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Neonatal pyknocytosis in a preterm dizygotic twin

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Abstract

Infantile pyknocytosis (IP) is a rare, self-limited neonatal haemolytic anaemia that may require multiple blood transfusions. Just over 50 cases have been reported in the medical literature, and the great majority of them concerns term infants. The aetiology of IP is not well understood, but most likely it results from a transient extra-corpuscular factor, whose nature is unknown. This factor could be transmitted from mother to child or, alternatively, could result from a deficiency of an anti-oxidative agent.

Here we report the case of 2 preterm infants, one of whom suffered from picnocytosis. The twin had severe anemia at the age of 2 weeks,, while the other twin was unaffected. A smelly greenish diarrhoea occurred just before the presentation of IP, suggesting that the same agent led to both the diarrhoea and the oxidative injury. Although no specific agent was identified as the cause of anaemia and IP, we speculate that the transmission of an agent from mother to child was unlikely, as only twin one suffered from the disease. IP may remain underdiagnosed, but should be considered in cases of early unexplained severe hemolytic anemia.

Key words: Infantile pyknocytosis, glucose-6-phosphate dehydrogenase deficiency, anemia, oxidative stress, hemolysis.

Core tip: This manuscript describes the first case of infantile pyknocytosis affecting only one of the twins, and contributes to clarify the etiology of infantile pyknocytosis.

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INTRODUCTION

Premature neonates commonly experience a fall in haemoglobin concentration. This has been termed "physiologic" anaemia of prematurity, since it is usually not associated with any abnormalities in the red blood cells (RBCs). Repeated blood sampling and diseases can worsen this "physiologic" anaemia of the premature newborn. However, more rare underlying diseases may mimic anaemia of prematurity or may increase its severity.

Infantile pyknocytosis (IP) was first described by Tuffy and co-workers and is characterized by a self-limited neonatal haemolytic anaemia, which may require multiple blood transfusions[1]. The aetiology of IP is unclear. Pyknocytes most likely result from a transient extra-corpuscular factor, whose nature is unknown[2]. An exogenous oxidative agent transmitted from mother to child or a deficiency of an anti-oxidative agent has been hypothesized[3].

We report the case of two Caucasian female preterm twins, one of whom suffered from IP and presented with severe anaemia at age 2 weeks. We discuss factors possibly associated with IP.

CASE REPORT

A dizygotic twin pregnancy resulted from an in vitro fertilization-embryo transfer. The family history did not present cases of neonatal anaemia.

Preterm labour occurred at 32 weeks' gestation, and an emergency caesarean section was required due to breech presentation.

Twin 1 (first born). The Apgar score was 8 and 9 at the 1st and 5th minutes respectively, birth weight was 1735 g, length was 39 cm and cranial circumference was 25 cm. At birth, the red blood cell count and haemoglobin levels were normal (Figure 1). On day three the neonate suffered from jaundice and required phototherapy. The clinical course was uneventful until day 10, when stools became smelly and the baby required further phototherapy. The faecal occult blood test was positive.

On day 17 the newborn was referred to our NICU because of jaundice, foul-smelling greenish diarrhoea and worsening anaemia, which required a packed RBC transfusion.

The reticulocyte count was 169 x 10^3/ul. Liver and renal function tests were normal. A direct antiglobulin test and search for irregular agglutinins were negative; haemoglobin electrophoresis as well as glucose-6-phosphate dehydrogenase (G6PD) and pyruvate kinase activity were normal, while lactate dehydrogenase was mildly abnormal (518 U/L). Bacterial cultures were sterile; detailed viral investigations yielded normal results.

A peripheral blood smear demonstrated high rates (>25%) of irregularly contracted, bite, and densely stained RBCs (Figure 2). The morphological changes in the RBCs accompanied with normal enzyme activity led us to suspect IP.

The jaundice worsened further on day 19, and additional phototherapy was administered. A further packed RBC transfusion was given on day 28. Subsequently the infant recovered spontaneously, and no further transfusions were given.

