

Diamond Blackfan Anemia A Rare Anemia of Infancy

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Introduction

Diamond Blackfan anemia (DBA) is a rare anemia characterized by failure of erythropoiesis, with normal production of white blood cell and platelets.

Children with anemia without pancytopenia were first described in 1936 and again in 1938^{1,2}. Many other names have been applied to this syndrome including congenital hypoplastic anemia, chronic congenital aregenerative hypoplastic anemia and erythrocytogenesis imperfecta. There are approximately 400 cases reported in the literature. Of the reported cases, male and female are equally affected. Most cases are Caucasian, but blacks, oriental and Indians have been reported.

Approximately 30 to 40% patients have congenital anomalies, most common finding is short stature followed by deformities in craniofacial region and upper limb, mostly involving thumb^{3,4}. The inheritance of Diamond Blackfan anemia is not clear, 10 to 15% of cases are familial⁵. Diamond Blackfan anemia (DBA) belongs to the emerging class of ribosomal disorder, it links to mutations in the ribosomal protein genes rps19, rps 24, and rps 17⁶. To date there are no definite tests to diagnose DBA. Prenatal diagnosis is currently only possible if there is mutation affecting Rps19. The diagnostic criteria include⁷:

- Normochromic, often macrocytic anemia with reticulocytopenia developing early in childhood.
- Bone marrow with normal cellularity and usually a deficiency of red cell precursors.
- Normal or slightly decreased leukocyte count.
- Normal or often increased platelet count.

Complete blood count and films shows a normochromic anemia but normal white cells and platelet count. The red cell MCV is often high. Bone marrow confirms aplasia. The enzyme adenosine

deaminase (eADA) in the red blood cell is usually raised. Radiological manifestations are those of the thumb malformation which is usually triphalangeal, and may be bifurcated, hypoplastic or subluxed.

About 30% of patient with Diamond-Blackfan anemia respond to oral prednisolon. High dose methyl prednisolon sometimes work. Cyclosporine alone with steroid also works in some cases⁸. Blood transfusion is only treatment who does not respond to steroid. Bone marrow transplantation^{9,10} and haematopoietic stem cell transplantation¹¹ are definitive mode of treatment.

At least five patients have been reported in India¹². Considering the rarity of the disease, we decided to report the case.

Case Report

A 4 months old male child of nonconsanguineous parents hailing from Tongi presented with gradual pallor for last 2 months along with cough and cold. He was a full term baby delivered by cesarean section with birth weight of 2.7kg. He developed convulsion on 3rd day of life and convulsion occur once only, all other



Fig.-1: Baby boy having no dysmorphic facies

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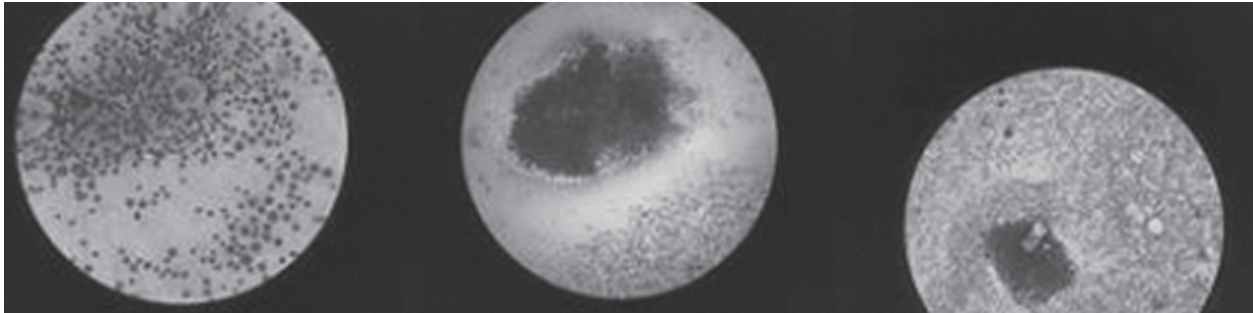


Fig.-2: Bone marrow slide of pure red cell aplasia (Diamond blackfan anemia)

investigation was normal except blood sugar level which was low. At one month of age the boy suffered from pneumonia. He was on formula milk along with breast milk. His milestone of development was age appropriate. His mother was on regular antenatal checkup and did not have any significant illness during pregnancy and had no family history of similar illness.

