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CASE REPORT

Hereditaryl Pyropoikilocytosis in the Neonatal Period - Case Report

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Abstract

The Hereditary Pyropoikilocytosis is a rare and severe form of Elliptocytosis, characterized by an alteration in the skeleton of the red blood cell membrane. It is an autosomal dominant condition with variable penetration in elliptocytosis, which may be in homozygosity or double heterozygosity in Pyropoikilocytosis, starting from the neonatal period, with clinical manifestations of persistent jaundice. We report here a case of a newborn with persistent jaundice, associated with anemia requiring blood transfusion. The clinical evolution and laboratory findings were conclusive for the diagnosis of Hereditary Pyropoikilocytosis.

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INTRODUCTION:

Hereditary Pyropoikilocytosis (HP) is a rare and severe form of Elliptocytosis[1]; it is characterized by an alteration in the red blood cell membrane skeleton. Its intensity varies from mild to fatal and, usually, begins in the neonatal period, with clinical manifestations of persistent jaundice and, in the long term, it can lead the patient to chronic dependence on blood transfusions[2].

The epidemiology is markedly described in the African continent[1], and although in Brazil there is no record of data on its prevalence, it is believed that it follows the African one due to the ethnic origin of our population. Its etiology most commonly lies in the association of severe elliptocytogenic defects in certain membrane proteins, including alpha-spectrin, or in homozygosity for defects solely in the spectrin gene[3]. It is an autosomal dominant condition with variable penetrance in elliptocytosis, and may be homozygous or double heterozygous in PH1, which should prompt investigation of the family history when a patient presents with anemia of unclear origin. With the natural evolution of the disease, hemolysis may disappear and poikilocytosis be replaced by the elliptocytes of common Hereditary Elliptocytosis, being genetically similar to a compound heterozygous autosomal recessive condition[4].

The clinical and laboratory manifestations of pyropoikilocytosis were first described in 1973 and 1975[5,6] and reported three patients with moderately severe congenital hemolytic anemia, containing unusual and bizarre red blood cells with anisocytosis, poikilocytosis and microspherocytosis. The red blood cells of these patients showed extensive fragmentation, budding of the cell membrane and formation of microspherocytes when exposed to a constant temperature greater than or equal to 45 °C for 15 minutes, which is in contrast to the usual, in which physiologically these changes are only of 49°C or above. The condition was named "congenital pyropoikilocytosis."

The care of babies with HP must be provided by an interdisciplinary team, hematologist and pediatrician[7], which is paramount for clinical management. The description of this case confirms its importance due to the rarity of the condition and the scarcity of scientific publications, especially in Brazil, and it aims to contribute to the early diagnosis and adequate management of these patients.

CASE REPORT:

This is a female newborn (NB), daughter to a 27-year-old mother, primiparous, with ASD and high blood pressure, who developed gestational diabetes with favorable control, without other complications. She was born at a gestational age of 36 weeks and 4 days, in normal conditions; without the need for neonatal resuscitation maneuvers, weighing 2710g. She developed early jaundice, after 15 hours of life, requiring phototherapy. She did not require exchange transfusion, but maintained persistent indirect hyperbilirubinemia. There was no visceromegaly. Her lab workup presented indirect hyperbilirubinemia (BT 7.9 mg/dL; BI 7.49 mg/dl, BD 0.41 mg/dL); microcytic anemia (Hb 9.5 g/dL) (MCV 74.3 fL); MCHC of 36.1 g/dL and RDW 28.9%, without reticulocytosis (0.6%), but increased lactic dehydrogenase enzyme (563 U/L). Her hematoscopy revealed the presence of marked anisopoikilocytosis, elliptocytes, schistocytes and spherocytes (Figure 1), suggesting the diagnosis. The complementary evaluation showed mother and newborn with blood type O positive, newborn with negative Direct Coombs, negative maternal Indirect Coombs, negative urine culture, normal G6PD measurement and normal thyroid function. The hemoglobin electrophoresis revealed FA pattern and global normocellularity myelogram, hypercellularity of the erythrocytic series and absence of dysplastic changes. There was no family history of anemia, splenomegaly and jaundice. Normal maternal and paternal blood counts, including hematoscopies. She remained on phototherapy until 8 days of age, requiring blood transfusion due to worsening anemia (Hb 7.4g/dL) at 20 days of age. She was discharged after 25 days, using folic acid and remained stable in outpatient follow-up, without complications. She did not require new transfusions to date and, in the evaluation of her serial blood counts, she maintained the forms found in the initial hematoscopy. At 7 months she presented Hb 10 g/dL on the blood count, MCV 71.9 fL and only ovalocytes (Figure 2), showing an improvement as expected. The clinical evolution and laboratory findings were thus conclusive for the diagnosis of Hereditary Pyropoikilocytosis.

