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Rare haematological presentation predating Non Hodgkins Lymphoma

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Abstract

Background: Non Hodgkin's Lymphoma (NHL) is a haematological malignancy with incidence varying from 1.5-2.9/lakh population, being common in male. The association of pure red cell aplasia along with cryoglobulinemia in a case of NHL is not known to the best of our knowledge

Case 1: 52 yr/M, presented with acute intestinal obstruction. Sections from hemicolectomy specimen showed diffuse sheets of atypical lymphoid cells splaying muscle fibres. Morphology and immunohistochemical markers suggested extranodal Diffuse large B-cell lymphoma. Peripheral smear examined showed marked clumping of Red Blood Cells (RBC) which disappeared on warming. Direct Coombs Test (DCT) - negative. Diagnosis of cryoglobulinemia in a case of extranodal diffuse large B-cell lymphomas (DLBCL) was given.

Case 2: 4 yr/M presented with fever and generalized weakness x15 days. Hb- 2.2g%. RBC showed clumping which decreased, post warming (37c). DCT - positive. BM showed erythroblastopenia with few giant normoblast. Diagnosis of Pure red cell aplasia with cryoglobulinemia was given**.** FNA from incidentally found left cervical lymphnode showed features of High grade NHL.

Keywords: NHL, Uncommon presentation, DLBCL.

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1. Introduction

Lymphoma forms 3% of all malignancies. Non Hodgkins lymphoma (NHL) – is commoner than Hodgkins Lymphoma. Of NHL, B cell type is commoner (80-85%). DLBCL is commonest of B cell NHL (40% - 60%). Common presentations of NHL are lymphadenopathy, splenomegaly, hepatomegaly and cytopenias with/without marrow involvement.

2. Case report

2.1 Case 1:

A 52 year male presented to surgery outpatient department with complaints of acute intestinal obstruction for 3 days. He had a history of refractory anemia for 1 year (extensively worked up outside). O/E there was no hepatosplenomegaly or lymphadenopathy. But abdomen was distended along with a palpable mass. No bowel sounds heard. Abdominal x -ray showed air fluid level. The patient underwent right hemicolectomy. A specimen of ileum, cecum and appendix measuring 10cm, 6x6x2cm & 4cm respectively was received, externally congested. On cutting open, mucosa was unremarkable elsewhere but the wall was thickened over a length of 8cm in the cecum with flattened mucosa. (Fig 1a & b)

Microscopic examination from the thickened intestinal segment showed atypical large cells infiltrating throughout the intestinal wall, from submucosa uptill serosa, splaying the muscle fibres (Fig 2 a, b & c). These cells had abundant cytoplasm with vesicular nucleus, prominent nucleoli & were positive for LCA, CD 20, CD

19, FOX P1, MUM1, Ki 67 and negative for CD 3, CD 10, Bcl2, Bcl6 (Fig 3a, b, c, d & e). Diagnosis of colonic DLBCL (Activated B cell type) was made. Meanwhile the peripheral smear examination showed poor spreading of smear and prominent red blood cells (RBC) clumping. On examining the vial grossly showed agglutinated on the wall (Fig 4 a, b & c). Smear prepared again after warming the sample and slide at 37^0C for 15 mins revealed marked reduction in clumping (Fig 5 a).

DCT done manually with poly-specific DAT reagent was negative. Hb-12.1g%, TLC-9700 cells/mm^3. Platelets-5.03 lakh/mm^3. Bone marrow aspirate was hypocellular for age, having hematopoietic cells of all lineages. No blast or atypical cells seen. No neoplastic/infiltrative/granulomatous pathology found in marrow biopsy (Fig 6 a, b, c, d, e, f).

A final diagnosis of cryoglobulinemia (DCT negative) in a case of colonic DLBCL was given. On reviewing the previous treatment history, it was found that during the work up of refractory anemia, he was diagnosed to have Cryoglobulinemia of Ig M type, was on treatment for 1 year but not responding to therapy. After the chemotherapy for lymphoma, the cryoglobulinemia resolved (Fig 4 c, d & Fig 5 a & b). 6 cycles of R-CHOP therapy was given till the time. After 2 cycles, cryoglobulinemia started resolving and the lymph node also subsided. Now the patient is free of symptoms.

