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Idiopathic pure red cell aplasia: A case series from India

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ABSTRACT

Pure red cell aplasia (PRCA) is a rare hematologic disorder characterized by normocytic normochromic anemia with reticulocytopenia and depleted erythroid precursors. It is reported mainly from western countries. We report our experience in two patients of PRCA from India, the clinical characteristics, differential diagnosis, and their management. Our patients showed improvements following treatment with corticosteroids, blood transfusion, and/or rituximab.

Key words: Pure cell red aplasia; PRCA; Rituximab; Corticosteroid; Prednisolone

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INTRODUCTION

Pure red cell aplasia (PRCA), an anemia caused due to failure of erythropoiesis, is a rare syndrome, which can be acquired or inherited (congenital).[1,2] The key characteristics of PRCA include normocytic normochromic anemia with decreased reticulocyte count (reticulocyte percentage <1%). Furthermore, erythroid precursor depletion from bone marrow is a prerequisite for PRCA.[2-4]

Congenital PRCA is mainly Diamond-Blackfan anemia whereas acquired PRCA is primary autoimmune PRCA primary myelodysplastic PRCA, or secondary to autoimmune or lymphoproliferative disorders, hematological malignancies, solid tumors, infections, certain medications, riboflavin deficiency, or pregnancy.[3,5]

In most cases, PRCA is idiopathic and the exact etiology of PRCA remains unknown.[6] PRCA has been reported to be associated with several other diseases, such as T-cell large granular lymphocytic leukemia, thymoma, myasthenia gravis, and Good syndrome, which may also affect the management of these patients.[7]

PRCA is treated as immunogenic disease and the first choice treatment is corticosteroids. Blood transfusion is used extensively in these patients. Immunosuppressive agents such as cyclosporine and monoclonal antibody rituximab have been successfully used in the treatment of PRCA.[4,7,8] Due to the rarity of the disease, only a few case reports, case series, or retrospective analyses are available on PRCA. These reports are majorly from the western countries, and the data on PRCA are scarcely reported from

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India. We here report our experience with two patients of PRCA from India. We describe the clinical characteristics, laboratory investigations, differential diagnosis and therapeutic management with corticosteroids, blood transfusion, and/or rituximab.

CASE PRESENTATION

Patient 1

A 38-year-old male patient was referred to medical oncology outpatient department for anemia under evaluation in view of bicytopenia and low hemoglobin (Hb) levels. The patient was asymptomatic 2 months before then he gradually developed fatiguability. He visited the local doctor. His Hb was 3 mg/dL and he was transfused one unit packed red blood cells (PRBC). Around 1 month later, the patient was admitted at Pacific Medical College and Hospital, Udaipur, for further evaluation and management.

His medical history showed ankylosing spondylitis, for which he had stopped the treatment 2–3 years back. The current general physical examination showed that pallor was present. The vitals on admission were: Blood pressure (BP) 110/770 mmHg, pulse rate 94/min, and oxygen saturation (SpO_2) 95% (radial artery). The initial laboratory investigations revealed: Hb 2.4 g/dL (range: 13.0–16.3 g/dL), red blood cell (RBC) count 0.92 million/μL (range: 3.8–5.0 million/μL), packed cell volume (PCV) 7.4% (range: 36–46%), reticulocytes (corrected for anemia) 0.1% (range: 0.5–2.5%), serum iron 249 (33–193) μg/dL (range: 60–170 μg/dL), serum ferritin 802 (30–400) μg/L (range: 240–450 μg/dL), total iron binding capacity (TIBC) 279 (259–388) μg/dL (range: 240–450 μg/dL), serum haptoglobin 2.8 mg/dL (range: 41–165 mg/dL), serum homocysteine 8.9 (3.7–13.9) μmol/L (range: 5–15 μmol/L), and LDH 127 (135–225) IU/L (range: 105–133 IU/L). The direct and indirect Coombs tests were negative. His renal function tests (RFTs), liver function tests (LFTs), serum electrolytes, and routine urine investigations were within the normal limits, and 2D echocardiogram was normal.

