CASE REPORT

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Positive autocontrol minor incompatibility in pure red cell aplasia patient: A case report

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ABSTRACT

Introduction: Pure red cell aplasia (PRCA) is a syndrome of normochromic normocytic anemia with severe reticulocytopenia and marked reduction or absence of erythroid precursors in the bone marrow. The serum of PRCA patients often contains immunoglobulin G (IgG) antibodies that suppress the growth of erythroid progenitor cells in vitro. This report focused on the diagnosis and management of a PRCA case.

Case Description: A 5-year-old boy presented with complaints of pallor for two days and generalized weakness for five days. Medical history included a tuberculosis infection, for which he underwent treatment with anti-tuberculosis drugs, including rifampicin and isoniazid. He had a history of recurrent pallor and multiple hospitalizations due to decreased hemoglobin levels, requiring routine blood transfusions since 2018 at Wahidin Sudirohusodo Hospital. Laboratory investigations revealed normochromic normocytic anemia, severe reticulocytopenia, and bone marrow aspiration findings of normocellular marrow with significantly reduced erythropoiesis activity. Crossmatch testing showed minor incompatibility (1+) and autocontrol positivity (1+), with the degree of minor incompatibility matching the positive autocontrol results, indicative of erythrocytes coated with autoantibodies. Monoclonal Direct Coombs Test (DCT) findings included IgG positivity (1+) and C3d negativity. Packed red cell (PRC) transfusion was successfully administered under medical supervision.

Conclusion: This case highlights a 5-year-old boy diagnosed with pure red cell aplasia based on clinical presentation, physical examination findings, and laboratory investigations. The patient's treatment involved blood transfusion, which was administered with appropriate precautions to manage the underlying anemia effectively.

Keywords: *crossmatch, incompatibility, pure red cell aplasia*.
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INTRODUCTION

Pure Red Cell Aplasia (PRCA) is a syndrome of normochromic normocytic anemia with severe reticulocytopenia and marked reduction or absence of erythroid precursors in the bone marrow.[1] The clinical presentation of PRCA is nonspecific, with signs and symptoms solely attributable to anemia. This reflects the pure underproduction of erythrocytes, leading to a gradual decline in hemoglobin concentration and total blood volume. It allows for some physiological adaptation and the subsequent manifestation of symptoms.[1]

Abnormalities in PRCA are limited to the erythroid lineage, and any abnormalities in other hematopoietic lineages typically indicate additional coexisting conditions.[1,2] Congenital PRCA primarily includes Diamond-Blackfan anemia and Pearson syndrome, linked to specific genetic defects affecting ribosome and mitochondrial function.[2,3] In contrast, acquired PRCA can be categorized as primary or secondary. Primary acquired PRCA is an autoimmune disorder where immune mechanisms impair erythroid differentiation.[4] Autoantibodies, such as those targeting erythroid progenitors or the erythropoietin receptor, have been implicated, though their exact targets are often unknown.[4,5] The presence of immunoglobulin G (IgG) antibodies in the serum of PRCA patients has been shown to suppress the in vitro growth of erythroid progenitor cells. At the same time, T-cell-mediated inhibition of erythropoiesis has also been demonstrated, indicating the involvement of both humoral and cellular immune mechanisms in its pathogenesis.[5] Secondary PRCA is associated with various conditions, including autoimmune or collagen vascular disorders, infections (notably parvovirus B19), pregnancy, hematological malignancies, non-hematological neoplasms, thymoma, and exposure to drugs or toxic agents.[6] Medications such as diphenylhydantoin, azathioprine, isoniazid, and rifampin have been linked to IgG-mediated inhibition of erythropoiesis.[1]

The diagnosis of PRCA involves laboratory evaluation, including a complete blood count with reticulocyte determination. A characteristic finding is an absolute reticulocyte count of less than 10,000/µL.[1] Bone marrow analysis reveals decreased or absent erythroblasts, while immunological and cytogenetic assessments, including T-cell receptor clone analysis, are performed to identify specific variants, such as myelodysplastic PRCA.[1,7] Clinically, PRCA presents as normochromic normocytic anemia resulting from reduced erythrocyte production.[8] Reticulocyte counts are markedly low, and erythrocyte

concentrations decline at approximately 1 g/dL per week, consistent with the average lifespan of erythrocytes.[8] This report focused on the diagnosis and management of a PRCA case.

