Infantile Pyknocytosis: A Rare Form of Neonatal Anemia

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Pyknocytes (*pykno-*, Greek for thick, compact, dense) are small fragmented red blood cells that stain densely on peripheral blood smear. Infantile pyknocytosis is a rare form of neonatal hemolytic anemia, first described by Tuffy et al. in 1959 [1]. We describe a child with infantile pyknocytosis and review the medical literature on this disorder.

PATIENT DESCRIPTION

A 17 day old male infant was admitted to the pediatric department because of prolonged jaundice. He was born at term (38 weeks) after an uncomplicated pregnancy; birth weight was 2.33 kg. The parents are Jewish of Libyan and Bulgarian/Persian origin. Two of the mother's brothers died of unknown causes, one antepartum and the other at age 1 month. The patient's serum bilirubin level at discharge from the nursery at age 3 days was 10.3 mg/dl. At age 16 days breast feeding was changed to milk formula.

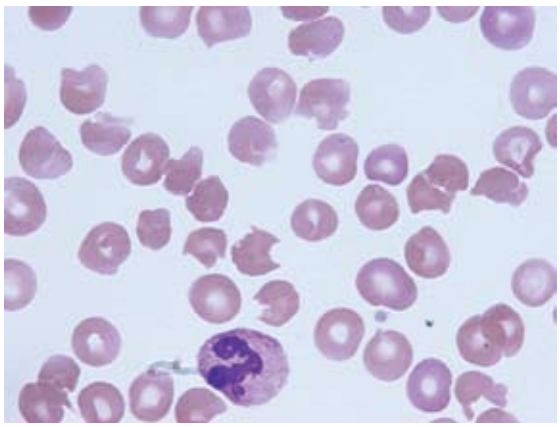
On admission, the patient appeared pale and icteric but showed no signs of acute distress; his vital signs were normal. Weight was only 60 g above birth weight. A 2/6 systolic heart murmur was heard at the left sternal border. Lungs and abdomen were normal. There was no organomegaly.

Laboratory tests showed a hematocrit of 27%, with a reticulocyte count of 4.5%. White blood cell count was 9900/mm^3 and platelet count 254,000/mm^3. Total bilirubin level measured 21.3 mg/dl (98% indirect). Liver and renal tests were within normal range. The child's blood type was O+, and his mother's A+. Coombs test, glucose-6-phosphate-dehydrogenase activity, hemoglobin, electrophoresis, levels of lactate dehydrogenase, aspartate transaminase, haptoglobin, thyroxine, thyroid-stimulating hormone and urinalysis were normal. Peripheral blood smear demonstrated numerous (~45%) distorted, contracted and densely stained RBCs as well as RBC fragments [Figure], and infantile pyknocytosis was diagnosed.

On the third day of hospitalization, hematocrit levels decreased to 20%, hemoglobin measured 6.0 mg/dl, and bilirubin levels remained constant. Transfusion of packed RBCs (15 ml/kg) led to an increase in hematocrit to 32%.

The infant was discharged but remained under close observation. He was admitted twice during the following 2 months because of lethargy and paleness related to an exacerbation of the anemia and he was treated with transfusions of packed RBCs. Since his last hospitalization, at age 11 weeks, he seems to have made a full recovery, with normal hemoglobin and bilirubin levels during 11 months of follow-up.

Peripheral blood smear of the patient at age 3 weeks



RBC = red blood cells

COMMENT

Infantile pyknocytosis is a rare form of neonatal anemia. Nevertheless, in a recent study this disorder accounted for 14 of 102 initially unexplained cases of hemolytic anemia in neonates (9.4%) [2]. Little is known about its etiology, epidemiology and clinical features. Since its first description in 1959, 53 cases of infantile pyknocytosis, including our patient, have been published [1-5]. We review the published medical reports of this disorder.

Analysis of the gender distribution of the reported children with infantile pyknocytosis revealed a 2:1 male predominance (35 males:18 females). In 90% of the affected infants, the first manifestation was indirect hyperbilirubinemia without accompanying splenomegaly, which appeared during the first days of life. At age 2 days, over 55% had indirect bilirubin values of more than 15 mg/dl. Mean maximal indirect bilirubin of the patients was 22.2 mg/dl (range 1.5–33 mg/dl). Between the second and fourth week of life, profound anemia was documented in about 70% of the babies with this entity, with a hemoglobin level of less than 8 mg/dl.

The average percentage of pyknocytes in the blood smear of patients

was 24%, with a range of 4–50%. Both the hyperbilirubinemia and the anemia resolved spontaneously by 4 months on average (range 1–15 months) and the pyknocytes disappeared. Additional laboratory anomalies in infants with infantile pyknocytosis included occasional mild leukocytosis and a mild elevation of liver enzymes.

The diagnosis is based on clinical findings of anemia and jaundice and the characteristic morphological appearance of the RBCs on peripheral blood smear. Its pathogenesis is unknown, but it is believed to be caused by a yet unidentified extracorpuscular factor. This hypothesis is based on the finding that labeled donor cells that were transfused to anemic patients soon assumed the distorted morphology of the recipients' RBCs [1,3]. A similar red blood cell morphology has been documented in heat stroke in adults, in elliptocytosis, in neonatal anemias related to vitamin E deficiency, and in G6PD deficiency in humans and horses. Small numbers (< 5%) of pyknocytes may also be detected in blood smears of healthy neonates. Percentages are higher in preterm than in full-term infants [3].

In at least 13 patients (24%), early jaundice and/or neonatal anemia was reported in a first-degree relative. A family history of death in a first-degree relative in early infancy was reported in three cases, including our patient. The diagnosis of infantile pyknocytosis in several patients with consanguineous parents [1,4] point at a possible genetic cause for this disorder. Low birth weight or prematurity do not seem to be independent risk factors for the development of this condition.

Treatment of infantile pyknocytosis is mainly supportive and consists of phototherapy and repeated blood transfusions. The anemia might respond to erythropoietin, although data on this treatment option are still preliminary [5]. Jaundice refractory to phototherapy may be treated by exchange transfusions.

The disorder is self-limited and no long-term complications have been documented. Nevertheless, one of the recently documented cases had a fatal outcome during infancy. The cause of death was found to be pulmonary hypertension, presumably secondary to the hemolysis. Four other patients who died from the disease were reported in the 1960s, which may be linked to a different standard of care at the time. These reports underline the need for increased awareness of this disorder in order to reach a timely diagnosis of infantile pyknocytosis.

G6PD = glucose-6-phosphate-dehydrogenase

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