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The Diagnostic Cascade Of Non Hodgkins Lymphoma Masquerading As Transfusion Dependent Anemia : A Rare Case Report

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Abstract

Background : Transfusion-dependent anemia is characterized by the need for continuous blood transfusion. Transfusion dependence occurs when more than one unit of blood is required continuously over a specified interval. Various diseases can lead to transfusion-dependent anemia.

Aims/Purpose : Pure red cell aplasia (PRCA) is a rare haematological disorder that causes anaemia by selective inhibition of red cell precursors in the bone marrow. PRCA causes are either congenital or acquired. Acquired conditions can be either primary (idiopathic) or secondary. The cause of secondary anaemia is due to autoimmune disorders, thymoma (and other solid tumors), infections (parvovirus B19), lymphoproliferative disorders, drugs, pregnancy, etc.

Method : A 62-year-old male presented with a history of transfusion-dependent anemia. After Routine haematological and biochemical investigations along with bone marrow examination, he was diagnosed as PRCA. **Result** : A repeat PET guided bone marrow biopsy was executed that revealed lymphoproliferative disorder and after immunohistochemistry, the final diagnosis was made as B-cell non-Hodgkin lymphoma with secondary PRCA.

Conclusion : An interdisciplinary approach is essential for prompt diagnosis and subsequent treatment in cases having diagnostic dilemmas.

Keywords: pure red cell aplasia, non-Hodgkin lymphoma, transfusion-dependent anaemia

Introduction

Pure red cell aplasia (PRCA) is a rare disorder of blood production in which the bone marrow fails to function in an adequate manner, resulting in anemia. It is a normocytic normochromic anaemia with severe reticulocytopenia and a marked reduction or absence of erythroid precursors from the bone marrow exclusively involving erythroid precursors, while myeloid and megakaryocytic lineages are spared.[1-4] The causes of PRCA are diverse. However, they can be divided into two categories: congenital and acquired.[5] Congenital, also known as Diamond–Blackfan syndrome, is estimated to have 5–7 cases per 1 million live births.

Primary (idiopathic) and secondary acquired conditions are the two types of acquired conditions. The cause of secondary anaemia is due to autoimmune disorders, thymoma (and other solid tumors), infections (Parvovirus B19), lymphoproliferative disorders (T-LGL, CLL, NHL, MPN), drugs, and pregnancy. The disease is thus heterogeneous in nature, and its aetiology varies in different parts of the world.[6,7]

Clinical History

A 62-year-old male presented to the hematology clinic *with chief* complaints of fatigue and generalised weakness. Diagnosed as having low haemoglobin at his native place, he had transfusions every month in the last 3 months, with a total of 8 units transfused before admission. When he presented at our institute, a detailed history was taken. There was no history of bleeding symptoms, black stools, fever, loss of appetite, weight loss, jaundice, bone pain, or joint pain. Bowel and bladder habits were normal, with no comorbidities or addictions. Also, there was no past history of transfusions 3 months ago. All vital signs were normal, and on examination, pallor was present with no evidence of icterus, lymphadenopathy, hepatosplenomegaly, or edema. The remaining systemic examination was normal. Biochemical tests revealed the following results: LDH 301units\l, urea 17mg\dl, creatinine 0.8mg\dl, bilirubin 0.8mg\dl, and iron 289mcg\dl.All viral markers (HIV, HBsAg, and HCV) were non-reactive. A hemogram demonstrated severe anaemia (Hb 4.7 g%) with a normal leukocyte count (5,700 cells/mm^3) and adequate platelets (2.16 l/mm^3). On peripheral blood examination, RBCs were normocytic, normochromic with normal differential leucocyte counts and no immature cells. The reticulocyte count was 0.4% (corrected to 0.15%).