At age 5 months both the haemoglobin level and RBC morphology were within a normal range. G6PD test yielded normal result, confirming overall the initial diagnosis of IP.

Twin 2 (second born). The Apgar score was 8 and 9 at the 1st and 5th minutes respectively. The birth weight was 1760 g, the length 45 cm and cranial circumference 30 cm. The newborn had mild jaundice (maximum bilirubin levels 9.04 mg/dl) on day five. Her subsequent clinical course was uneventful, and she never suffered from anaemia. The haemoglobin level was 13.5 g/dl on day 25.

DISCUSSION

Pyknocytes are small, irregular, distorted erythrocytes, which are densely stained in a peripheral blood smear. A low percentage of pyknocytes is commonly found during the first weeks of life in healthy full-term neonates (from 0.3 to 1.9%) or in preterm neonates (from 0.3 to 5.6%) [1].

IP is a transient, but often severe neonatal haemolytic anaemia associated with a rise of the physiologic presence of pyknocytes. Factors that increase oxidative stress may damage erythrocyte membranes, resulting in the formation of pyknocytes[3]. Since IP was first described, just over 50 cases have been reported in the literature and the great majority of them concerns term infants[4]. The rarity of the disease as well as the lack of awareness about this neonatal anaemia may lead to an underestimation.

IP may account for ~10% of cases of unexplained neonatal haemolytic anaemia[3]. Most cases present during the first days of life, with neonatal jaundice as the first finding,Approximately 70% of newborns present with severe anaemia from the

second to the fourth week of life, commonly requiring one or more packed RBC transfusions[1,3]. Anaemia resolves spontaneously by the age of 4 to 6 months[5].

The aetiology of IP is unclear. A transient extra-corpuscolar factor damaging the erythrocyte membrane, rather than an intrinsic factor, has been implicated in the pathogenesis of the disease. Indeed, flow cytometric analysis shows that morphological changes do not affect reticulocytes, suggesting that erythropoietin treatment could prevent severe anemia[3,6]. Furthermore, two of the seven cases of pyknocytosis reported by Ackermanshowed the same morphological anomalies after exchange transfusion, suggesting that erythrocytes of donor origin may also be affected[2].

Pyknocytes most likely result from a transient extra-corpuscular factor, whose nature is unknown. Causes such as an exogenous oxidative agent or a deficiency of an anti-oxidative agent have been hypothesized[3].

There are only 2 reports of IP in twins and all newborns were affected[7,8]. In the current case, only twin one suffered from IP. Therefore the transmission of an oxidative agent from the mother to the baby, as well as a familial susceptibility or a hereditary factor[8,9] seem unlikely. Even if we could not confirm any specific agent, a smelly greenish diarrhoea occurred just before the decrease in haemoglobin and the rise in bilirubin levels. These findings suggest that an exogenous (and probably infectious) agent, acquired after birth, led to both the diarrhea and the oxidative injury. Preterm birth possibly contributed to worsening the IP, as premature infants are more susceptible to oxidative stresses.[9]

In conclusion, this is first case of IP affecting only one of the twins. The most likely cause of IP was an exogenous oxidative agent associated with diarrhoea and not transmitted from the mother to the baby.

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COMMENTS

Case characteristics

A preterm female twin was born at 32 weeks' gestation; she presented with recurrent jaundice and severe hemolytic anemia at age 2 weeks.

Clinical diagnosis

The diagnosis was based on clinical findings and exclusion of common causes of jaundice and hemolytic anemia. Pyknocytosis was confirmed through a peripheral blood smear.

Differential diagnosis

Liver and renal tests were normal. Bacterial cultures were sterile; detailed viral investigations yielded normal results.

Laboratory diagnosis

Common causes of neonatal jaundice and hemolytic anemia were excluded.

Imaging diagnosis

A peripheral blood smear demonstrated high rates (>25%) of irregularly contracted, bite, and densely stained RBCs (supporting the diagnosis of pyknocytosis).

Pathological diagnosis

No pathological diagnosis were required.

Treatment

The newborn underwent blood transfusions.

