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Case Presentation

Preterm infant with a late presentation of blueberry muffin lesions secondary to recombinant erythropoietin

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Abstract

Our patient is a 26-week-old preterm female infant delivered by caesarean section secondary to severe maternal preeclampsia who had been receiving subcutaneous recombinant erythropoietin (r-EPO) for anemia of prematurity. At 8 weeks of age after 8 doses of r-EPO, the infant developed numerous non-blanching erythematous macules and patches located on the back, posterior shoulder, and posterior arms, concerning for late-onset blueberry muffin lesions. Biopsy of the lesions confirmed dermal hematopoiesis. After r-EPO was discontinued all skin lesions gradually resolved over a period of 2 weeks and never recurred.

Keywords: recombinant erythropoietin, extramedullary dermal hematopoiesis, blueberry muffin lesions, anemia of prematurity

Case synopsis

Our patient is a 26-week-old preterm female infant delivered by caesarean section secondary to severe maternal preeclampsia. In addition to prematurity, the early clinical course was complicated by severe respiratory distress, severe intrauterine growth retardation, grade three intraventricular hemorrhage, anemia, and thrombocytopenia. Over the next several weeks the female infant’s development progressed very well without any medical setbacks. However, at 8 weeks of age the patient suddenly developed an alarming rash on her back for which a dermatology consultation was consulted.

Prior to the onset of the rash the patient had been receiving subcutaneous recombinant erythropoietin (r-EPO) injections to treat anemia of prematurity at a dose of 400 units/kg three times a week for 9 doses. It was after the 8th dose of r-EPO that the rash appeared. Physical exam revealed numerous non-blanching erythematous macules and patches located on the infant’s back, posterior shoulder, and posterior arms concerning for blueberry muffin lesions (Figure 1). A 4mm punch biopsy demonstrated polychromatophilic erythroblasts within the hypodermis with no immature myeloid cells, dysplastic erythroblasts, or viral inclusions, confirming the diagnosis of dermal hematopoiesis (Figure 2).

The neonatal ICU team suspected that the dermal hematopoiesis was secondary to r-EPO because they recently had a similar male preterm infant with late-onset blueberry muffin lesions secondary to r-EPO administration. After r-EPO was discontinued in our patient, her skin lesions gradually resolved over a period of 2 weeks and never recurred. The patient is now 9 months of age and continues to do well.
Discussion

Blueberry muffin lesions typically present at birth or appear in the first few days of life as non-blanching blue-purple macules or dome-shaped papules that favor the trunk, head, and neck [1,2]. These lesions usually clear 3-6 months after birth and are the result of extramedullary dermal hematopoiesis [2]. Cutaneous biopsy shows aggregates of normoblastic erythroid precursors in the dermis of affected skin [2]. These lesions are most commonly seen in neonates with congenital infections, but have also
occurred in neonates with hemolytic conditions like hereditary spherocytosis, twin-twin transfusions, and blood group incompatibility disorders such as RH isoinmunization. These findings are also seen in neoplastic diseases such as neuroblastoma, langerhans cell histiocytosis, and congenital leukemia [2,3]. For the classic presentation, the most important part of the work up for blueberry muffin lesions is to rule out TORCH infections, which include congenital rubella, toxoplasmosis, syphilis, enterovirus, parvovirus B19, and cytomegalovirus. These can usually be detected by serologies, including IgM, or by viral PCR [4]. Other labs such as complete blood count can be helpful for hematologic malignancies. Skin biopsy confirms the diagnosis of extramedullary hematopoiesis.

Late-onset blueberry muffin lesions and dermal hematopoiesis have only been reported twice in neonates, once in a case report of a congenital rubella syndrome and the other as a result r-EPO administration [1,5]. To our knowledge there is only one published report of rEPO-induced blueberry muffin lesions other than the case we present here [5]. Our patient was a female born at 26 weeks gestational age that developed non-blanching erythematous macules on the back at 8 weeks of age after her 8th dose of r-EPO. Similarly, the previously reported male preterm infant was born at 22 4/7-weeks gestational age and developed purple non-blanching papules on the back at approximately 10 weeks of age after his 4th dose of r-EPO.

In preterm infants, the hematocrit drops after birth owing to expected breakdown of red blood cells and frequent blood draws. Erythropoietin in neonates is found to be low, so r-EPO was initially used to increase the levels in neonates and stimulate native red cell production [6]. Recombinant erythropoietin is also thought to reduce the need for red blood cell transfusions. The evidence for the use of r-EPO is somewhat mixed, but it has become a common tool for treating preterm infants with anemia [7]. As the age of viability is pushed earlier, it is important for the consulting dermatologist to be aware of the dermatologic effects of r-EPO in the preterm population.

References