CASE

A 5-year-old boy presented with complaints of pallor that began two days prior and generalized weakness persisting for five days before admission to the hospital emergency department. The weakness was continuous and unrelieved by rest. The patient denied symptoms such as nausea, vomiting, shortness of breath, cough, chest pain, palpitations, epistaxis, gum bleeding, petechiae, or reduced appetite. There were no complaints of urination, and the feses were soft and yellow-brown in consistency. The patient had a history of tuberculosis infection and had undergone treatment with anti-tuberculosis drugs, including rifampicin and isoniazid. He also had a recurrent history of pallor, frequent hospitalizations due to decreased hemoglobin levels, and regular blood transfusions since 2018 at Wahidin Sudirohusodo Hospital. No transfusion reactions were reported during these routine procedures.

On physical examination, the patient appeared moderately ill but alert and conscious (compos mentis), with a body weight of 17.7 kg and a height of 110 cm, indicating good nutritional status. Vital signs were within normal limits: blood pressure 90/60 mmHg, pulse 100 beats per minute (regular), respiratory rate 24 breaths per minute (regular), temperature 36.8°C, and oxygen saturation 99%. Anemic conjunctiva was observed, but the sclera was non-icteric, and there were no signs of cyanosis, dyspnea, or lymphadenopathy. Chest examination revealed symmetrical expansion, normal vocal fremitus, sonorous percussion in both lung fields, and bronchovesicular breath sounds without rhonchi or wheezing. Cardiac examination showed pure and regular heart sounds (S1/S2) with no murmurs. Abdominal examination revealed a distended abdomen, normal peristalsis, and hepatomegaly, with the liver palpable 6 cm below the costal arch and 4 cm below the xiphoid process. The liver surface was smooth, with sharp edges and no tenderness. The spleen is palpable *Schuffner 4* and has a rubbery consistency. Genital examination found 2 testes in the scrotum, each measuring 1.5x1x0.5 cm with a rubbery consistency. On examination of the extremities, both hands' palms appear pale and warm.

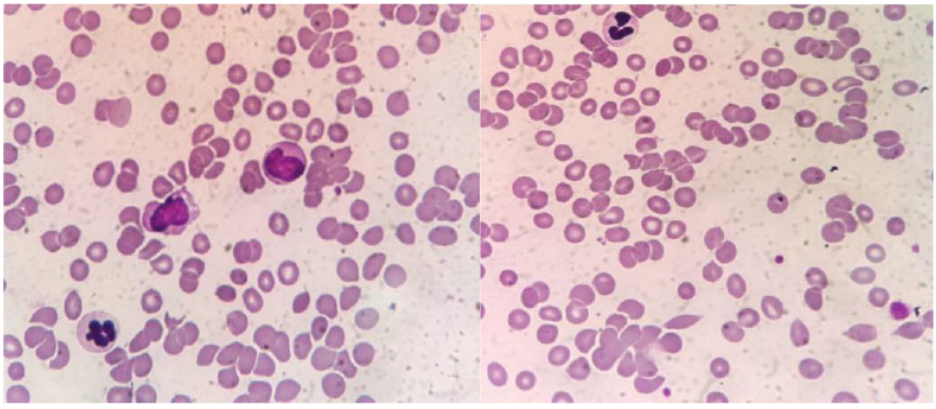

Figure 1. Blood smear result (Objective magnification 100x).

