Pure Red Cell Aplasia in a Three-Months-Old Infant Possibly Secondary to Cytomegalo Virus Infection

Devki Nandan · Afsana Jahan · Vivek Dewan ·
Sarman Singh · Gurdeep Buxi

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Abstract We report a 3 months old child who presented with severe anemia due to pure red cell aplasia (PRCA). After ruling out other known causes of PRCA, congenital cytomegalovirus (CMV) infection was diagnosed to be the cause. The child responded to Ganciclovir and is doing well. CMV infection should be considered as differential diagnosis in PRCA during infancy.

Keywords Pure red cell aplasia · Cytomegalovirus

Introduction

Pure red cell aplasia (PRCA) is a specific entity characterised by anaemia, reticulocytopenia and reduced or absent erythroid precursor cells with preservation of other haematopoietic lineage in bone marrow [1]. PRCA is

characterised by decreased or absent red cell production which may be due to primary defect in erythroid progenitor cell e.g. Diamond-Blackfan syndrome (DBS) [2] or secondary to transient erythroidblastopenia of childhood (TEC), infections, drugs, collagen vascular diseases, leukaemia, lymphoma, thymoma, solid tumours, haematopoietic stem cell transplantation etc. [3–5]. As such it is a rare entity in infants and its association with congenital cytomegalovirus (CMV) infection, to the best of our knowledge has only once been reported in children [6]. We here in report a three-months-old infant with severe PRCA and active congenital CMV infection who responded to treatment with Ganciclovir and is doing well in follow up.

Case Report

A three-months-old male infant born to a second gravid mother out of non-consanguineous marriage by full term normal vaginal delivery in hospital with a birth weight of 2.899 kg, presented with increasing pallor and breathing difficulty for last 2 months. Antenatal period of mother was uneventful. Patient had a history of receiving blood transfusion on fortieth day of life for severe anaemia. There was no history of recurrent blood transfusions among the family members. On admission, infant was conscious, had severe pallor, heart rate of 138/min, respiratory rate of 64/min, chest retractions and pedal oedema but no lymphadenopathy, cyanosis or clubbing were noted. Cardiovascular system examination revealed a short systolic flow murmur over apical area. Liver was palpable 4 cm. Below the right costal margin and spleen was palpable 3 cm. Below the left costal margin. Investigations showed haemoglobin 2 gm/dl, total leukocyte count (TLC) of 26,000/mm³, differential

D. Nandan · A. Jahan · V. Dewan
Department of Pediatrics, Post Graduate Institute of Medical
Education and Research, Dr. Ram Manohar Lohia Hospital,
New Delhi, India 110001

D. Nandan (✉)
D-3/3210, DDA SFS Flat, Vasant Kunj, New Delhi 110070,
India
e-mail: devkinandan2002@yahoo.com

S. Singh
Division of Clinical Microbiology, All India Institute of Medical
Sciences, New Delhi, India

G. Buxi
Department of Pathology, Post Graduate Institute of Medical
Education and Research, Dr. Ram Manohar Lohia Hospital,
New Delhi, India 110001

Fig. 1 Peripheral blood smear showing normocytic normochromic anemia with no evidence of haemolysis

count (DLC) polymorphs, 86 %; lymphocytes, 12 %; eosinophil, 02 % platelet count of $3.8 \times 10^5/\text{mm}^3$ and peripheral smear revealed normocytic normochromic anaemia (Fig. 1). C-reactive protein was negative, urine and blood culture were sterile. Patient was given antibiotics, packed cell transfusion (10 ml/kg) and furosemide. The reticulocyte count was found to be persistently below 0.5 %. Bone marrow biopsy report was suggestive of erythroid aplasia (Fig. 2) Investigations were done to find out causes of PRCA (Table 1). TORCH profile of mother and baby was positive for CMV Ig M. CMV PCR in baby's urine was also positive. In the absence of common causes of PRCA such as Diamond Blackfan syndrome, viral infections like Parvo virus B19, Rubella, HIV, viral hepatitis, but a positive Ig M CMV in mother's and baby's sera as well as a positive CMV PCR in baby's urine, a diagnosis