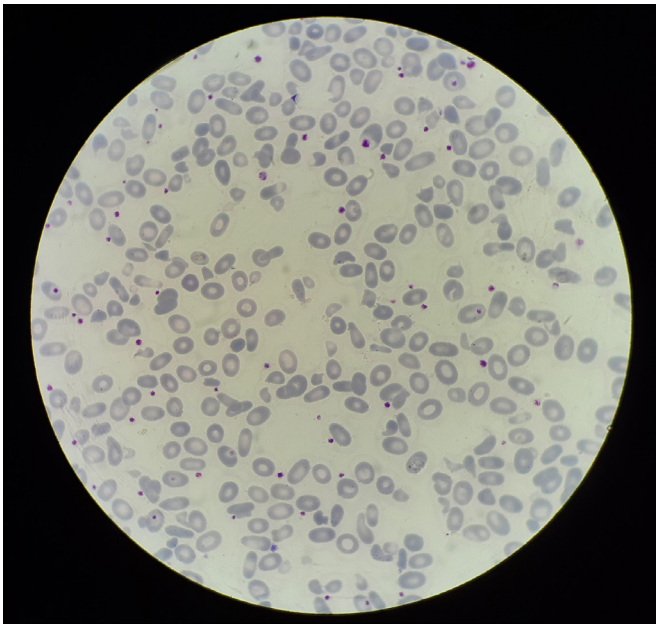


Figure 1. Hematoscopy in the neonatal period showing marked anisopoikilocytosis, elliptocytes, schistocytes and spherocytes.

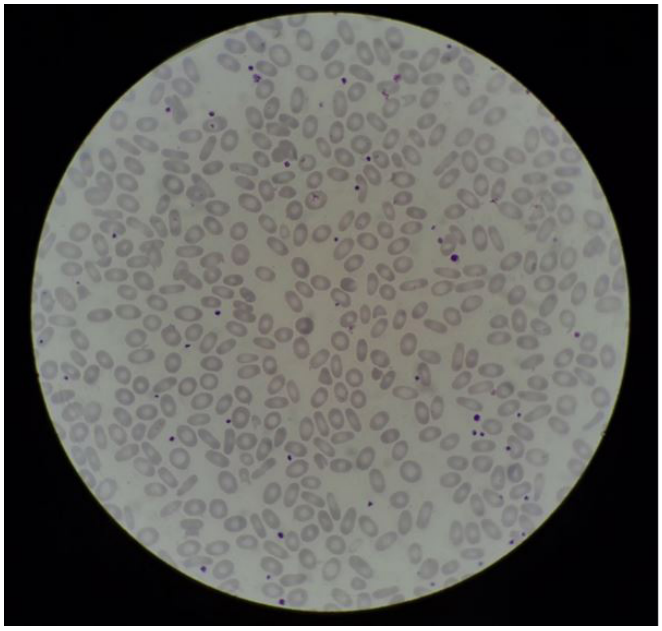


Figure 2. Hematoscopy at 7 months of age showing only ovalocytes.

