DOI: 10.7860/JCDR/2014/7840.4250

Case Report

Internal Medicine Section

Recurrent Severe Anaemia: A Rare Presentation of Parvovirus B19 Infection

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ABSTRACT

Secondary pure red cell aplasia is usually seen in immunocompromised hosts or patients who have chronic haemolytic anaemia, which is caused by blood transfusion related transmission. The present patient, a 30-year-old immunocompetent female, presented several times with recurrent severe anaemia, over a period of one and half years. Her history, clinical examination and investigations did not reveal any indigenous drug intake, previous blood transfusions, haemolytic disorders, myeloproliferative disorders, pregnancies, autoimmune diseases or thymoma. She was found to have a thalassaemia minor trait, on the basis of which severity and recurrence of anaemia could not be explained, and on further evaluation, she was diagnosed to have acute aplastic crisis caused by Parvovirus B19 induced, acquired pure red cell aplasia. The co- existence of these two haematological disorders in an immunocompetent, non-transfusion dependent individual is rare, which makes our case report unique.

Keywords: Secondary pure red cell aplasia, Beta thalassemia minor trait, Non transfusion dependent, Immunocompetent individual

CASE REPORT

A 30-year-old, non-pregnant female from Himachal Pradesh, northern India, presented to Medical Outpatient department in March 2011 with chief complaints of progressively increasing generalized weakness and easy fatiguability, of 3 months duration. Patient denied having any history of upper or lower gastrointestinal bleeding, menorrhagia, jaundice, passage of worms in stools or bleeding from any other site, fever, rash, joint pains, drug intake, neck lumps or swellings or weight loss. There was no history of decreased urine output, passage of frothy urine, early morning facial puffiness or pedal oedema. There was no past history of blood transfusions or of any indigenous drug intake. Physical examination revealed a markedly pale looking female who had a regular pulse rate of 84 beats per minute and a blood pressure of 130/84 mm of Hg. Icterus, clubbing, oedema, lymphadenopathy, haemorrhagic spots, malar rash and gum hypertrophy were absent. Thyroid was not enlarged. There was no sternal tenderness or any joint deformity. Systemic examination did not reveal any organomegaly. Investigations showed Hb- 3.4 gm%, TLC- 4200/ cu mm, DLC- 54% Neutrophils, 44% Lymphocytes, 1% Monocytes and 1 % Eosinophils. Platelet Count - 1.8 lac/ cu mm, RBC count- 3.2 million/ cu mm, MCV- 83.9, MCH-30.1, MCHC- 35.9. PBF showed a marked degree of anisopoikilocytosis, with normocytic RBCs with moderate hypochromia, with few microcytes and few large oval macrocytes. Corrected reticulocyte count was 0.8%. Serum Bilirubin was 0.8 mg/dl, SGOT-15 IU/L, SGPT-18 IU/L. B. Urea-25 mg/dl, S. Creatinine-0.8 mg/dl. LDH-248 U/L. Direct and indirect Coomb's tests were negative. HBsAg, anti HCV and HIV were non reactive. Serum Iron studies showed normal findings, as did serum Vit. B12 (843.11 pg/ml) and serum folic acid (> 20 ng/ml) studies. Serum electrolytes were normal and so was the urine complete examination. Stool for occult blood showed negative results. Bone marrow aspiration showed a normocellular marrow with micronormoblastic and megaloblastic changes and a myeloid: erythroid ratio of 4:1. Chest radiographs and ultrasonography of abdomen showed normal results. Patient was transfused 3 units of blood and she was also put on oral haematinics. Patient was discharged in a stable condition with her Hb level measuring 11.2 gm % and she was advised follow up in Medical Outdoor Dept, which she failed to do.

Two months later, she again presented to Medical Outdoor department with gross pallor and generalized weakness. Her Hb was 3.6 gm%. Her peripheral blood smears and bone marrow findings were same as before. She was given 4 units of blood along with oral haematinics and was discharged with Hb levels of 10.8 gm%. Her subsequent weekly OPD visits revealed a progressive fall in Hb and at six weeks of follow up, her Hb level was 7.6 gm%. Haemoglobin electrophoresis was done three months after last blood transfusion, which showed HbF< 0.01% (N), Peak A2- 4.60% (N), Hb Adult- 81.40% (slightly low), HbA2–6.20% (2×ULN) findings, which were suggestive of a diagnosis of Beta Thalassaemia Minor. Her haematological indices were normal, except for Hb-4.1 gm%, Haematocrit-30% and RBC counts of 2.7 million/cu mm. She denied having any family history which was suggestive of haemolytic anaemia. Patient refused bone marrow examination and was discharged after getting three units of blood transfused. Patient was lost for follow up again.