The patient was transfused 6 units of PRBC. Bone marrow aspiration and biopsy were done. Bone marrow aspiration showed reactive cellular marrow aspirate with suppressed erythropoiesis. Bone marrow biopsy showed hypercellular marrow with suppressed erythropoiesis, which was suggestive of red cell aplasia (RCA). The patient was discharged with an Hb level of 8.7 mg/dL.

One month later, he was again admitted as a follow-up case (FUC) of PRCA with Hb level of 4 mg/dL and was transfused five units of PRBC. His ultrasonogram (USG) of abdomen showed mild hepatomegaly and moderate splenomegaly. The patient was treated with tab prednisolone 70 mg in 24 h. He was discharged with Hb level of 8.9 mg/dL.

Six months later, he was again admitted as a FUC of PRCA with Hb level of 8.2 mg/dL. His treatment plan for PRCA included weekly intravenous rituximab administration at a dose of 650 mg. His Hb levels were: 8.2 mg/dL at the 1st rituximab dose, 11.1 mg/dL at the 2nd rituximab dose, 11.4 mg/dL at the 3rd rituximab dose, and 11.4 mg/dL at the 4th rituximab dose.

Patient 2

A 22-year-old female presented to the medicine out-patient department with the complaints of fatiguability, giddiness, and shortness of breath on exertion from the past 3 months.

The history of present illness showed that the patient was asymptomatic 3 months before and then gradually developed the aforementioned symptoms. She visited a local doctor and her Hb was 2.7 g/dL, PCV was 5.64%, RBC count was 0.76 million/μL, and platelet count was 4.7 lakhs/μL. She was diagnosed with severe iron deficiency anemia. She was admitted to Ravindra Nath Tagore Medical College, Udaipur, for treatment. Her laboratory investigations were as follows: Hb 1.9 (13.5–18) g/dL, reticulocyte count 1.2% (0.5–1.5%), serum iron 301 (33–193) μg/dL, serum ferritin 944 (30–400) μg/L, and TIBC 310 (259–388) μg/dL. She was transfused with 4 units of PCV and received treatment with tab. Iron folic acid, tab. multivitamin B complex, and tab albendazole. With this treatment, her laboratory parameters improved: Hb 8.3 g/dL, RBC Count 2.6 (3.8–5.8) million/μL and PCV 22.4 (35–50)%.

The current general physical examination revealed that pallor was present. The vitals on admission were: BP 96/64 mmHg, pulse rate 94/min, and SpO_2 98% (radial artery). Initial investigations revealed that Hb was 4.6 g/dL (range: 13.0–16.3 g/dL), RBC 1.66 million/μL (range: 3.8–5.0 million/μL), PCV 13.9% (range: 36–46%), reticulocyte count (corrected for anemia) <0.5% (range: 0.5–2.5%), and erythrocyte sedimentation rate 145 mm/h (range: 0–29 mm/h). The peripheral blood film test reported normocytic normochromic anemia. Her RFTs, LFTs, serum electrolytes, routine urine examination, and USG of abdomen were normal. Her 3-h fecal occult blood test and COVID-19 tests were negative. Serum iron was 216 μg/dL (range: 60–170 μg/dL), serum ferritin was 573 μg/L (range: 240–450 μg/dL), TIBC was 241 μg/dL (range: 240–450 μg/dL), and unsaturated iron-binding capacity was 25 μg/dL (range: 111–343 μg/dL). Hb electrophoresis

test was normal. She was treated with ferrous ascorbate and folic acid. She was transfused 2 units of PRBC.

