waldenström's Macroglobulinemia (WM) is a clonal disorder of small lymphocytes that show maturation to plasma cells synthesizing IgM. It is the biological activity of IgM protein that determines most of the clinical manifestations of the disease. WM most closely corresponds to lymphoplasmacytic lymphoma or immunocytoma of the REAL classification of lymphoma. Here, we report a case of a 50 year old male with squamous cell carcinoma of buccal mucosa. On routine investigations we found autoagglutination of RBCs; on workup with this feature we had suspicion of Waldenström's Macroglobulinemia. The diagnosis of WM was established after cytomorphology and immunohistochemistry (IHC) analysis of the bone marrow which revealed the presence of a lymphoid/lymphoplasmacytoid-like bone marrow infiltrate along with an elevated serum IgM level. Waldenström's Macroglobulinemia and its co-existence with autoimmune diseases and non hematological malignancies has already been described in the literature, but the present case was asymptomatic for WM with carcinoma of buccal mucosa, which is the first case reported so far.

Keywords: lymphoplasmacytic lymphoma, REAL classification, autoagglutination, immunohistochemistry analysis

1. Introduction

WM is a pleomorphic lymphoproliferative disorder characterized by the elevated levels of monoclonal immunoglobulin (IgM) protein secreted by malignant B-cells and paratrabecular lymphoplasmacytic infiltration in the bone marrow. The classical presentation of WM's patient includes anemia, hepatosplenomegaly, lymphadenopathy and hyperviscosity.[1)] Infiltration of the bone marrow and extramedullary sites by malignant B-cells and elevated IgM levels account for the symptoms associated with this disease. Patients may develop constitutional symptoms, pancytopenia, organomegaly, neuropathy, and symptoms associated with immunoglobulin deposition or hyperviscosity.[2,3)] WM is incurable with current therapy, and half of the patients die of disease progression; median survival is approximately 5 years.[(4)] The incidence of development of second cancers was not significantly different between asymptomatic and symptomatic WM and between treated and untreated patients.[5)]

1. Case Report

A 50 year old male, known patient of hypertension and diabetes mellitus, on treatment; non-smoker, occasional alcoholic, had undergone TURP 3years ago, now presented with buccal mucosal lesion. On examination, the patient was average built with mild pallor, no palpable lymph nodes or cutaneous lesions, no icterus, no cyanosis or clubbing. Examination of CNS/RS/per abdomen was normal. On examination of oral cavity, a cystic lesion found on right side, inside the cheek. Biopsy of the lesion performed and diagnosed as squamous cell carcinoma. Surgery was planned and investigations were advised. Initial laboratory workup revealed anemia (Hb-10.5%), ESR was raised (130mm in 1st hour) by Westergren's method. Peripheral blood smear showed autoagglutination of RBCs (Fig. 1) with mild leucocytosis and normal platelet count. Serum iron and vitamin B12 were within normal range. Serum LDH was within normal range with negative Coomb's test. Liver function tests and renal function tests were normal. Chest X-ray and Ultrasound abdomen was normal. Further workup for cold agglutinins was advised. Result of Direct Agglutination Test at 4°C was positive with 1:128 titers of cold agglutinin. On further investigation, there was a sharp M band in the gamma globulin detected on serum protein electrophoresis. Urine was negative for Bence Jones proteins. Monoclonal gammopathy was seen in IgM and kappa region on Immunofixation. Bone Marrow aspirate findings were normal, except for mild and focally increased lymphocytes with normoblastic and megaloblastoid erythropoiesis. Trephine biopsy was adequate with normal bony trabeculae and intervening marrow showing 60% cellularity. Trilineage haematopoiesis seen. Focal nodules of lymphoid/lymphoplasmacytoid aggregates seen ?reactive/neoplastic. IHC was done by using L26 clone antibody to CD20 (ready to use) and the result showed the presence of CD20 positive cells (Fig. 2). Skeletal survey was advised which was normal study with no evidence of any osteolytic lesions.

On correlating all the findings with IHC results, thus a final diagnosis of Waldenstrom's Macroglobulinemia was made.

