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Case Report

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Blackfan diamond anemia: Case presentation

Abstract

Introduction: Blackfan Diamond Anemia is a congenital disorder characterized by normochromic macrocytic anemia, with decreased or absent erythroid precursors in the bone marrow, which occurs in the early stages of life, once diagnosed, steroids and red blood cells transfusions are mainstays of treatment, although some patients require bone marrow transplantation.

Objective: To describe the characteristics of a female infant with Blackfan Diamond Anemia.

Case presentation: A 5-month-old female patient with severe macrocytic anemia and reticulopenia with transfusion requirements from two months of age, in addition to variable phenotypic abnormalities, for which a medullogram was performed, confirming a selective depression of the erythropoietic system.

Conclusions: The diagnosis of Diamond Blackfan Anemia should be suspected in infants with or without malformations who present anemia and reticulopenia from early stages of life.

Keywords: diamond Blackfan anemia, lymphocytes, hemoglobin

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Introduction:

Blackfan Diamond Anemia is a congenital disorder, genotypically and phenotypically heterogeneous, which presents a decrease or absence of erythroid precursors, variable congenital malformations and predisposition to malignant diseases.[1] It is characterized by macrocytic, normochromic anemia, usually diagnosed in early childhood, reticulocytopenia, decrease or absence of erythroid precursors in the bone marrow, and increased erythrocyte adenosine deaminase.[2] There are established diagnostic criteria for this disease which must all be met, and if not, major and minor supporting criteria are used.[3] Corticosteroids and red blood cell transfusions constitute the essential therapeutic pillars. Although some patients develop resistance to treatment and require long-term transfusions or bone marrow transplant.[4] A clinical case of a five-month-old female infant with Blackfan Diamond Anemia is presented. The objective of the presentation is to describe the characteristics of this patient. The girl's legal guardians were informed, informed consent was requested and, respecting ethical principles, the data of the patient and her relatives will not be published.

Case presentation

A five-month-old female patient with prenatal diagnosis of multicystic renal dysplasia right, she went to the emergency room two months after birth due to a common cold, she was admitted to the pediatric hospital where significant pale skin mucosa, a heart murmur and the presence of phenotypic malformations (low-set ears with cartilage malformation, bridge flattened nose, mongoloid-looking eyes, hypertelorism, flat occiput, wide anterior fontanel, wide and thick nuchal fold, syndactyly in the toes of the left foot) (Figure 1), studies were carried out and the presence of severe anemia was corroborated (Hb: 52 g/l), peripheral lamina: hypochromia, aniso-poikilocytosis, normal leukocytes with a predominance of lymphocytes and slight thrombocytosis, it was decided to transfuse red blood cells and follow-up in consultation after discharge, it was evaluated by genetics who referred to renal dysplasia multicystic and with a karyotype of 46 XX in 8 metaphases. At three months of age he went to the clinic and again found severe anemia, Hb: 66g/l, peripheral lamina: macrocytosis xxx, hypochromia x, normal leukocytes with a predominance of lymphocytes and slight thrombocytosis. Reticulocyte count: 4 x 10^{-3}/L, negative direct coombs test, normal liver and kidney function, she was transfused with red blood cells for the second time and a medullogram was performed, showing depression of the erythropoietic system with integrity of the granulopoietic and megakaryopoietic system without other alterations in the bone marrow, which is why it is concluded as Blackfan Diamond Anemia.

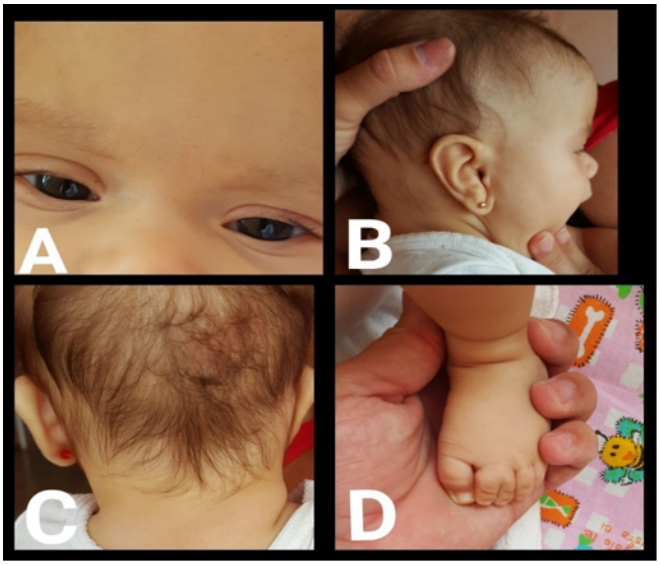

Figure 1 Phenotypic malformations of the patient.

