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A case report of B cell NHL (Mantle Cell Lymphoma)

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ABSTRACT
A 60 years old male came to the medicine department of tertiary care hospital with the chief complains of generalized weakness, easy fatigability and dyspnea on exertion and routine activity since 1 month. Patient also complained of on and off fever since 15 days. On admission his vitals were within normal limits. Routine hematological tests showed decreased hemoglobin with other parameters normal. Other tests like iron profile, Vit B12 and folic acid study, liver function tests, renal function tests, Coomb's test, stool examination for occult bleeding, urine routine examination and routine radiological tests like USG-KUB, USG- Abdomen, ECHO and Chest X-ray were done to rule out the common causes of anemia like bleeding, hemolytic anemia, anemia of chronic disease. On examination splenomegaly and lymphadenopathy was present which was also confirmed on USG-Abdomen. Reticulocyte count was raised that ruled out bone marrow suppression. Peripheral blood smear picture revealed normocytic hypochromic RBCs with few microcytes, elliptocytes, occasional tear drop cells and nucleated RBCs. Few atypical lymphoid cells with indented nuclei and pale blue cytoplasm were seen along with many smudge cells. Differential count was as following; Neutrophils: 28%, Lymphocytes: 47%, Monocytes: 09%, Eosinophils: 08%, Basophils:00% and Atypical cells:08% Platelets were adequate on smear. Malarial parasite was not seen.
At last Bone marrow aspiration and biopsy was planned and performed. Bone marrow aspiration was diluted with peripheral blood but many atypical lymphoid cells were noted. Further the bone marrow biopsy showed nodular paratrabecular and interstitial infiltration by small to medium sized atypical lymphoid cell with indented nuclei and inconspicuous nucleoli. A temporary diagnosis of Lymphoma was given. On further testing immunophenotyping was done which confirmed Mantle cell Lymphoma (B-cell NHL) as the diagnosis.
KEY WORDS*: Lymphoma, mantle cell lymphoma, cyclin D1*

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I. Introduction

Bone marrow is affected by a variety of hematological and non- hematological conditions. Non Hodgkins Lymphoma is a group of malignant neoplasms originating from lymphoid tissue. These tumors result due to chromosomal translocations, various toxins, infections and chronic inflammation. NHL can have a B- cell or a T-cell origin and among them it can be precursor B-cell/T-cell or mature B-cell/T-cell origin.

II. Case Report

A 60 year old male was admitted with nil co-morbidity and relatively asymptomatic 1 month before was admitted with the chief complains of breathlessness (on routine activity), generalized weakness, easy fatigability since 1 month. He also complained of low grade fever which was on and off since 15 days. Except for being a tobacco chewer since 15 years he had no other significant past medical or surgical history. On admission his vitals were stable and within normal limits. Routine blood tests were done with the following results; Hb: 5.6 g/dl (12-18 g/dl), WBC: 7.07 (5.2-12.4 x103/microlt), Platelet: 151 (130-400 x103/microlt), MCV: (83-101 fL), MCH: 27 (27-32 pg), RDW: 21.6 (11.5-14.5%), HCT: 28.9 (40-50%), RBC: 2.06 (4.5-5.5 x106/microlt). Reticulocyte count : 8.0% with corrected reticulocyte count: 3.12, (Liver function tests were within normal limits) Total bilirubin: 1.91 (0.3-1.2 mg/dl), Direct bilirubin: 0.62 (0-0.3 mg/dl), Indirect bilirubin: 1.29, SGPT-22 (10-49 U/L), SGOT-33 (0-34 U/L), ALP-127, S.protein-5.77 (5.7-8.2 g/dl), S.albumin-3.87 (3.2-4.8 g/dl), S.globulin: 1.74 (2-3.5 g/dl), S.albumin/globulin ratio: 2.03 (1.5-2.5), S.LDH- 476 (100-250 U/L), PT-17.2, INR-1.26, D-dimer-2.06. Iron profile S.ferritin - 291.6 (10-282 ng/ml), S.TIBC - 263 (250-420 microg/dl), S.Vitamin B12: 136 (160-950 pg/ml), Stool examination for occult bleeding was negative. Urine

routine examination revealed no significant pathology. Malarial parasite was negative and dengue NS1 antigen were negative. Direct and indirect Coombs test were negative. Peripheral findings showed normocytic hypochromic RBCs with few microcytes, elliptocytes, occasional tear drop cells and nucleated RBCs. Few atypical lymphoid cells with indented nuclei and pale blue cytoplasm were seen along with many smudge cells. Differential count was as following; Neutrophils: 28%, Lymphocytes: 47%, Monocytes: 09%, Eosinophils: 08%, Basophils:00% and Atypical cells:08% Platelets were adequate on smear. Malarial parasite was not seen.

On examination patient was noted to have mild hepato-splenomegaly and bilateral neck, axillary and inguinal lymph nodes enlargement. Patient was advised ultrasonographic evaluation to further confirm the findings; USG local part showed few subcentimeter sized lymph nodes bilaterally in neck, axilla (largest in left axilla measuring 28x10 mm) and inguinal region (largest in right inguinal region measuring 23x1 mm).

The routine causes of decreased hemoglobin like hemolysis were ruled out by negative coombs test and normal LFTs. No schistocytes were noted in the peripheral smear. Bleeding was ruled out by a normal USG-KUB, USG- Abdomen and negative stool occult test. Nutritional anemia was excluded as the patient had within normal iron profile and slightly low serum vitamin B12 and folate levels. Infectious causes like malaria was ruled out after specific negative test.