Her anti-nuclear antibody profile was negative. Bone marrow aspiration showed cellular marrow aspirate with suppressed erythropoiesis. Bone marrow biopsy showed hypercellular marrow with suppressed erythropoiesis-suggestive of RCA. She was diagnosed with severe anemia with PRCA. She was discharged 5 days later with Hb level of 7 g/dL.

Two days later, the patient was again admitted under oncology department with Hb level of 6.6 g/dL, RBC 2.3 million/μL and LDH 183 (135–225) IU/L. Polymerase chain reaction test for detection of human parvovirus B19 was negative. Her erythropoietin level was >750 (5.4–31) mU/mL. She was transfused one unit PRBC and received treatment with prednisolone 20 mg twice a day. Three days later, she was discharged with an Hb level of 10.6 g/dL and RBC 3.6 million/μL.

DISCUSSION

PRCA is a rare hematological disorder which shows the characteristics of severe normocytic anemia, reticulocytopenia, and absence of erythroblasts from bone marrow. PRCA can be differentiated from aplastic anemia in having integral precursors for thrombocytes and leukocytes, which in the peripheral blood are normal in number and morphology.[1] PRCA was first described in 1922 by Kaznelson but till date has not been evaluated in clinical trials due to the rarity of the disease.[1] We reported the clinical characteristics and treatment outcomes in two patients, who developed idiopathic PRCA. PRCA lack the specific signs and symptoms. Swollen lymph nodes, hepatomegaly, and splenomegaly are indicative but not definitively diagnostics for PRCA. Pallor is also present in all PRCA patients.[1] Similarly, our patients reported pallor.

Iron levels, ferritin levels, and TIBC are done to determine the iron overload in PRCA patients, which were also performed in our patients. The differential diagnosis of PRCA from hemolytic anemia includes reticulocytopenia. Both our patients had reticulocytopenia.[1]

Bone marrow examination is required to distinguish acquired from congenital PRCA and also to rule out MDS pathology for acquired PRCA.[1] Bone marrow examination revealed hypercellular marrow with suppressed erythropoiesis, which suggested PRCA in our patients. Coombs test is indicative of hemolytic anemia and these can be used for differential diagnosis with PRCA. In our patient, negative Coombs test supported the PRCA.

PRCA has been reported in patients having Severe Acute Respiratory Syndrome coronavirus 2 infections.[9] In our patient, COVID-19 test was negative.

Shao et al., have reported that acquired PRCA can be secondary to ankylosing spondylitis, which is an autoimmune disorder and combination treatment of immunosuppressants with hematopoiesis stimuli is effective in these patients.[10] One of our patients had a history of ankylosing spondylitis.

Considering the immune based pathologic mechanism of PRCA, immunosuppressive agents are the first-line therapy; cyclosporine and corticosteroids combination have reported high response rates ranging from 66% to 95%.[2] Several other agents such as rituximab, sirolumab, and daratumumab have shown improved response rates in PRCA patients. Recently, a retrospective evaluation (n=64) from China reported successful treatment of PRCA with sirolimus-based therapy in terms of hemoglobin improvement.[11] Daratumumab demonstrated rapid and sustained response in treatment-refractory acquired idiopathic PRCA in a 74-year-old patient.[12] Daratumumab also successfully managed a patient of post-transplant PRCA with responses observed within 3 weeks.[13] Rituximab successfully managed two patients with PRCA secondary to CLL, and the patients became transfusion independent.[8] As per the treatment algorithm for acquired PRCA by Gurnari and Maciejewski, rituximab should be used in refractory PRCA patients with B-cell lymphoproliferation.[7] In our report, one patient with PRCA demonstrated response to the weekly rituxuimab therapy with improved Hb levels. Another patient was managed with corticosteroid therapy and blood transfusion.

CONCLUSION

PRCA is a recurrent disease and requires long-term treatment, frequent blood transfusions, and iron chelation therapy. PRCA patients generally respond to immune based therapies. Patients and physicians should be made aware on the disease and management aspects considering the rare and long-term nature of PRCA.

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