Results

Looking at the selective suppression of haemoglobin with a reduced reticulocyte count and no evidence of peripheral destruction of RBCs or blood loss, a bone marrow examination was conducted after taking proper consent of the patient. Bone marrow aspirate from the right iliac bone was done, which showed erythroid hypoplasia and increased lymphoid cells that came out to be reactive by flow cytometry and IHC on the bone marrow biopsy.[Figure 1] This confirmed the diagnosis of pure red cell aplasia. As a result, additional research was conducted to determine the etiology. Parvovirus-B19 DNA was not detected by qualitative PCR. The ANA test by immunofluorescence was negative. Whole-body PET/CT showed mildly FDG-avid sub-centimetric cervical, left supraclavicular, infraclavicular, mediastinal, pelvic, and inguinal lymph nodes along with a marrow lesion in the left iliac bone, likely indicative of metabolically active disease. A PET/CT-guided biopsy was conducted of the left iliac bone. H&E stained section showed atypical lymphoid cell proliferation. On immunohistochemistry (IHC), these lymphoid cells were diffusely immunopositive for CD 20 and immunonegative for CD-3 and CD-10.[Figure 2] So, the final diagnosis was B-cell non-Hodgkin lymphoma with secondary PRCA.

Follow Up

After this, the patient was subjected to R-CHOP chemotherapy (Rituximab 375 mg/m2, Cyclophosphamide 750 mg/m2, Doxorubicin 50 mg/m2, and Vincristine 1.4 mg/m2 (max 2 mg)) and oral steroids (tablet prednisolone 60 mg OD for 4 weeks, tapering over the next 4 weeks). Following this treatment, Hb improved steadily, and the patient became transfusion-free after the 2^{nd} cycle of R-CHOP. After three cycles of R-CHOP, an interim PET-CT was performed to assess treatment response. A complete metabolic response to treatment was noted as compared to the initial PET-CT. Another 3 cycles of the R-CHOP regime were given, and a 3^{rd} PET-CT was done, in which there was no definite evidence of abnormal hypermetabolism elsewhere in the body. A long-term follow-up was done. At the 18-month follow-up, the patient had completed 6 cycles of chemotherapy and was doing well; his haemoglobin was consistently greater than 11 g/dL.

Discussion

Pure red cell aplasia (PRCA) is a syndrome defined by normocytic normochromic anemia with severe reticulocytopenia and marked reduction or absence of erythroid precursors from the bone marrow. It is a condition that is usually detected when all other causes of anaemia have been considered and ruled out. The diagnosis usually requires a high index of suspicion, especially when the standard investigations do not give a lead or the routine management of anaemia fails to improve the patient's haemoglobin. Any patient presenting with isolated anaemia and reticulocytopenia requires evaluation for PRCA. The low reticulocyte count helps differentiate PRCA from haemolytic anemia, which can also have isolated anemia, albeit with reticulocytosis.

Within PRCA, a differentiation should be made between inherited, acquired, and transient PRCA.[1,2,3] For acquired PRCA, look for secondary causes, as listed in the aetiology above. Bone marrow

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should be examined thoroughly to rule out MDS, which can present with isolated anaemia and reticulocytopenia. In addition, if there is no evidence of any other cause of PRCA, we should do PET CT so that we can see the metabolic active site. As in this case, we were able to diagnose B non-Hodgkin lymphoma using a radiological approach.

Conclusion

Interaction among pathologists, radiologists, clinicians, and other specialists on a regular basis will undoubtedly improve diagnostic accuracy in difficult cases. This would enhance diagnostic skills, minimise misinterpretations, and improve the overall quality of patient life. Increased collaboration among clinicians, radiologists, and pathologists can also lead to greater understanding and more accurate conclusions in diagnostically challenging cases[8].

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Figure no. 1 A)Bone marrow aspiration from right iliac bone (Giemsa stain 100x view) : Show increased lymphoid, 1 B) Bone marrow biopsy from right iliac bone (H&E stain 40x view) : show erythroid hypoplasia, increased megakaryocytes and lymphoid cells.