2.2 Case 2:

A 4 year boy presented to the paediatric outpatient department with complaints of fever and generalised weakness x 15 days. On examination he had marked pallor, icterus, and splenomegaly. Hb- 2.2 g/dl. TLC- 16200 cells/mm^3. Platelet- 2.31 lakh/mm^3. Peripheral smear examination showed marked clumping of RBC which resolved after preparing the smear with a warmed sample on a warmed slide (Fig 7 a & b). DCT was positive. Bone Marrow aspirate was Normocellular for age but with erythroblastopenia and few giant normoblast showing dog ear appearance (Fig 8 a & b). Other lineages were normal. No atypical cells or blast seen. Diagnosis of Pure red cell aplasia with cryoglobulinemia was given. On complete clinical examination of the patient, a left cervical lymphadenopathy was found. FNAC from the lymph node- showed many atypical cells with polylobated nuclei. A diagnosis of high grade NHL possibly anaplastic large cell lymphoma was suggested (Fig 9 a & b). Severe persistent anaemia in a case of NHL due to marrow infiltration by malignant cells is a known entity. But the absence of atypical cells in the marrow, instead having few pseusopod like projections raises the suspicion of parvovirus B19 infection. The patient was given one dose of chemotherapy and was advised to undergo serology test for Parvovirus B19. But he did not show up for further evaluation or therapy.

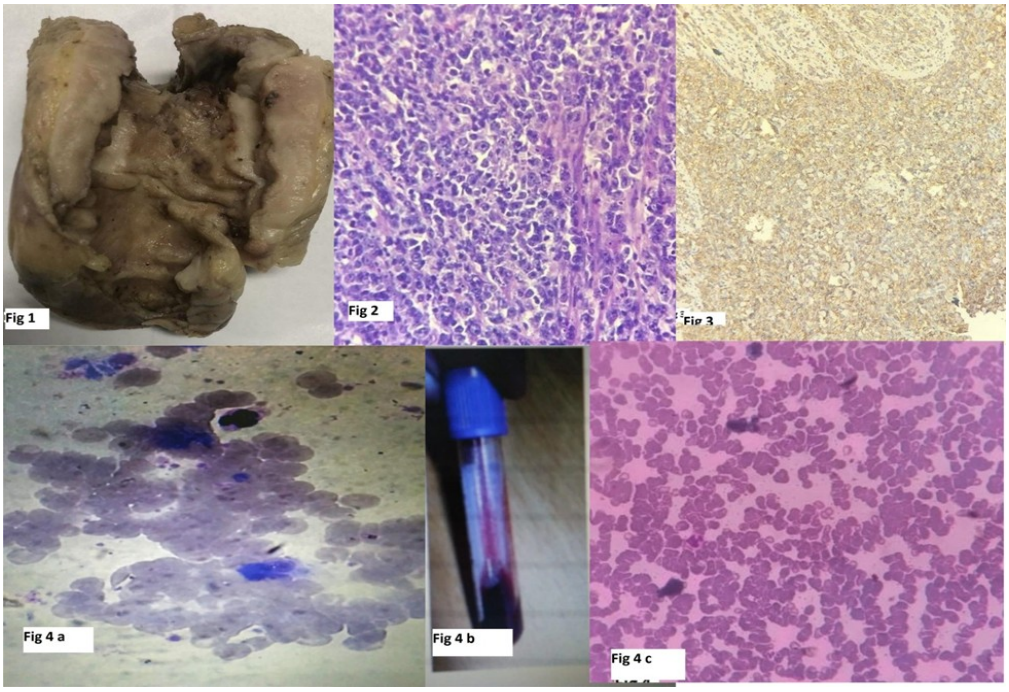

Fig 1: case 1-Mucosa flattened, no growth identified but intestinal wall thickened.
Fig 2: case 1-H & E stain 400x, Atypical lymphoid cell splaying the muscle fiber
Fig 3: case 1-IHC- CD19, 400X membrane positivity (CD 20 membrane positivity 100x)
Fig 4 a: case 1- Giemsastain - 400 x smear showing prominent RBC clumping (before chemotherapy, without incubation).
Fig 4 b: case 1 – EDTA vial showing agglutinates on the wall
Fig 4 c: case 1- smear showing marked reduction in RBC clumping (after chemotherapy, without incubation).

