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# Unraveling the Conundrum: A Case Report of Hodgkin Lymphoma Masquerading as Pure Red Cell Aplasia Secondary to Parvovirus Infection in a Pediatric Patient

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## ABSTRACT

Pure Red Cell Aplasia (PRCA) is a rare hematological disorder characterized by a marked reduction or absence of erythroid precursors in the bone marrow. It often presents with severe anemia and reticulocytopenia, necessitating a comprehensive diagnostic workup to elucidate its etiology. Parvovirus B19 infection has been recognized as a common cause of transient PRCA in children, typically resolving spontaneously with the clearance of the viral infection. We present a unique case of a pediatric patient initially presenting with features consistent with PRCA following parvovirus B19 infection. Despite the resolution of the viral infection, the patient continued to exhibit persistent anemia and lymphadenopathy, prompting further investigation. Subsequent bone marrow biopsy revealed an unexpected diagnosis of Hodgkin lymphoma, highlighting the intricate diagnostic challenges that can arise in the evaluation of hematologic disorders in pediatric patients. This case underscores the importance of maintaining a high index of suspicion for alternative etiologies in patients with refractory anemia, even after the resolution of the inciting infection. Through this report, we aim to elucidate the clinical

course, diagnostic challenges, and management considerations in this rare and intriguing presentation of Hodgkin lymphoma masquerading as PRCA secondary to parvovirus infection in a pediatric patient.

**Keywords:** Hodgkin lymphoma; Pure red cell aplasia; Parvovirus B19; Pediatric patient; Haemtological disorders

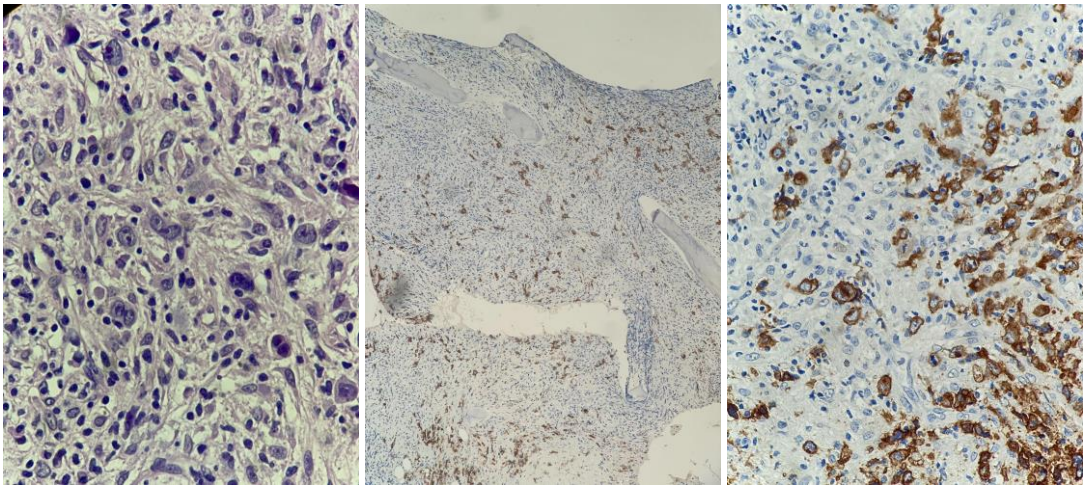
## INTRODUCTION

Approximately 40% of people diagnosed with Hodgkin's lymphoma (HL) exhibit anemia as a presenting symptom[1]. The aforementioned condition is commonly detected in later phases and is typically accompanied by B symptoms, including fever, night sweats, and weight loss. Typically, the anemia observed is characterized by normocytic and normochromic features and tends to be of mild severity, with hemoglobin (Hb) values ranging from 10 to 12 g/d[2]. The occurrence of anemia in chronic disease is observed in a diverse range of inflammatory conditions, such as chronic infections, acute systemic inflammatory response syndrome, inflammatory disorders, and some types of malignancies. The condition known as iron-refractory anemia is distinguished by the presence of low levels of iron in the blood (known as hypoferremia), a decrease in iron-binding capacity, and lower-than-normal transferrin saturation[3,4]. However, the iron content in the bone marrow remains largely intact. The utility of conventional biochemical iron markers, such as serum iron, ferritin, and transferrin saturation, is constrained due to the influence of inflammation, which can skew their measurements[5]. Serum ferritin levels serve as valuable indicators of iron status in individuals lacking chronic underlying conditions; nevertheless, they exhibit an increase in individuals with inflammatory diseases. Elevated ferritin levels have been observed in patients diagnosed with Hodgkin's lymphoma, particularly in advanced stages and during the development of the disease[6]. This report presents a case study of a pediatric child who experienced the development of hemolytic anemia as an initial indication of Hodgkin lymphoma. In the present report, we emphasize this observation as a paraneoplastic symptom of Hodgkin lymphoma, which warrants consideration while investigating the etiology of anemia.