Related reports

Infantile pyknocytosis is a rare, self-limited neonatal haemolytic anaemia that may require multiple blood transfusions.

Term explanation

Pyknocytes are small, irregular, distorted erythrocytes, which are densely stained in a peripheral blood smear. A low percentage of pyknocytes is commonly found during the first weeks of life in healthy full-term neonates (from 0.3 to 1.9%) or in preterm neonates (from 0.3 to 5.6%).

Experiences and lessons

Infantile pycnocytosis may remain underdiagnosed; it should be considered in cases of early unexplained severe hemolytic anemia.

Peer-review

The paper is well written.

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Figure 1: Twin 1 haematocrit, haemoglobin and bilirubin levels during the first month of life. Ht: haematocrit; **Hb**: haemoglobin; **Bil**: bilirubin level; **Pt**: phototherapy; **PRBCs**: packed red blood cell transfusion.

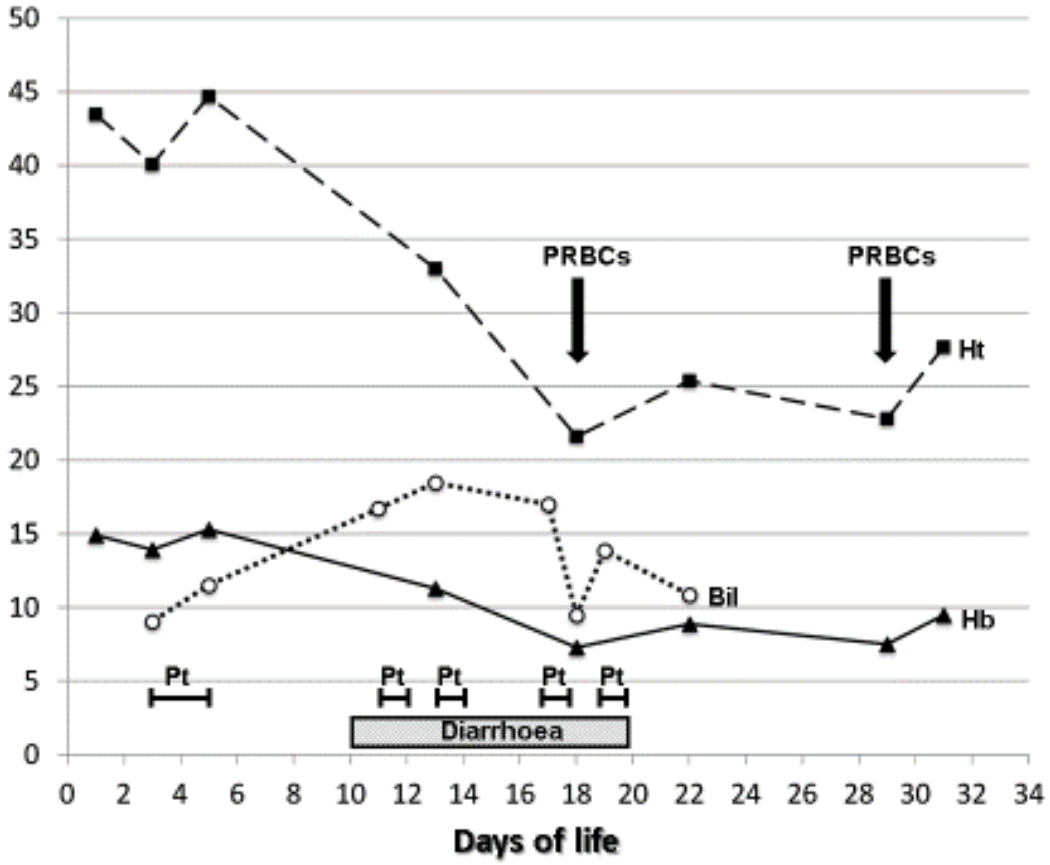

Figure 2: Twin 1 peripheral blood smear during the haemolytic phase of infantile pyknocytosis (MGG 400x). Erythrocyte morphological changes: bite cells, irregularly contracted cells (pyknocytes). Changes are comparable to G6PD deficiency.