Diamond-Blackfan Syndrome: A case report

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Abstract:

Diamond-Blackfan syndrome is a rare hereditary (AR/AD) disorder characterized by an intrinsic defect in erythroid precursor cells with relative insensitivity to erythropoietin. It is also known as Blackfan-Diamond anemia, inherited pure red cell aplasia. It is a rare disorder which presents with anemia in early infancy. This disorder is genetically and clinically heterogeneous in nature. The inheritance is mainly autosomal dominant. Approximately 25% of the cases are associated with craniofacial anomalies and some cases may end up in malignancy. The diagnosis is made by blood investigations, and bone marrow studies in which red cell precursors are reduced or absent. Screening for the mutations including those encoding for ribosomal proteins in the patient and the family members confirms the diagnosis. Human Leukocyte Antigen (HLA) matched hemopoietic stem cell transplantation is the treatment of choice. In other cases, corticosteroids and cyclosporine A have been tried. The haemoglobin level is maintained with packed red cell transfusion. We are presenting here a female baby who had anemia at birth and was brought to us at the age of 2 months. The diagnosis of Diamond-Blackfan syndrome was made since the patient presented with anemia and showed reticulocytopenia, gross reduction in Red Blood Cell (RBC) count, and reduction in red cell precursors in the bone marrow.

Introduction : Diamond-Blackfan syndrome is a disorder of the bone marrow. First noted by Hugh W. Josephs in 1936, the condition is however named for the Paediatricians Louis K. Diamond and Kenneth Blackfan, who described congenital hypoplastic anemia in 1938. The major function of bone marrow is to produce new blood cells.[1] In Diamond-Blackfan syndrome, the bone marrow malfunctions and fails to make enough red blood cells, which carry oxygen to the body's tissues. The resulting shortage of red blood cells (anemia) usually becomes apparent during the first year of life. Symptoms of anemia include fatigue, weakness, and an abnormally pale appearance (pallor). Diamond–Blackfan syndrome is characterized by normocytic or macrocytic anemia (low red blood cell counts) with decreased erythroid progenitor cells in the bone marrow. This usually develops during the neonatal period. About 47% of affected individuals also have a variety of congenital abnormalities, including craniofacial malformations, thumb or upper limb abnormalities, cardiac defects, urogenital malformations, and cleft palate. Low birth weight and generalized growth delay are sometimes observed. Here we report a case of a child presented with difficulty in breathing and pale appearance.[(2)]

Case report : A 2-month-old female baby born of a third degree consanguineous marriage was brought to our hospital with complaints of being pale and difficulty in breathing. The developmental milestones were appropriate for age. There was no history of jaundice.

On examination she was anemic but there was no icterus. The baby weighed 3.1kg and the head circumference was 32 cm against the expected weight of 3.7 kg and head circumference of 36-38 cm. Anterior fontanelle was very small and posterior fontanelle was closed. The occipital region was flat. Cleft palate was present. Examination of respiratory system revealed crepitation on auscultation and pansystolic murmur on cardiovascular system examination. Other system examination did not reveal any

abnormalities. The haemoglobin level was 2.8gm/dl and hematocrit was 8.5%. The blood counts showed reduction in both RBC count (0.81million/cmm) and the reticulocyte count (0.3%). The White Blood Cell (WBC) count and platelet count were normal. The red cells were normocytic and HbF was within normal limits. Erythrocyte adenosine deaminase (eADA) estimation were elevated. Total serum bilirubin level was 0.6mgm/dl. Bone marrow aspiration showed normocellular marrow with red cell precursors were grossly reduced. Ultrasound abdomen and ultrasound cranium did not reveal any abnormality.

We made a diagnosis of Diamond-Blackfan syndrome, since the baby presented with anemia at birth, reticulocytopenia, normal white cell count and platelet counts, normal marrow cellularity with paucity of red cell precursors, supporting criteria of elevated erythrocyte adenosine deaminase (eADA). In addition, the baby had microcephaly and flat occiput. There was no evidence of any other bone marrow failure syndrome.

Since, the patient is not having another sibling, and also cannot afford the costs involved, we could not consider the possibility of hemopoietic stem cell transplantation. The patient was started on prednisolone therapy and is receiving packed red cell transfusion for the past 4 months.