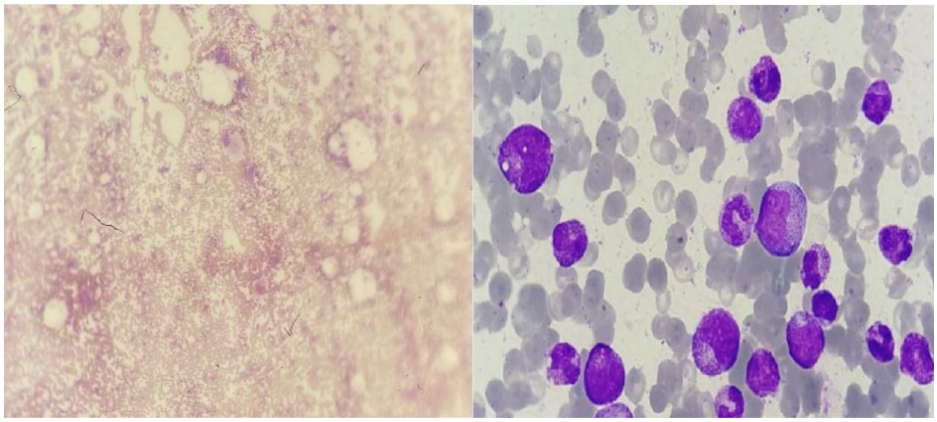

Figure 2. Bone marrow aspiration (left, objective magnification 10x; right, objective magnification 10x).

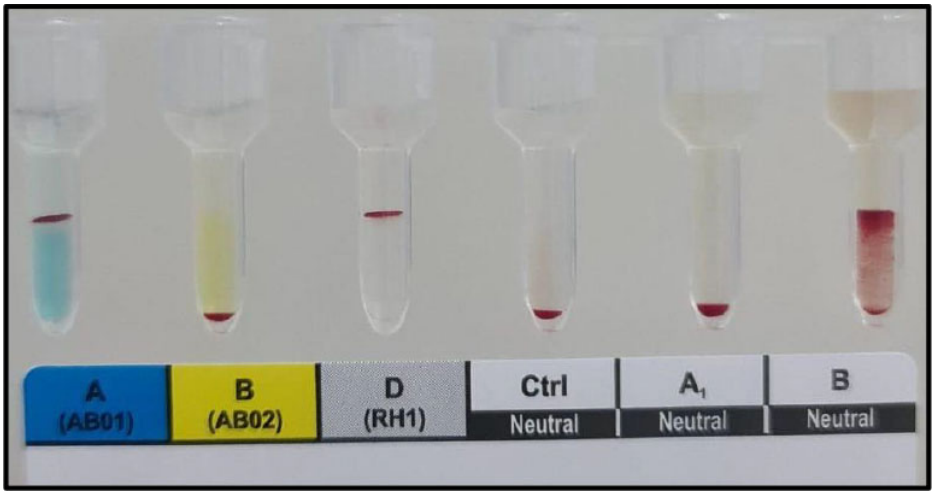

Figure 3. Blood type examination with gel test (colum agglutination test).

Blood laboratory examination showed hemoglobin 7.0 gr/dl, leukocytes 4.7 x 103/µL, platelets 148 x 103/µL, MCV 85 fL, MCH 28 pg, MCHC 33 g/dL, reticulocytes 0.20 x 103/µL with the impression of normochromic normocytic anemia and reticulocytopenia. The peripheral blood smear examination found suspected biscytopenia myelodysplastic

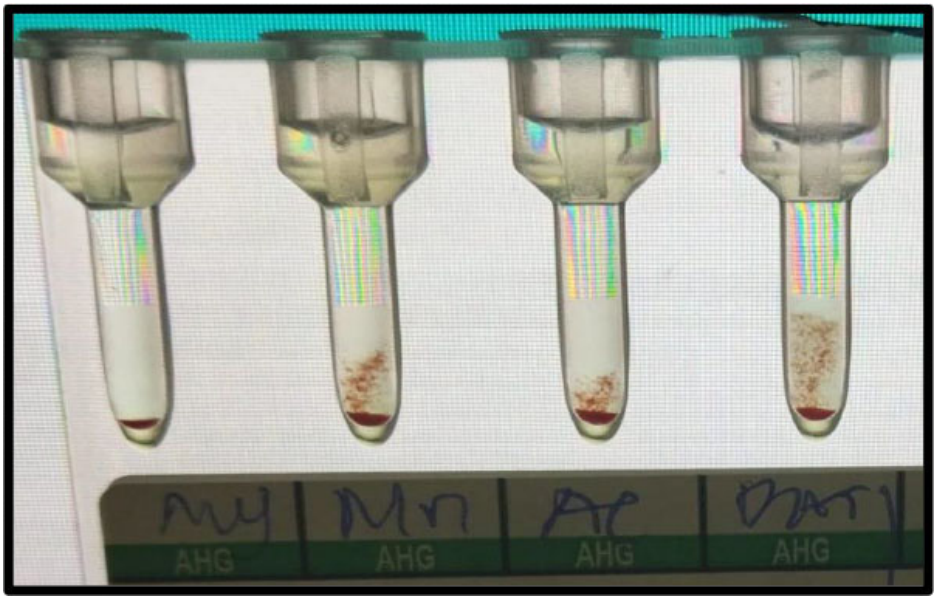

Figure 4. Crossmatch with gel test (column agglutination test).