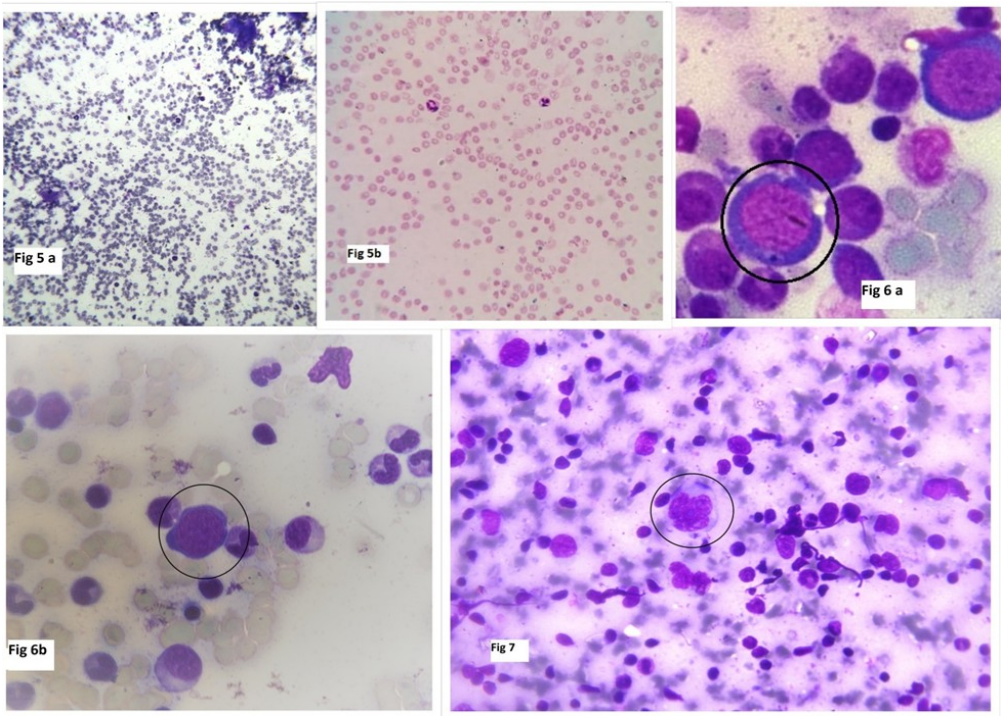

Fig 5a: case 2-Giemsa stained smear 100 x Prewarming – marked agglutination of RBC
Fig 5b: case 2-Giemsa stained smear – 100 x Post warming at 37c – marked reduction in agglutination
Fig 6a & b: case 2 - Giemsa stained smear if Bone marrow aspirate - 1000 x, Giant pronormoblast with dog ear appearance and prominent nucleoli
Fig 7: case 2-Giemsa stained FNA smear – 400 x, Atypical cells in a background of reactive lymphoid cells

3. Discussion

Cryolgobulinemia - large immunoglobulin that precipitates in cooled serum. It is commonly associated with Liver diseases (predominantly HCV), Infection (predominantly HCV). [Most common association is HCV – 40 -90%][1]. Also associated with Connective tissue disorder-SLE 25%, systemic sclerosis 12.5% Rheumatoid arthritis 46% Sjogrens syndrome 16 – 37% Lymphoproliferative disorders (5-10%). NHL-1.1-4.8%. [4] It is detected by coombs test but recently autoimmune hemolytic anemia which is DCT negative is becoming the common entity encountered. [3]

Pure red cell aplasia-Normocytic normochromic anemia with reticulocytopenia (<1%) and erythroblastopenia (<0.5% in BM). The common congenital cause is Diamond Blackfan Anaemia. There are a lot of acquired causes. In adults, it can be primarily caused by autoimmune disease / idiopathy. Secondary causative agents are divided into chronic and transient. The former is by Thymoma, CLL, Pernicious anaemia, SLE, Rheumatoid arthritis, malnutrition with riboflavin deficiency. Later is by Parvovirus B19, Cytomegalovirus, HIV, many drugs. It is uncommonly seen with NHL [2]. To the best of our knowledge this is a rare presentation of NON Hodgkin Lymphoma predating the manifestation of lymphoma, so high index of suscpicion is required to avert the misdiagnosis.

4. Conclusion

Thus 2 very rare presentations of NHL are highlighted, presenting in 2 extremes of age.

1) NHL presenting as cryoglobulinemia (DCT negative)
2) Cryoglobulinemia and Pure Red cell aplasia in a case of NHL.

Cryoglobulinemia- Incidence being low (1.1 to 4.8% of NHL)makes it a rare association that too predating the manifestation for significant time in a case of NHL, Thus awareness of the entity which is already existing makes for a better survival which happened in the index case. Cryoglobulinemia and PRCA together in NHL are not yet published to the best of our knowledge.

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