On physical examination, baby was malnourished with weight 4kg (WAZ-3.1 (SD) and length 56cm, OFC 38.5cm (LAZ 2.5SD). He had severe palor without any dysmorphic facie (Fig.-1) and had tachycardia and tachypnoea. There was no organomegaly. Investigation showed anemia (haemoglobin 3.9g/dl), with normal red cell morphology (Red cell count $01.10^{12}/L$, MCV: 84.6fl MCH: 27.40pg, MCHC: 32.30gm/dl). Normal white cell and platelet count ((TC: $4500/mm^3$, Neutrophil 14% lymphocyte 50%, Eosinophil 04%, Monocyte 06%, ESR:68, Platelet count: $5,10,000/mm^3$). Reticulocyte count 0.2%, Hb electrophoresis and TORCHS screening are normal. Serum Iron level is 210 mg/dl. On bone marrow examination (Fig.-2), erythropoiesis is depressed with reduction of red cell precursors, granulopoiesis is hyperactive, myelocytes and megakaryocytes are increased.

Baby was managed with blood transfusion. Prednisolone was started with 2mg/kg/day but after 6 week there was no improvement and hemoglobin was dropped again. Methyl prednisolone was started on a tapering dose and given 6 doses, followed by oral prednisolon, now the child is on fortnightly follow up and maintain Hb around 10mg/dl for last two month.

Discussion

Diamond-Blackfan anemia is a rare etiology for congenital anemia¹². But this diagnosis should be considered when hypoplastic anemia occurs in infancy. This disorder is very heterogeneous in character, only 10-20% cases; it is inherited as

autosomal recessive manner⁵. Our patient also a child of nonconsanguinous patient. Recently being discovered that DBA is linked to mutation in the ribosomal protein gene rps19, rps24, and rps17. The missense mutations in DBA primarily attract the capacity of the protein to be incorporated into pre-ribosome, thus blocking maturation of the pre-40s particles⁶.

The case reported here, diagnosed at 4 months of age, when he present with severe palor, but his neonatal period is not uneventful.

The diagnosis of DBA made most commonly in infancy. Twenty five percent of reported infant were anemic at birth, 65% by 6 months, and 90% by one year. Rare cases were diagnosed between 2 and 6 year of age⁷.

The anemia of DBA is usually profound at the time of diagnosis. Hemoglobin level average 6.5gm/dl, in patients diagnosed in the first two months of life and 4gm/dl in those diagnosed later. In our patient Hemoglobin level was 3.9gm, at the age of 4 month.

The anemia is normocytic, but it is macrocytic in one third with reticulocyte counts are usually zero. White blood counts are normal or slightly decreased, while platelet counts are normal or increased⁷. Our patient have normocytic anemia with reticulocyte count 0.2%, white blood cell count are normal with increased platelet count. Bone marrow cellularity with erythroid hypoplasia in 90% of cases as well as our patient also has.

Our patient had no congenital anomalies, usually in 30-40% patient with DBA anemia have congenital anomalies, particularly of the upper limb and craniofacial regions⁴.

Prednisolon is the initial treatment, the dose is 2 mg/kg, divided doses until Hb reaches 10gm/dl. Then the

dose is tapered and treatment is given on alternate days. A few puzzling patients respond to corticosteroids initially, but then fail to maintain erythropoiesis on doses that are less than toxic. Our patient does not respond oral prednisolon, but later on response to high dose methyl prednisolon (30 mg/kg) for 4 day. Then 20 mg/kg for 3 days, later on methyl prednisolon is replaced by oral prednisolon (the pulse therapy could not complete). A low dose corticosteroid plus androgen occasionally useful. Recently cyclosporin A in combination with prednisolon improves success rates and can be steroid sparing⁸. Interleukin 3 has been tried.

If all medication fails blood transfusion is only option. Regular blood transfusions lead to problems of iron overload. Bone marrow transplantation is only definitive treatment but it is not always successful. A recent study in Japan found an 85% success rate with haemotopoietic stem cell transplantation¹¹.

Remission has occurred in approximately 17% of DBA patient reported by Diamond Blackfan Anemia Registry (DBAR). Remission occur following both steroid and/or transfusion therapy.

There is an increased risk of leukemia of these patient¹². So life long follow up is necessary.

The reported mortality rate is approximately 15% although it is undoubtedly higher. Most death was from complication of chronic transfusion, haemosiderosis, such as heart disease, pneumonia, infection. Our patient now on follow up, maintains Hb around 10gm/dl, with oral prednisolon.

Conclusion

Early infantile anemia should be carefully investigated and close follow-up should be performed during the first few months of life, even if there is an obvious etiology.

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