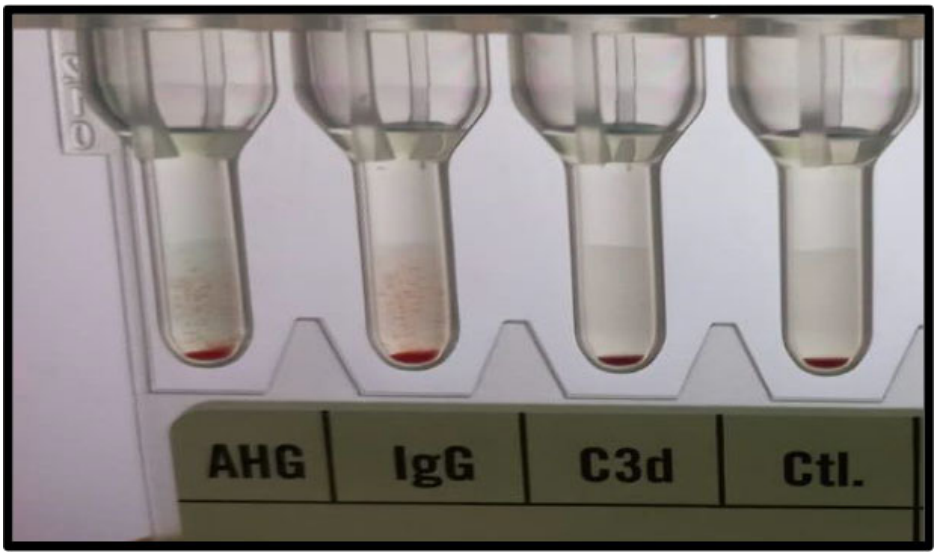

Figure 5. Monoclonal direct Coombs test (DCT) examination.

syndrome (MDS) and bone marrow aspiration suggestion (Figure 1). Bone marrow aspiration examination found normocellular marrow with significantly decreased erythropoiesis activity differential diagnosis/Pure Red Cell Aplasia (Figure 2).

Blood typing (Figure 3) identified the patient as blood type A with Rhesus D positive. Crossmatch testing (Figure 4) revealed one positive minor incompatibility, one positive auto control, and two positive direct Coombs tests (DCTs). A prior crossmatch test one month earlier showed similar results, with two positive minor incompatibilities, two positive autocontrols, and two positive DCTs. Monoclonal DCT analysis (Figure 5) identified one positive IgG and negative C3d, indicating immune antibody involvement. The findings suggested sensitization of red blood cells in vivo by immune antibodies, including IgG and complement (C3d).

The patient was diagnosed with PRCA complicated by positive minor incompatibility and autocontrol. Despite the crossmatch results showing minor incompatibility (1+), autocontrol positivity (1+), and a positive DCT (2+), a packed red cell (PRC) transfusion was administered after premedication with intravenous dexamethasone (5 mg) and diphenhydramine (10 mg). Follow-up laboratory results on day 4 showed hemoglobin 8.8 g/dL, leukocyte count 5.3 × 10^3/µL, and platelet count 156 × 10^3/µL.

