Blueberry Muffin Rash in a Patient with Hemolytic Disease of the Newborn Due to Anti-Cw

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Abstract
Blueberry muffin rash is a characteristic multiple bluish skin nodules associated with perinatal infection, severe and chronic anemia, and neoplastic infiltrative diseases. We present an unusually severe case of hemolytic disease of the newborn. He required exchange transfusions for several times. The complete work up led to the diagnosis of anti-Cw. The skin lesion regressed spontaneously within one month.

Keywords ● Isoantibodies ● newborn ● hemolytic disease of the newborn

Introduction
The blueberry muffin rash can be seen with intrauterine infection, severe and chronic anemia, and neoplastic infiltrative diseases.1-10 These lesions can be found in various hematological disorders and hemolytic syndromes such as twin-to-twin transfusion, Rh hemolytic disease of the newborn, diffuse neonatal hemangiomatosis, congenital leukemia, and neuroblastoma.4,6,8,11,12 Blueberry muffin rash is never idiopathic and the prognosis depends on the cause. Cw is a low frequency red cell antigen, which belongs to the Rh antigen system.

We report blueberry muffin rash in a patient with hemolytic disease of the newborn due to anti-Cw. To the best of our knowledge this association has not been previously reported.

Case Report
A full-term male neonate was born through a cesarean section to a 29-year-old mother (gravida 4, para 3, living 0). The neonate’s blood group was O positive. He weighed 2600 gram and his Apgar scores at 1 and 5 minutes were 6 and 9 respectively. He had been resuscitated at the time of birth because of thick meconium stained amniotic fluid. He was then transferred to the neonatal intensive care unit for further management within a few hours of life.

The parents had no consanguinity and did not have any previous medical diseases. Both of them were of Afghani immigrants. The mother had three previous deliveries in which all of the neonates – a girl and two boys- had died one day after birth due to unknown causes but all had pallor and presented with severe jaundice. There was not any data available from the previous birth history in Afghanistan.

Physical examination of the neonate on admission revealed a pale and yellowish skin, edematous infant with many
scarlet-bluish macule, papule, and nodules on his face, chest, abdomen, and extremities (figure). He had hepatosplenomegaly with a liver and spleen palpable 6 cm (with liver span of 9 cm) and 8 cm below costal margins, respectively. His heart was hyperdynamic and a systolic murmur (grade III/VI) was detected. He was supported by mechanical ventilation.

**Figure:** Blueberry muffin rash on the face presented at birth due to extramedullary hematopoeisis.

Initial lab data showed: white blood cell count (WBC)=21000/mm$^3$, hemoglobin=12.3 g/dl, hematocrit=36.9%, reticulocytes=17.8%, and platelet count=13000/mm$^3$. The peripheral smear revealed nucleated red blood cells (NRBC), spherocytosis, and anisocytosis. There were 350 NRBC per 100 WBC. The coagulation times were within normal limits. Blood chemistry revealed normal electrolytes, elevated creatinine (1.6 mg/dl), AST 245 U/l (normal: 0-40), ALT 118 U/l (normal: 0-40), and albumin 2.8g/dl (normal: 3.5-5). Total and direct bilirubin were 12.1 and 2.1mg/dl respectively, which were increased to 21 and 6.8 after 3 hours of birth.

Prenatal screening for infectious diseases was negative. Antinuclear and Antiphospholipid antibodies were negative. Vaginal culture was also negative. Both father and mother had blood group O positive. An assay for maternal antibodies against red cells was not done during pregnancy.

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**Discussion**

Blueberry muffin is a petechial, purpuric, magenta colored macules, papules, and plaques as well as blueberry colored ecchymoses, which resolve gradually over a period of several days to weeks. The clinical significance and prognosis of this lesion in the newborns is variable and depends on its etiology. The hemorrhagic-purpuric looking skin lesions reflect extramedullary hematopoeisis. These may reactivate hematopoeisis in organs where it previously occurred in embryonic and fetal life due to compensatory demand, deficient replacement, or either loss or dysfunction of corpuscular blood elements. Therefore the skin lesions are due to the presence of hematopoeitic aggregations within the dermis and not due to true hemorrhage. These lesions must be differentiated from those seen in malignant diseases such as con-
Blueberry muffin rash due to anti-Cw

Genital monoblastic leukemia, neuroblastoma, congenital alveolar rhabdomyosarcoma, and congenital histiocytosis or neonatal hemangiomatosi,