Five months later, she got admitted to Emergency department in a comatosed and tachypneic state with a history of high grade fever, with rigors and chills, low back ache, myalgias and pain in both the knee joints, of two days duration. She had recieved twenty units of blood transfused in past five months. She was normotensive and pale looking and had a respiratory rate of 46 per min. Her pupils were dilated but they were responsive to light. There was no neck stiffness. Her chest was clear. Patient had exaggerated reflexes and both the plantars were extensor. Her oxygen saturation was 32 %. Patient was intubated and shifted to intensive care unit, considering a possibility of Systemic Inflammatory Response Syndrome with Hypoxaemic Encephalopathy. Hb was 2.0 gm%, TLC was 25,970/cu mm, DLC was 68% with polymorphs without any toxic granulations, band forms or shifts to the left, 28% lymphocytes, 4% monocytes, platelet count was 6,36,000/ cu mm, RBC count was 1.2 million per cu mm, MCV-106.2 fL, MCH- 30.8 pg, MCHC- 29.0 g/dl. Her LFT and RFT studies showed normal pictures. ABG showed hypoxaemia. Her iron studies were suggestive of an iron overload state which was reflected by *S. Ferritin*- 1068 ng/ml (5 * ULN), S.Iron- 121 µg/dl (N), TIBC- 305 µg/dl (N), Percentage Saturation- 40% (N). She was empirically given intravenous imipenem, ciprofloxacin and metronidazole. She was also administered 2 units of packed RBCs on day 1, followed by one unit per day for a week, along

with iron chelator, Deferasirox. Her bone marrow aspiration showed a paucicellular marrow with an M:E ratio of 30:1, normoblastic erythropoiesis, a borderline blast count and occasional granulocytic precursors. Bone marrow trephine biopsy which was done, revealed a reduced erythroid series, an adequately represented granulocytic series and presence of immature cells interstitially, along with a relative increase in marrow reticulin content, which were suggestive of pure red cell aplasia. Blood sample taken for Real Time PCR which was done for Parvo virus B19, was sent in view of her clinical setting and it was positive. CT scan of chest did not reveal any thymic enlargement. Patient was prescribed oral prednisolone 60 mg/day, which was planned to be tapered over a period of one month. Patient's general condition improved gradually and she was discharged after 3 weeks of admission. Patient was also advised a quantitative estimation of the Parvovirus and she was counseled about i.v.immunoglobulins, which she could not afford due to financial constraints. Patient is on regular follow-up since then and she is persistently maintaining Hb levels in range of 11.2 ± 0.8 gm/dl without any haematinics, since past seven months.

DISCUSSION

Pure red cell aplasia, also known as regenerative anaemia, erythroblast hypoplasia, erythroblastopaenia, red cell agenesis, is defined as erythropoietic hypoplasia which occurs in the absence of abnormalities in the leukopoietic or thrombocytopoietic systems. The first case of pure red cell aplasia was described by Kaznelson in 1922. Congenital variant of this disorder is known as Diamond Blackfan Anaemia and it is rarely seen in adulthood. Its acquired form is associated with autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, myasthenia gravis, autoimmune haemolytic anaemia, acquired hypoimmunoglobulinaemia, and thymoma, and with lymphoproliferative processes such as CLL and Hodgkin's disease, in which immune dysregulation is common, Parvovirus infection or drugs like diphenylhydantoin, sulfa and sulfonamide drugs, azathioprine, allopurinol, isoniazid, procainamide, ticlopidine, ribavirin, and penicillamine. Pure red cell aplasia which occurred in pregnancy and in CKD patients who underwent haemodialysis and received recombinant erythropoietin, which caused eprex epidemic in 2002 due to auto antibody mediated phenomenon, has also been reported [1-3]. Parvovirus B19 is toxic to erythroid progenitor cells and it specifically infects them. Normally, Parvovirus infection is terminated by the humoural immune response within 1 to 2 weeks of infection, but in the absence of an effective antibody response, infection persists and causes pure red cell aplasia [4]. The usual bone marrow findings in acute parvovirus infections are marked erythroid hypoplasia and occasional giant erythroblasts. Intranuclear inclusions seen in developing erythroid precursors have been rarely described in children or adults with Parvovirus infection, although abundant intranuclear inclusions are commonly observed in the placentae and other tissues in infected foetuses [5].

Present case had recurrent episodes of severe anaemia over a period of one and a half years, which eventually turned out to be secondary pure red cell aplasia caused by persistent Parvovirus B19 infection, which eventually manifested as an acute aplastic crisis. An extensive study of literature showed the association of Parvovirus with thalassaemia in a majority of cases which belonged to paediatric age group, which was considered to result from multiple blood transfusions given to thalassaemic children. The unique features seen in our case report were an adult patient having a thalassaemia minor trait, who had acquired Parvovirus infection through an alternative route other than repeated blood transfusions, the usual cause which was considered in thalassaemic individuals. The possibility of an alternative route was considered, since she had not received any blood transfusion prior to her first presentation, which implied that she had active infection at her first visit itself, which was a rare presentation in an immunocompetent adult and hence, this case is being reported.

The main treatment options are transfusion therapy with appropriate iron chelators, immunosuppressants in the form of corticosteroids, cyclosporine or azathioprine. In refractory cases, rituximab (anti- CD 20 monoclonal antibody) or alemtuzumab (anti-CD 52 monoclonal antibody) can be used [6]. Role of plasmapheresis has also been described by some authors [7]. In cases with persistent Parvovirus infections, i.v. immunoglobulins play a major role in treatment, especially in immunocompromised individuals [8].

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Oct 08, 2013**
Date of Peer Review: **Dec 30, 2013**
Date of Acceptance: **Feb 01, 2014**
Date of Publishing: **Apr 15, 2014**