DISCUSSION

The clinical diagnosis of pure red cell aplasia (PRCA) in this patient was established based on the patient's complaints, physical examination findings, and laboratory results. The patient presented with pallor for two days and generalized weakness for five days before admission, with clinical signs including pale conjunctiva. Anemia in PRCA arises due to ischemia in target organs and compensatory mechanisms triggered by decreased hemoglobin levels.[9] The patient's medical history included tuberculosis infection and treatment with anti-tuberculosis drugs, specifically rifampicin and isoniazid. These medications, along with diphenylhydantoin and azathioprine, are known to be associated with secondary PRCA through inhibition of IgG-mediated erythropoiesis.[1]

Physical examination findings included pale conjunctiva, tachycardia, hepatomegaly (liver palpable 6 cm below the costal arch and 4 cm below the xiphoid process, with a flat surface, sharp edges, and no tenderness), and splenomegaly (Schuffner grade 4, with a rubbery consistency). The presence of organomegaly in this patient is likely attributable to extramedullary hematopoiesis. This compensatory process occurs when the bone marrow cannot adequately meet the body's demands for blood cell production.[10]

Laboratory findings revealed hemoglobin 7.0 g/dL, mean corpuscular volume (MCV) 85 fL, mean corpuscular hemoglobin (MCH) 28 pg, mean corpuscular hemoglobin concentration (MCHC) 33 g/dL, and reticulocyte count 0.20 × 10^3/µL. These results are consistent with normochromic normocytic anemia and reticulocytopenia, supporting the laboratory diagnosis of Pure Red Cell Aplasia (PRCA). Anemia and reticulocytopenia in PRCA result from the absence of erythroid precursors in the bone marrow, which impairs erythropoiesis.[1] The abnormalities observed in PRCA are restricted to the erythroid lineage, and abnormalities in other hematopoietic

lineages typically indicate the presence of other concurrent disorders.[1,2] Peripheral blood smear analysis confirmed normochromic normocytic anemia, with normal leukocyte formation and platelet counts.[1,7]

Bone marrow aspiration revealed normal marrow cellularity with markedly reduced erythropoietic activity. Isolated erythroid precursors were identified. In primary autoimmune PRCA, normal marrow cellularity with preserved myeloid and megakaryocyte maturation is characteristic, along with an absence or significant reduction of erythroblasts. In some cases, rare proerythroblasts or basophilic erythroblasts may be present, accounting for no more than 5% of the differential count.[1] The pathogenesis of PRCA involves autoimmune mechanisms, with patient serum demonstrating the presence of immunoglobulin G (IgG) antibodies that inhibit the in vitro growth of erythroid progenitor cells. Additionally, T-cell-mediated inhibition of erythroid proliferation has been implicated, with evidence pointing to anti-erythroid precursor cell antibodies and T-cell-mediated suppression of erythropoiesis.[5]

The diagnosis of PRCA is established based on the diagnostic triad of normochromic normocytic anemia, reticulocytopenia (<1%), and bone marrow aspiration findings demonstrating a significant reduction in erythropoietic activity.[1,8] In this patient, routine blood tests revealed hemoglobin 7.0 g/dL, mean corpuscular volume (MCV) 85 fL, mean corpuscular hemoglobin (MCH) 28 pg, mean corpuscular hemoglobin concentration (MCHC) 33 g/dL, and reticulocyte count 0.20 × 10^3/µL. Peripheral blood smear findings confirmed normochromic normocytic anemia, while bone marrow aspiration showed normocellular marrow with markedly decreased erythropoiesis.

Monoclonal Direct Coombs Test (DCT) findings included positive IgG (1+) and negative C3d, indicating the presence of autoantibodies bound to the patient's erythrocyte surfaces. The Coombs test detects antibodies or complement proteins attached to erythrocytes. These antibodies, specific to erythrocyte surface antigens, cause agglutination of the erythrocytes.[11] Crossmatch testing in this patient identified one positive minor incompatibility and one positive auto control. The degree of minor agglutination incompatibility matched that of the positive autocontrol, further supporting the presence of autoantibodies coating the erythrocytes.[11]

Blood transfusion was administered under medical supervision using packed red cell (PRC) products. PRCA results in anemia due to severely reduced erythrocyte production, with reticulocyte counts markedly diminished and erythrocyte concentration decreasing at an approximate weekly rate of 1 g/dL, consistent with the average erythrocyte life span.[8] Transfusion of one unit of PRC per week is typically required to prevent severe anemia and maintain adequate hemoglobin levels.[8] In this case, the patient received a total PRC transfusion volume of 485 mL intravenously in three stages: 95 mL in the first, 185 mL in the second, and 205 mL in the third. The transfusion was conducted successfully, improving the patient's clinical condition and achieving the target hemoglobin level of 10 g/dL. No transfusion reactions were observed during or immediately after PRC administration, and the patient demonstrated a satisfactory hematological response.