Bone marrow aspiration and biopsy was done which showed a hypercellular marrow with markedly reduced fat spaces. There was interstitial and nodular paratrabecular infiltrates of small to medium sized lymphoid cells with irregular nuclei, clumped chromatin, indistinct nucleoli and scant to moderate cytoplasm (Figure 1). Erythroid and myeloid series showed decrease in number but with normal maturation whereas the megakaryocytes were adequate in normal with normal maturation. On IHC, it was CD 20 (B-cell marker), CD 5 (CLL/SLL, Mantle cell marker) was positive along with Cyclin-D1 positive (specific for Mantle cell Lymphoma) and Ki-67 showed 10-15% activity. CD 3 was positive showing mild infiltrates (Figure 2 & 3). It was negative for CD 23, CD10, Bcl-6 and CD 117, Tdt, which concluded it to being Mantle cell lymphoma (B-cell NHL)

III. Discussion

The term "non-Hodgkin's lymphomas" defines a heterogenous group of malignant tumors of lymphatic tissue with specific biological, morphological and clinical features, as well as with various responses to therapy, prognosis and survival of patients. In general, today about half of such clinical and morphological types of lymphomas originate from tumorous analogues of B-lymphocytes, the remainder account for T-cell and a very small part for NK-cell tumors. **(1)** Mantle cell lymphoma is a B-cell tumor consisting of monomorphic small to medium lymphoid cells with uneven contour of nucleus and translocation of CCND1 gene. **(2)** The most common "classical" variant of Mantle cell lymphoma was first described in 1973 by a German pathologist, K.Lennart. **(3,4)**

Mantle cell lymphoma may present with marked involvement of marrow and blood, and blood involvement is present in approximately half of the cases with marrow disease. **(5)** The blood findings may resemble CLL/PL, PLL and small cleaved cell lymphoma. The lymphoma cells may be quite pleomorphic with variation in size, nuclear cytoplasmic ratio, degree of nuclear irregularity and prominence of nucleoli. **(6)** The differential diagnosis includes small cell lymphoma, lymphoplasmacytic lymphoma, nodal, hairy cell lymphoma and extra-nodal and splenic marginal zone lymphomas. . The most important pathogenic stage of MCL is translocation of genes encoding cyclin D1 (CCND1) and heavy chains of immunoglobulins-t (11;14) (q13;q32). **(1,4)** In most cases, these disorders can be separated from one another on basis of morphology alone. The lymphocytes express pan B-cell antigens (CD19, CD20, CD 79a and PAX5 as well as BCL2 (anti-apoptotic marker). T-cell markers such as CD3, CD4 and CD8 were negative. In addition, these cells had aberrant expression of CD 5. The lymphocytes usually do not express CD 23 and CD 10.

The bone marrow involvement may be diffuse or focal. The lymphoma cells express cyclin-D1 by IHC and t(11;14) (q13:q32) chromosome abnormality by FISH.

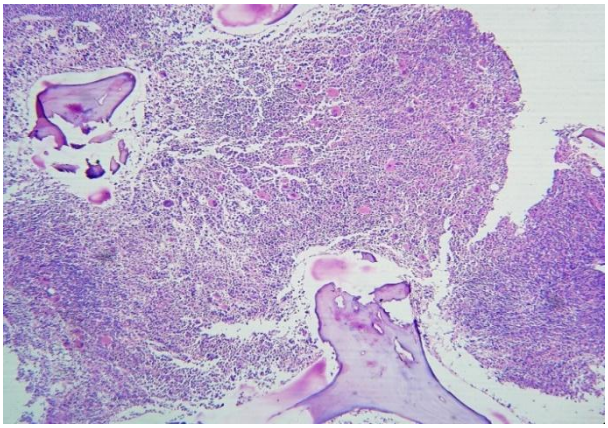

Figure: 1 Mantle cell lymphoma - Para trabecular and interstial region involvement

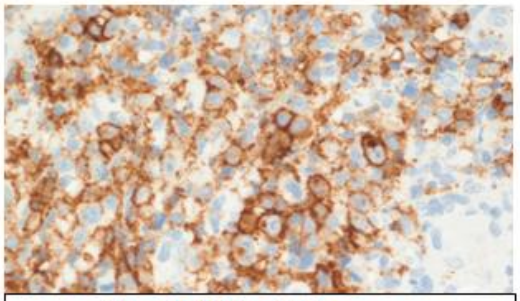

Figure 2: CD20 positivity

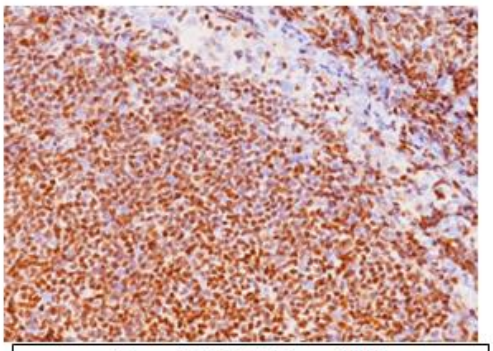

Figure 3: CYCLIN-D1 positivity

IV. Conclusion

Mantle cell lymphoma is a distinct entity recognizable on the basis of morphological, clinical, immunophenotypic and molecular genetic features. The clinical presentation of leukemia and lymphomas can vary drastically depending on the type of leukemia or lymphoma. Common clinical features are generalized lymphadenopathy, splenomegaly (often marked), hepatomegaly and involvement of gastro intestinal tract and Waldeyer's ring. Lymphomas can be B-cell and T-cell lymphoma out of which B-cell lymphomas are more common. For small B-cell lymphomas the differential diagnoses to consider are CLL/SLL, Hairy cell lymphoma, Mantle cell lymphoma, Follicular lymphoma and Marginal Zone lymphoma. The best way to distinguish is by immunophenotyping either by flow cytometry or immunohistochemistry.

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