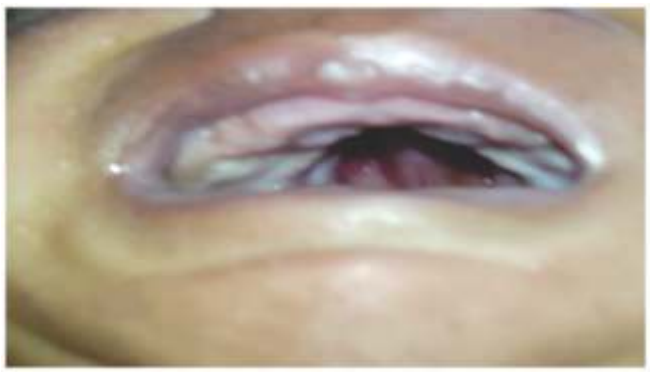

Figure:1 Cleft palate

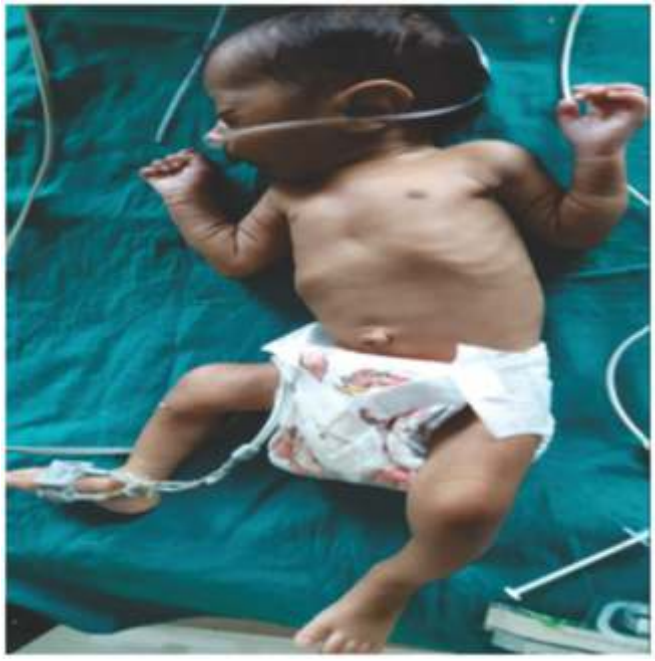

Figure:2 Clinical photo

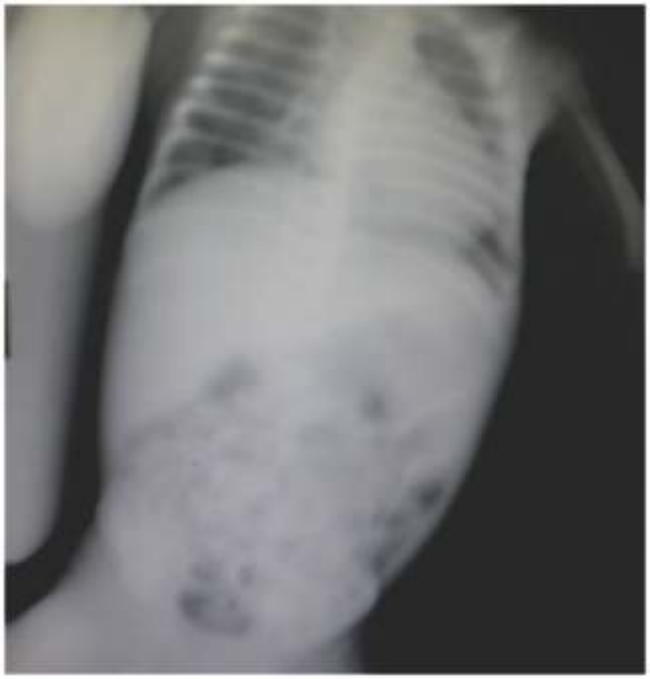

Figure: 3 Chest Xray

Discussion : Diamond-Blackfan syndrome is a rare genetic disorder distinguished by proapoptotic hematopoiesis and congenital anomalies involving craniofacial region, eyes, neck, thumb, urogenital tract, heart, and musculoskeletal structures. Some cases may present with short stature, growth retardation and learning difficulties. It usually presents in infants,

although presentation can vary from severe fetal anemia requiring transfusion to anemia detected as late as 6 years of age. Most cases are sporadic with a dominant or, rarely recessive pattern.[2,3]

People with Diamond-Blackfan anemia have an increased risk of several serious complications related to their malfunctioning bone marrow. Specifically, they have a higher-than-average chance of developing myelodysplastic syndrome (MDS), which is a disorder in which immature blood cells fail to develop normally. Affected individuals also have an increased risk of developing certain cancers, including a cancer of blood-forming tissue known as acute myeloid leukemia (AML) and a type of bone cancer called osteosarcoma.[3]

Approximately half of individuals with Diamond-Blackfan anemia have physical abnormalities. They may have an unusually small head size (microcephaly) and a low frontal hairline, along with distinctive facial features such as wide-set eyes (hypertelorism), droopy eyelids (ptosis); a broad, flat bridge of the nose; small, low-set ears; and a small lower jaw (micrognathia). Affected individuals may also have an opening in the roof of the mouth (cleft palate) with or without a split in the upper lip (cleft lip). They may have a short, webbed neck; shoulder blades which are smaller and higher than usual; and abnormalities of their hands, most commonly malformed or absent thumbs. About one-third of affected individuals have slow growth leading to short stature.[4,5]

The differential diagnosis in our case (anemia at birth) is haemolytic disease of new born (HDN) but investigations done at the hospital where transfusion was given first has not revealed any evidence of isoimmune hemolytic anemia. Transient Erythroblastopenia of Childhood (TEC) which is another differential diagnosis for DBA presents usually after 6 months of age and is an acquired condition.[6,7]

Conclusion: The severity of Diamond-Blackfan syndrome may vary, even within the same family. Increasingly, individuals with non-classical Diamond-Blackfan syndrome have been identified. This form of the disorder typically has less severe symptoms that may include mild anemia beginning in adulthood. The child has not shown any satisfactory response to corticosteroid treatment.

References

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