CONCLUSION

A case of a 5-year-old boy presenting with pallor for two days and generalized weakness for five days before hospital admission was reported. Based on clinical complaints, physical examination findings, laboratory investigations, and bone marrow aspiration results, the patient was diagnosed with PRCA. In PRCA, the serum typically contains IgG antibodies that inhibit the growth of erythroid progenitor cells in vitro. Crossmatch testing in this patient revealed one positive minor incompatibility and one positive auto control. At the same time, the Direct Antiglobulin Test identified one positive IgG and negative C3d, indicating the presence of autoantibodies on the surface of the patient's erythrocytes. Blood transfusion therapy, specifically PRC transfusion, was administered under close medical supervision to address the patient's severe anemia. Further studies should focus on the long-term management of PRCA, including the efficacy of immunosuppressive therapies and alternative treatment options to minimize transfusion dependency.

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ETHICAL CONSIDERATION

The patient has provided informed consent and has agreed to this writing.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

All authors equally contributed to the preparation of this report.

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REFERENCES

1. Means RTJ. Pure red cell aplasia. Blood. 2016 Nov;128(21):2504–9. Available from : DOI: 10.1182/blood-2016-05-717140.
2. Arbiv OA, Cuvelier G, Klaassen RJ, Fernandez C V, Robitaille N, Steele M, et al. Molecular analysis and genotype-phenotype correlation of Diamond-Blackfan anemia. Clin Genet. 2018 Feb;93(2):320–8. Available from : DOI: 10.1111/cge.13158.
3. Bergmann AK, Campagna DR, McLoughlin EM, Agarwal S, Fleming MD, Bottomley SS, et al. Systematic molecular genetic analysis of congenital sideroblastic anemia: evidence for genetic heterogeneity and identification of novel mutations. Pediatr Blood Cancer. 2010 Feb;54(2):273–8. Available from : DOI: 10.1002/pbc.22244.
4. Cerchione C, Catalano L, Cerciello G, Avilia S, Picardi M, Risitano AM, et al. Role of lenalidomide in the management of myelodysplastic syndromes with del(5q) associated with pure red cell aplasia (PRCA). Vol. 94, Annals of hematology. Germany; 2015. p. 531–4. Available from : DOI: 10.1007/s00277-014-2192-z.
5. Keithi-Reddy SR, Kandasamy S, Singh AK. Pure red cell aplasia due to follow-on epoetin. Kidney Int. 2008 Dec;74(12):1617–22. Available from : DOI: 10.1038/ki.2008.230.
6. Yang XY, Chen L, Gu JN, Zeng CJ, Pan DM. Linezolid-Induced Pure Red Cell Aplasia:

A Case Report. Vol. 15, Infection and drug resistance. New Zealand; 2022. p. 3847–56. Available from : DOI: 10.2147/IDR.S362358.
7. Balasubramanian SK, Sadaps M, Thota S, Aly M, Przychodzen BP, Hirsch CM, et al. Rational management approach to pure red cell aplasia. Haematologica. 2018 Feb;103(2):221–30. Available from : DOI: 10.3324/haematol.2017.175810.
8. Gurnari C, Maciejewski JP. How I manage acquired pure red cell aplasia in adults. Blood. 2021 Apr;137(15):2001–9. Available from : DOI: 10.1182/blood.2021010898.
9. Widaya K and Pardjono E. Immune Hemolytic Anemia. In Setiati S, Alwi I, Sudoyo AW, Simadibrata M, Stiyohadi B, Syam AF. Textbook o. Jakarta: Interna Publishing; 2014. 2607–13 p.
10. Cenariu D, Iluta S, Zimta AA, Petrushev B, Qian L, Dirzu N, et al. Extramedullary Hematopoiesis of the Liver and Spleen. J Clin Med. 2021 Dec;10(24). Available from : DOI: 10.3390/jcm10245831.
11. Mulyantari, NK. Yasa I. Pretransfusion Laboratory Update. Udayana University Press. Bali; 2016.