(A) Hypertelorism, flattend nasal briedgand monogoloid- looking eyes.

(B) Low set ears with cartilague malformations.

(C) Thickend nuchal fold and flat occiput.

(D) Sundactyly of 3rd and 4th toes of left foot.

Discussion

Blackfan Diamond Anemia is a rare cause of hereditary bone marrow failure (6-7 per million live births) characterized by hypoplastic anemia, congenital anomalies and predisposition to cancer, initially described as an anemia of early childhood by Hugh W. Joseph in 1936 and later recognized as a specific clinical entity by Louis Diamond and Kenneth Blackfan in 1938 (Diamond & Blackfan, 1938).[5, 6] It has an autosomal dominant inheritance pattern in 45% of cases, in the remaining 55% the presentation pattern is sporadic with autosomal recessive inheritance or linked to the X chromosome, affecting both males and females.[1] It is due to damage to the gene that encodes the ribosomal protein RPS19 (25% of cases), although 19 other mutations are described, the most studied being RPS24, RPS17, RPL5 and RPL11. Mutated genes that do not involve ribosomal proteins have been identified: mutations in the erythropoietin gene, in genes linked to the X chromosome (GATA-1) and in the TSR gene.[1,7,8] This disorder is characterized by inadequate hematopoiesis accompanied in 30-50% of cases with congenital, ocular, neck, thumb, urogenital tract, heart and craniofacial anomalies. Some cases present short stature, delayed growth and learning difficulties.[9,10] In the case presented, several congenital anomalies were found (kidney, eye, craniofacial, and toe). In addition, he began with severe macrocytic anemia since he was two months old, reticulopenia and selective depression of the erythropoietic series in the bone marrow, which coincides with what has been reported in the literature in these cases.[11] There are criteria for diagnosis, which are established if they are met:[2] all diagnostic criteria; three diagnostic criteria plus one major supporting criterion; two diagnostic criteria and three minor support criteria; one major support criterion and three minor support criteria.

Diagnostic criteria[2]

1. Macrocytic-normochromic anemia in the first year of life.
2. Reticulopenia.
3. Bone marrow, normocellular with selective deficiency of erythroid precursors.
4. Normal or slightly decreased leukocyte count.
5. Normal or slightly increased platelet count.

Major support criteria[2]

1. Classic Blackfan Diamond Anemia Genetic Mutation
2. Positive family history

Minor support criteria[2]

1. Elevated fetal hemoglobin
2. Congenital anomalies
3. Elevated erythrocyte adenosine deaminase activity
4. No evidence of another spinal cord failure syndrome

The diagnosis was made in the case presented since all the diagnostic criteria were met, it also presented other minor supporting criteria such as congenital anomalies and no evidence of another spinal cord failure syndrome, it was not possible to determine the adenosine deaminase activity of the erythrocytes, nor could fetal Hb be determined due to the need to transfuse the girl. There is no evidence of other family members with this disease. The essential pillars of treatment are red blood cell transfusions, steroid therapy and hematopoietic stem cell transplantation. Approximately 80% of cases have an initial response to steroids, however, 20% would require chronic transfusion therapy or a bone marrow transplant. In general, the use of steroids is recommended after one year of age, due to adverse effects, although on certain occasions their use is justified.[12] Initially, in our patient, it was necessary to transfuse concentrated red blood cells on two occasions in a period of one month. Subsequently, it was decided to begin the use of steroids (due to the high transfusion requirement) with a good response so far, with stable blood levels. Hemoglobin (maintained above 90 g/L) and independence from transfusions. It can be concluded that in an infant with macrocytic anemia, with or without associated malformations and reticulopenia, the diagnosis of Blackfan Diamond anemia should be kept in mind.

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Conflicts of interest

The authors declare that there is no conflicts of interest.

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