COMMENTS:

The pathophysiology of Pyropoikilocytosis arises from a defect in the tetramerization of the spectrin protein or in the junctional complex, leading to weakness in the red blood cell membrane skeleton and its consequent extravascular fragmentation, similar to that observed in burns after destruction of cytoskeletal interactions by heat[1]. In the neonatal period the hemolysis is markedly worse. It is hypothesized to be due to high concentrations of fetal hemoglobin (HbF) in red blood cells. HbF does not bind to the RBC compound 2,3-diphosphoglycerate (DPG) and, as a result, large amounts of free 2,3-DPG are available to interact with and destabilize the RBC cytoskeleton, producing poikilocytosis and hemolytic anemia. As HbF levels decline in the first months of life, the contribution of 2,3-DPG to the hemolytic process decreases, hemolysis disappears and poikilocytes are replaced by the elliptocytes characteristic of Elliptocytosis[1], as evidenced by a serial hematoscopy analysis of the patient.

In rarer and more severe cases, it may occur during pregnancy, progressing to hydrops fetalis[7], probably due to broader defects in spectrin. In the neonatal period, pyropoikilocytosis manifests itself as severe hemolytic anemia, leading to significant anisopoikilocytosis. Children are commonly born at term with a hemoglobin level within normal parameters when collected from umbilical cord blood[8]. However, in the first days of life, the hemoglobin level decreases rapidly, which may even require transfusions, as described in this case. Jaundice is the most important sign in newborns, which triggered the investigation in this case mainly due to the prolonged period of time, most often requiring phototherapy, and in some cases exchange transfusion.

Examining blood smears for erythrocyte morphology in the laboratory has been a practical and productive diagnostic method for evaluating newborns with hyperbilirubinemia[9]. In pyropoikilocytosis, there is severe anisocytosis, cell fragments, micropoikilocytosis, microspherocytes and developing erythrocytes. This data proved to be of great clarification in elucidating the case reported here, reinforcing the effectiveness of this analysis. However, a low MCV (30 to 75 fL), due to fragmented red blood cells, is characteristic in some cases, it may be at the upper limit, as in the patient described here and in a literature report of a 17-day-old newborn[10] who presented with jaundice, resulting from severe anemia (Hb 6.9 g/dl), whose MCV was 87.5 fL, with a diagnosis of pyropoikilocytosis suggested by the smear. Osmotic fragility is generally normal in individuals without hemolysis, but it may show increased fragility in severe forms, but this is not an essential test for diagnosis[1,10].

In a follow-up report of eight newborns and infants with Pyropoikilocytosis, carried out at the Children's National Med National in Washington[5], neonatal hyperbilirubinemia was present in all cases, including the need for medical intervention such as phototherapy or exchange transfusion, which is in agreement with this case report and the literature. In these patients, the hypotheses of hemolytic disease of the newborn, sepsis, G6PD deficiency, autoimmune hemolytic anemia and spherocytosis were ruled out, as it occurred in the investigation of the case in question, because these are important and prevalent differential diagnoses in the neonatal period. When evaluating the peripheral blood smears at birth of the eight patients, the presence of microcytosis, fragments of red blood cells and marked poikilocytes was decisive in the diagnosis, as in the patient described.

In older children, infections or concurren illnesses can trigger degrees of hemolysis, including anemia, requiring occasional transfusions. For example, parvovirus B19 infections, in which anemia worsens, leading to pallor, asthenia, dyspnea, fever and classic skin rash, sometimes requiring hospitalization to compensate and manage the anemia[7]. Supplemental folic acid is usually recommended for individuals with more than a minimal degree of hemolysis, in order to prevent folate deficiency, as used by the patient reported, although this practice has not been studied in depth for cases of elliptocytosis[2] . When there is chronic anemia, which requires periodic transfusions, other therapies are considered, such as total or subtotal splenectomy[11], which are effective, or the use of erythropoietin, although there are still no studies with sufficient evidence[2] in patients with pyropoikilocytosis.

GENERAL CONSIDERATIONS:

Pyropoikilocytosis is a rare and potentially serious form of elliptocytosis, which must be recognized by pediatricians, due to its manifestation of jaundice in the neonatal period.

Monitoring these children shows stabilization of hemoglobin values, varying from one patient to another and, in the absence of other symptoms, an annual visit to the specialist is indicated. Parents should be warned about the risk of worsening anemia, which can occur especially during viral infections, when they should seek medical attention for better monitoring and care. The diagnosis also allows family exploration and genetic counseling for parents, because this is a hereditary condition.

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