

Anemia of Blackfan Diamond in an infant at the Albert Royer National Children's Hospital in Dakar and Review of the Literature

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ABSTRACT

Blackfan Diamond anemia is the only known congenital erythroblastopenia. Following the discovery of the genes involved, it has become the leader in ribosomal diseases and this has opened the way to a great deal of basic research into erythropoiesis. It is defined by severe erythroblastopenia with less than five percent of erythroid precursors in a single-cell marrow. Blackfan Diamond's anemia manifests early before the age of two and its incidence is low in Africa, we report a case with early onset in a 03-month-old infant with RPS19 mutation. The diagnosis often remains difficult due to the unavailability of genetic tests. Corticosteroid therapy was prescribed for two weeks without significant improvement. The patient is currently on a transfusion routine while awaiting a bone marrow transplant.

Keywords: Blackfan Diamond anemia; Pediatrics; Ribosomopathies

INTRODUCTION

Blackfan-Diamond anemia, first described by Josephs in 1936, then clearly identified in 1938 in Dana Farber by Louis Diamond and Kenneth Blackfan is the only recognized form of erythroblastopenia [1,2]. Despite a very marked erythroid tropism, it is a global damage of the bone marrow and it belongs in fact to the group of constitutional pathologies of the bone marrow. The recent discovery of the genes involved has made it the leader of a new group of diseases: ribosomopathies or ribosomal diseases. Blackfan Diamond's anemia starts early before the age of two and its incidence is low in Africa, we report a case which will be presented in the form of a medical observation.

OBSERVATION

He is a 03-month-old female infant born to a 28-year-old primitive mother, primiparous without known tares. There is no notion of parental consanguinity found, the pregnancy was well monitored with five prenatal consultations, serologies made negative returns, term delivery by low transverse cesarean section, birth weight at 2760g size 50 cm. He was hospitalized during the neonatal period for anemia that required a blood transfusion. Received for anemic syndrome with very marked

skin and mucous pallor, tachycardia at 170 beats per minute with a systolic murmur at all foci, good neurological behavior and a fair general condition. The assessment had found: on the hematological level an anemia normochromic normocytic arégénérative with 2, 8g / dl and a rate of reticulocyte at 1144 by mm³, the normal white blood cells and a thrombocytosis with 1153000 by mm³, it is of the blood group A rhesus positive. The biochemical balance returned with a positive C-reactive protein at 48 mg / l, the martial balance returned normal and the electrophoresis of hemoglobin found a drepanocytic trait with the AS profile. The rest of the biochemical balance returned normal (Figure 1)

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Figure 1: Facies of the child with anemia of Blackfan Diamon

Virologically, the search for parvovirus B19 infection returned negative. The medullogram made under local anesthesia showed an abundant non-dysmorphic presence of cells of the granular line, lymphocytes and by the absence of the erythroblastic line making evoked a genetic erythroblastopenia; confirmation by molecular biology with a search for an RPS19 ribosomal mutation was confirmed. Therapeutically he benefited from blood transfusion sessions, corticosteroid therapy with prednisolone at 2 mg / kg for two weeks without obtaining a reticulocytic crisis. Corticosteroid therapy was continued for one month with no significant improvement in anemia. The latter was stopped and the child was put on a transfusion program allowing us to have a hemoglobin level between 7 and 8 g/dl. The evolution at six months under treatment. On the evolutionary level, she presented at 06 months of life a delay in weight and height with weight and height less than -2 DS on the WHO weight and height curves. Transfusions were done monthly with repeated checks of the blood count. A martial assessment was made in order to detect an iron overload but the latter returned to normal. She is reviewed every three months for clinical evaluation and monitoring of hemoglobin levels.

DISCUSSION

Blackfan-Diamond anemia (ABD) is secondary to a blockage of erythroid differentiation at a stage that is still discussed. It is conventionally accepted that this blockage occurs at the erythropoietin (EPO) stage - independent to the EPO-dependent stage (3). This blockage is directly responsible for erythroblastopenia defined by less than 5% of spinal precursors on the myelogram. The involvement of ribosomal protein genes and the consequences observed following their mutation, in particular the lack of maturation of ribosomal RNAs make ABD the first disease of the ribosome [4].

The age at diagnosis is often less than a year as reported in a European study of 229 cases with 88% [5]. We found a similar result with an age at diagnosis at 03 months of life. Often the ABD falls into a syndromic setting with often abnormalities of the cephalic extremity such as microcephaly, cleft palate or other malformation of the head. None of his malformations were found in our case. Heart, bone and spinal malformations may be associated with it [5]. Abnormal blood counts in other lines are possible in the ABD. The small infant may present with sometimes major thrombocytosis [6]. This thrombocytosis was

found in our patient at the time of diagnosis. On the genetic level, we had found a mutation on the RPS19 gene as in most studies [7]. Other mutations are possible and are often responsible for syndromic ABD with maxillary and facial malformations suggestive of Treacher-Collin syndrome [8,9]. Finally, RPL31 has recently been reported as a deletion in a patient [10]. Furthermore, the absence of a molecular diagnosis does not rule out the diagnosis [11].

Management is based on the transfusion support. There is a consensual effect of not using corticosteroids during the first year of life; taking into account the toxicity of corticosteroids at this age. This may explain the fact that this corticosteroid therapy even returned ineffective in our patient. In transfusion dependent patients, the transfusion threshold must be adapted to each patient and take into account the general condition, the speed of growth and also the quality of life criteria [12]. Chelation should be started in all patients with a ferritin between 500 and 1000 ng / ml and deferoxamine is the first-line drug without exceeding 25 to 30 mg / kg in children [13]. From one year on, it makes sense to offer corticosteroid therapy in patients who are still dependent on transfusions [14].

Prednisolone at 2mg / kg / day can be offered and a reticulocytic crisis should be observed between the 10th and 16th days to testify to the effectiveness of corticosteroid therapy. The objective is then to decrease the dose in steps of 0.5 mg / kg / d under control of the reticulocyte rate up to 0.5 mg / kg / d. the decrease will then be slower until the minimum effective threshold dose is identified. In our patient, despite all these therapeutic approaches, his evolution remains marked by complications with a delay in weight and weight and dependence on blood transfusions. Hope is placed on an allograft of marrow, unavailable in our context, often gives good results [15].

CONCLUSION

Blackfan Diamond anemia is a rare but not exceptional condition. The challenge is to avoid complications like stunting and post transfusion hemochromatosis. The long-term prognosis can be improved by good genetic counseling with the hope of treatment targeting at least one of the ribosomal proteins. This fat case started from the rare cases found in Senegal and it arises especially the non access to treatments like immunotherapy and bone marrow transplant.

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