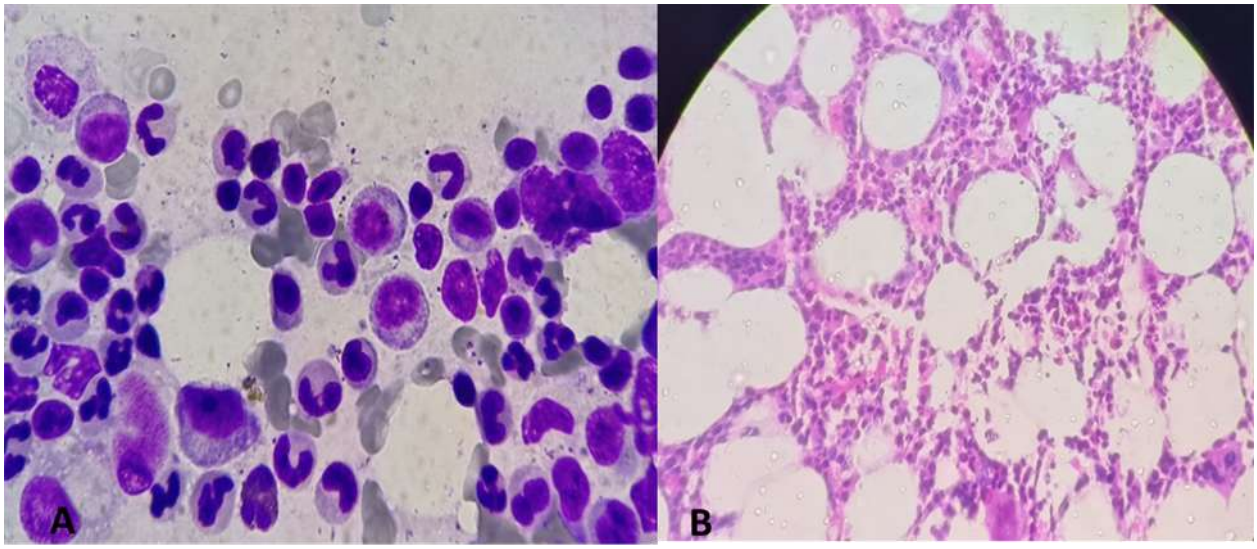

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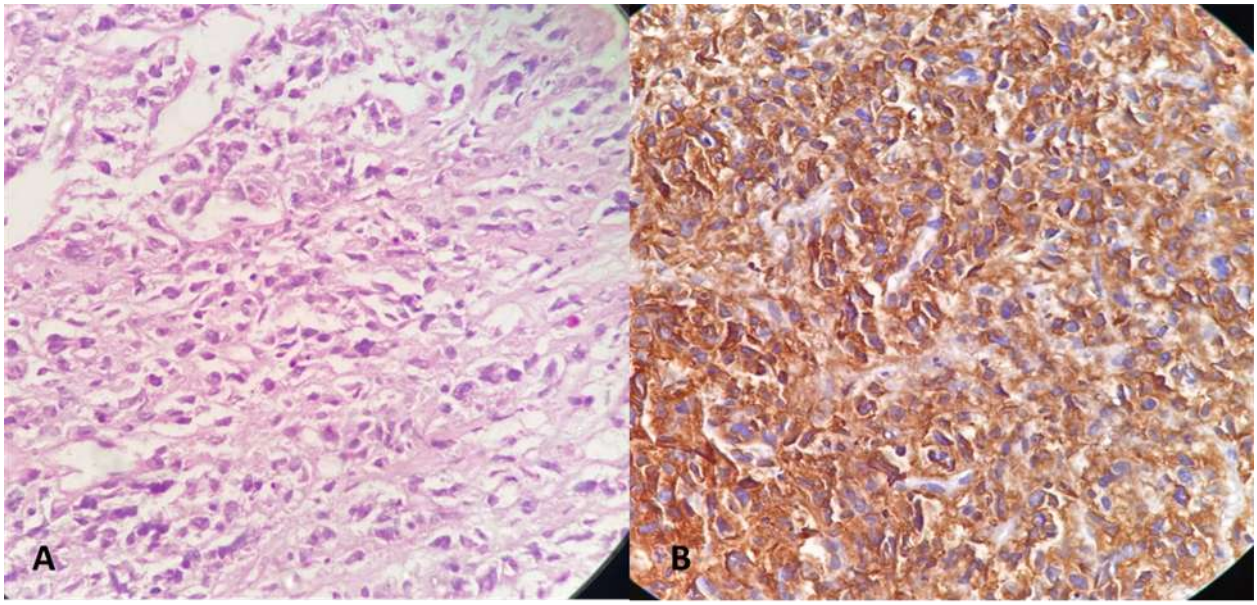
Figure no. 2 A) Bone marrow biopsy from left iliac bone (H&E stain 40x view) : Atypical lymphoid cell proliferation B) IHC on bone marrow biopsy from left iliac bone – Diffuse CD 20 positive



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