## CASE PRESENTATION

A 9-year-old boy presented to the Armed Forces Institute of Pathology, Rawalpindi, with a twenty-day history of high-grade fever associated with chills, cough, and reduced appetite. He was transfused 04 units of RCC and was started on ATT (based on cough and infiltrate on chest X-ray) 06 days ago before reporting to us. On examination, his cervical lymph nodes were palpable and moderate splenomegaly was found. His HRCT chest revealed extensive anterior and middle mediastinal lymphadenopathy which was suggestive of a lymphoproliferative disorder. At AFIP, his complete blood picture showed hypochromic microcytic anemia with a total leucocyte count (TLC) of $8.17x10^9$/L, red blood cell counts of $4.85x10^{12}$/L, hemoglobin level 9.9g/dL, and platelets count was 300 $x10^9$/L. The absolute reticulocyte count was $24x10^{12}$/L (0.5%). For further work, his bone marrow examination was done which revealed a normocellular aspirate with markedly depressed erythropoiesis (<5%), myelopoiesis was hyperplastic showing maturation and megakaryocytes were increased. Trephine biopsy showed similar findings with no evidence of lymphocytic infiltrate. The diagnosis of red cell aplasia (most likely acquired) was made. PCR for Parvovirus B19 was carried out which came to be positive with a quantitative count of 1297 copies/ml. He was started on antiviral therapy but after one month of treatment with steroids, antivirals, and antibiotics his fever did not settle. Meanwhile, his cervical lymph node biopsy and histopathology were also done

which was suggestive of chronic granulomatous lymphadenitis. His MTB gene Xpert was done to rule out tuberculosis which also came out to be negative. The persistent symptoms led to a decision to repeat a CT scan Chest and CT abdomen and Pelvis which revealed marked interval progression in the number and size of mediastinal lymph nodes and increasing hepatosplenomegaly. Follow-up bone marrow examination was recommended after one month of previous marrow examination. In the second bone marrow examination, red cell aplasia was diminished, with a recovered normoblastic (>30%). However, bone marrow trephine biopsy revealed a well-defined focal area of infiltrate consisting of scattered Reed Sternberg (RS) cells and mononuclear Hodgkin cells with an inflammatory background of reactive T cells, plasma cells, eosinophils, and fibroblasts, as shown in (Figure 1)(a). Immunohistochemistry (IHC) showed CD 30 positive and differential staining of PAX-5 in the Hodgkin infiltrate, as shown in Figure 1(b) and 1(c). Thus, final diagnosis of Hodgkin Lymphoma infiltrating bone marrow was made and the patient was treated accordingly.



(a) (b) (c)

**Figure 1:** (a) Low-power (40x magnification) hematoxylin and eosin (H&E) stained image showing scattered Reed Sternberg (RS) and mononuclear Hodgkin cells in the trephine biopsy. (b) 10x magnification Immunohistochemistry (IHC) staining showing CD 30 positivity in the Hodgkin infiltrate. (c) 40x magnification Immunohistochemistry (IHC) staining revealing CD 30 positivity.

## DISCUSSION

Anemia, a frequent presenting symptom, affects around 40% of Hodgkin's lymphoma patients[7]. The etiology of severe anemia in the majority of patients seems to be associated with the underlying primary disease. However, in certain cases, the administration of alkylating drugs or irradiation, infections, uremia, or blood loss may contribute as aggravating factors. The anemia associated with Hodgkin lymphoma has been characterized morphologically as normochromic and hypochromic[8]. There is often observed evidence of heightened haemolysis, as indicated by the presence of reticulocytosis, elevated levels of serum bilirubin, increased excretion of fecal urobilinogen, and an augmented need for transfusions[9,10]. Spherocytosis and heightened osmotic fragility have been observed in certain individuals, although these irregularities are often not prevalent[11]. The Coombs antiglobulin test often yields negative results, although a small number of cases have been documented where positive outcomes were observed[12,13]. The investigation of red cell survival in four patients diagnosed with

Hodgkin lymphoma-associated anemia demonstrated an elevated rate of red cell destruction, ranging from two to four times higher than the standard rate[14,15]. The development of anemia in Hodgkin lymphoma seems to be influenced by an elevated rate of red blood cell breakdown[16]. Nevertheless, the limited data on red cell survival in a small number of patients indicate a slightly higher rate of erythrocyte breakdown. However, this alone does not seem to be enough to account for the occurrence of anemia. This is because the bone marrow, which is considered to be functioning normally, is believed to have the ability to increase the production of erythrocytes adequately to offset red cell destruction rates that are six to eight times higher than the usual rate[17]. This implies that there exists a certain factor that restricts the capacity of the bone marrow to significantly enhance the rate of erythropoiesis to offset the modestly heightened rate of haemolysis. There is a lack of documented quantitative investigations examining the erythropoietic activity of the bone marrow in individuals with Hodgkin disease[18]. Nevertheless, it is worth noting that untreated anemic patients typically exhibit normoblastic hyperplasia of the marrow and moderate to considerable reticulocytosis[9,19]. This suggests that the marrow possesses the ability to enhance erythropoiesis to a certain degree as we observed in our case study. Several aberrant results observed in patients with anemia of chronic infection have also been documented in individuals diagnosed with Hodgkin disease[20]. Therefore, it can be observed that both kinds of anemia exhibit hypoferremia, elevated erythrocyte protoporphyrin levels, hypercupremia, increased urine coproporphyrin levels, and heightened tissue iron reserves in the liver and spleen. The results of this study indicate that a potential cause restricting the production of hemoglobin in Hodgkin lymphoma-related anemia could be a malfunction in iron metabolism, resembling the identified iron metabolism abnormalities in chronic infection-related anemia[17].

## CONCLUSION

Anemia can present as a paraneoplastic condition in the context of lymphoproliferative disorders such as Hodgkin lymphoma. It is imperative to investigate the fundamental etiology of anemia, even in cases when it proves resistant to therapeutic interventions. Through this report, we highlight the diagnostic challenges and the significance of interdisciplinary collaboration in managing complex hematologic conditions in children.

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