Fig. 1: Photomicrograph of peripheral smear showing prominent Rouleaux formation (Leishman, X100)

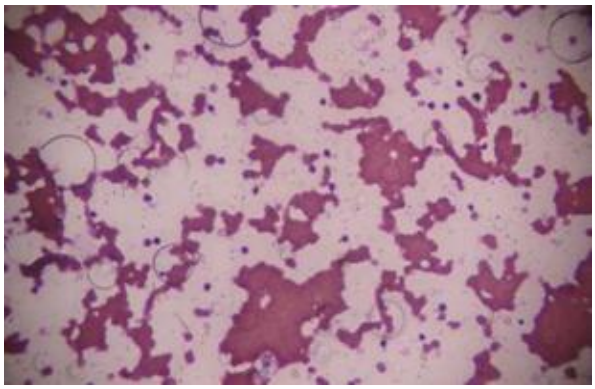
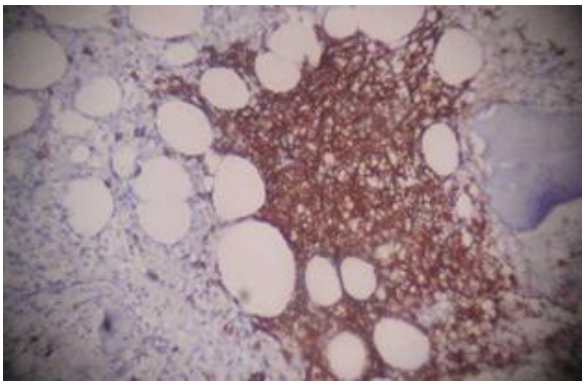


Fig. 2: Photomicrograph of Bone Marrow biopsy section showing CD20 positive cells (CD20, X100)



2. Discussion

The WHO includes Waldenstrom Macroglobulinemia in lymphoplasmacytic lymphoma category and excludes other subtypes of specific lymphoma with plasmacytic differentiation.[6,7] Secretion of monoclonal IgM is common but IgA and IgG or an immunoglobulin light chain is also seen in some patients.[8] In our case, we report a sharp M-band seen in gammaglobulin region detected by protein electrophoresis. The incidence of WM is approximately 5 cases per 1 million persons per year, and this disease accounts for approximately 1% to 2% of hematologic cancers.[9,10] The incidence of WM is more commonly seen in white people compared to other groups of population.[11] The median age at diagnosis varies between 63 and 68 years, and slightly more common in males.[2] Our patient was 50 year old male, which is slightly younger than the cases described in other studies. The disease was originally described by Waldenstrom in 1944.[12] In the original description of WM, Waldenstrom described two patients with oronasal bleeding, lymphadenopathy, anemia and thrombocytopenia, and an elevated ESR.[13] Bone marrow and lymph nodes show infiltration of pleomorphic B–lineage cells at different stages of maturation.[14] The cells express pan B-cell markers (e.g., CD19 and CD20) and typically test negative for CD3 and CD103.[15] In the described case, IHC analysis of bone marrow biopsy showed infiltration of lymphoplasmacytoid CD20 positive cells.

A study by Alexanian *et al*. was done to evaluate the frequency and history of Waldenstrom's Macroglobulinemia. They found 27% patients to be asymptomatic with slow disease progression. They concluded that the outcome was similar for both asymptomatic and symptomatic WM.[16] This case differs from the cases reported in literature, as here, the patient is having pre-existing WM without any symptoms but he presented with cystic lesion of buccal mucosa. This association is not therapy related development of second malignancy (carcinoma of buccal mucosa) because the patient received neither chemotherapy nor radiotherapy except for the biopsy of lesion.

Waldenstrom's macroglobulinemia is a lymphoid malignancy and the association between lymphoid malignancies and solid malignancies has been discussed in the literature.[17] Co-existence of hepatic carcinoma, lung carcinoma, and some other malignancies with WM have been reported previously.[18,19,20] Most of these case reports belong to patients in whom a second malignancy developed during the course of WM except the case reported by Hasegawa *et al*.[18] An alternative explanation for the preponderance of second cancers in WM patients is disease-related immune suppression. The immunologic impairment associated to lymphoproliferative disorders could contribute to the pathogenesis of WM as well as to the development of additional malignancies.[8] There might be a common genetic mutation or an immunomodulatory role of the first malignancy predisposing to the second. This could suggest that the existence of two malignancies in a patient could be a co-incidence. Regardless of the cause and the pathogenetic mechanism, the awareness of an increased risk of second malignancy needs a careful oncohematological examination of WM patients.

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