of congenital CMV infection was made and patient was treated with 6 mg/kg/dose 12 hourly intravenous Ganciclovir for 6 weeks [7]. Over next 6 weeks, patient improved remarkably showing improvement of anemia and regression of hepatosplenomegaly. Repeat haemogram after 6 weeks showed a hemoglobin of 8.3 g/dl, TLC of $15,600/\text{mm}^3$, DLC of polymorph, 41 %; lymphocyte, 53 %; eosinophil, 6 %, platelet count of $7 \times 10^5/\text{mm}^3$ and reticulocyte count of 1.2 %. He is doing well in follow up.

Discussion

As this patient had severe normocytic normochromic anaemia with persistent reticulocytopenia and bone marrow was showing evidence of PRCA, he was evaluated for the causes of PRCA in infancy, reported till date [2–5]. DBS was ruled out by presence of normocytic normochromic anemia and normal fetal hemoglobin [8]. Other acquired causes of PRCA that present during infancy, that were ruled out were Parvo virus B 19, hepatitis A, B, C infection, vitamin B12, folic acid deficiency and immunodeficiency states. TEC, the most common cause of PRCA, usually presents after 6 months of age and resolves without treatment. Therefore, this case was diagnosed to be PRCA possibly secondary to CMV infection. It may be recommended that in a case of PRCA in infants a thorough review of the diagnostic possibilities both congenital and acquired causes including CMV infection should be done in a very young infant.

Fig. 2 Bone marrow biopsy showing cellular marrow, marked preponderance of myeloid precursors seen in various stages of maturation variable numbers of lymphocytes, plasma cells and very

occasional normoblast are seen. Megakaryocytes are adequately functioning and iron stores are normal

Table 1 Investigations to rule out other causes of anaemia

Investigations	Report.
Serum Total/direct/indirect Bilirubin (mg/dl)	0.7 (0.2–1.2)/0.2 (0.1–0.3)/0.5 (0.2–1.1)
SGOT/SGPT (IU/l)	502 (15–50)/376 (15–50)
Blood culture and sensitivity	Sterile
Osmotic fragility	Normal
Serum LDH (IU/l)	300 (220–400)
Serum Iron/TIBC/UIBC (µg/dl)	170 (60–150)/300 (250–400)/200 (150–250)
Percentage saturation (%)	25 (15–50)
Serum vitamin B12 (pg/ml)	300 (211–911)
Serum Folate (ngm/ml)	25 (5–38)
Bone marrow biopsy	Cellular with marked preponderance of myeloid precursors in various stages of maturation, variable number of lymphocytes and plasma cells, very occasional normoblasts, and adequately functioning megakaryocytes were seen
G6PD (U/gm Hb)	8 (4.6–13.5)
IgM Toxoplasma	Negative
IgM Rubella	Negative
IgM HSV	Negative
IgM Parvo virus B 19	Negative
IgM CMV	Positive
HBS Ag (ELISA)	Negative
ANTI HCV (ELISA)	Negative
X-RAY & CT scan CHEST	Normal with normal thymus shadow
Mothers	
TORCH profile	Positive for CMV
HIV I & II	Negative
Hemoglobin electrophoresis	HbA0-90.8 %, Hb F-6.5 % and HbA2-2.7 %.
Serum immunoglobulin levels (mg/dl)	Ig G: 800; Ig M: 56; A: 110

LDH Lactate dehydrogenase, *TIBC/UIBC* Total/unsaturated iron binding capacity, *G6PD* Glucose 6 phosphate dehydrogenase, *HSV* Herpes simplex virus, *CMV* Cytomegalo virus, *HBs ag* Hepatitis B surface antigen, *Anti HCV* Anti hepatitis C virus antibody

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Conflict of interest None.

Fund None.

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