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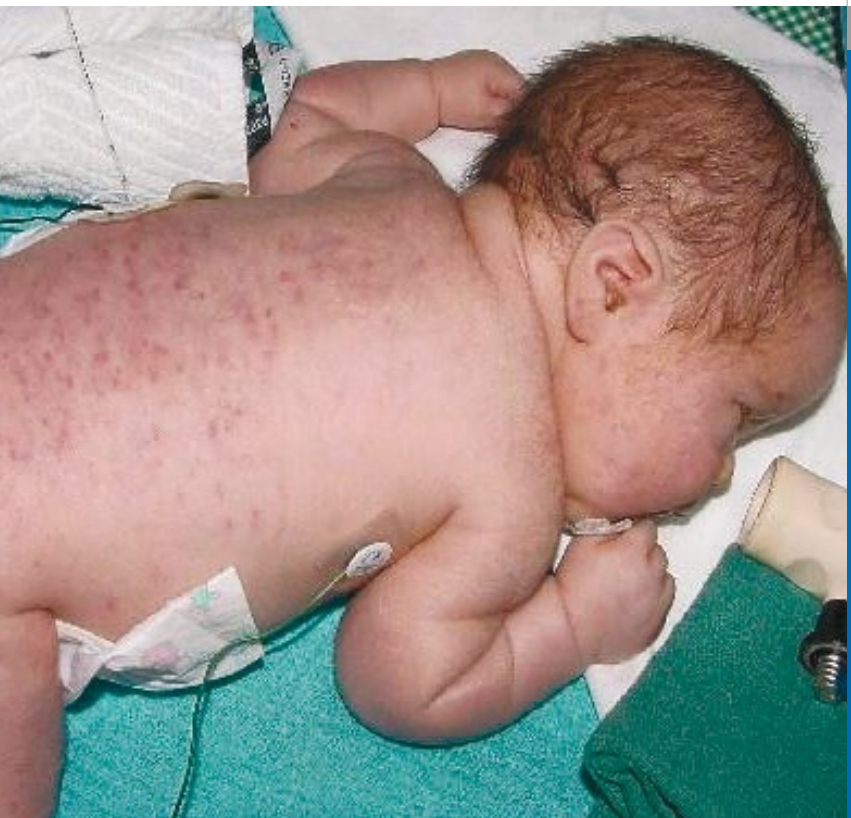
Blueberry muffin baby in anti-Kell alloimmunisation



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Kroiss-Benninger S, Daetwyler K, Berger TM, Neonatal and Pediatric Intensive Care Unit, Children's Hospital of Lucerne, Switzerland

This male infant was born to a 29-year-old G 5/P4 at 34 weeks of gestation by Cesarian section for non-reassuring fetal monitoring. Anti-Kell antibodies had been detected during the preceding pregnancy. Titers had remained constant at 1:128 during the current pregnancy. At 28 weeks of gestation, hydrops with moderate ascites developed (Fig. 1 A, B). Serologies for toxoplasma, hepatitis B, lues, rubella and parvovirus B19 were negative.

Cordocentesis revealed severe anemia with a hemoglobin of 56 g/l. Subsequently, 4 intrauterine transfusions were performed at the University Hospital of Basel (Table) and hydrops resolved.

Apgar scores were 8, 8 and 9 at 1, 5 and 10 minutes, respectively. Birth weight was 2840 g (P 90). He developed mild respiratory distress with tachypnea and a transient oxygen requirement. His skin was pale with multiple plane reddish-blue eruptions, mainly localized on the trunk. These were felt to represent blueberry muffin spots (Fig. 2 A, B). In addition, there was hepatomegaly without splenomegaly.

Initial laboratory investigations revealed severe anemia (hemoglobin of 75 g/l) without evidence of ongoing hemolysis (bilirubin stable at < 100 mcmol/l) and a negative direct Coombs' test. A blood smear showed almost exclusively circulating transfused adult red blood cells with as few as 0.2% HbF-positive erythrocytes (Fig. 3 A).

Table

Gestational age (weeks)	Fetal hemoglobin (g/l)	Transfusion (ml)
28 2/7	56	70
29 1/7	99	60
31 0/7	50	95
33 0/7	72	60

Timing of cordocenteses with fetal hemoglobin concentrations and volume of PRBC transfusions.

Hematopoiesis seemed to be suppressed with a low reticulocyte count (0.3%) and no peripheral erythroblasts. On the other hand, erythropoietin concentration in umbilical cord blood was extremely high with 3240 U/l (normal: 5-25 U/l). In addition, there was mild thrombocytopenia (65 G/l) and leukopenia (4.5 G/l). CMV-cultures of urine were negative and ultrasound examinations of brain and abdomen revealed no pathology.

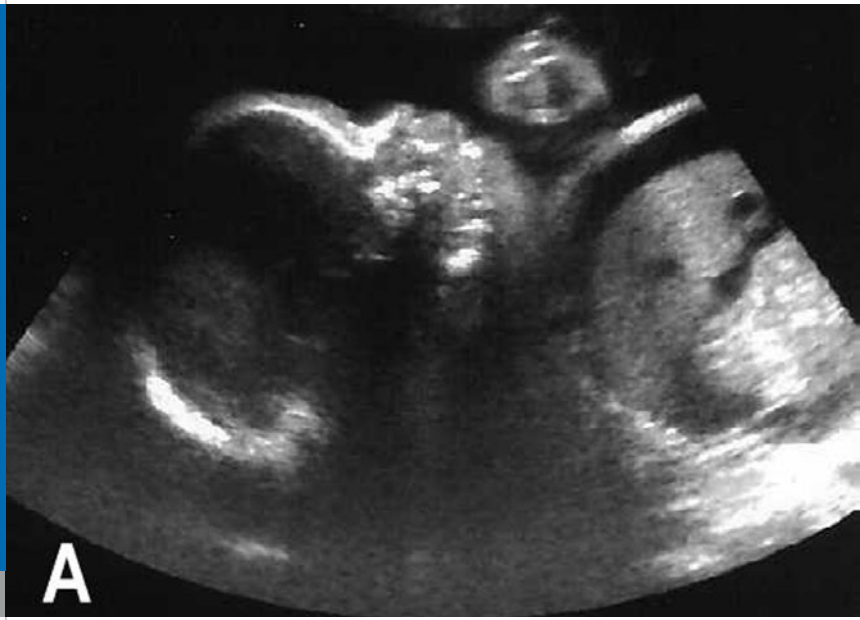
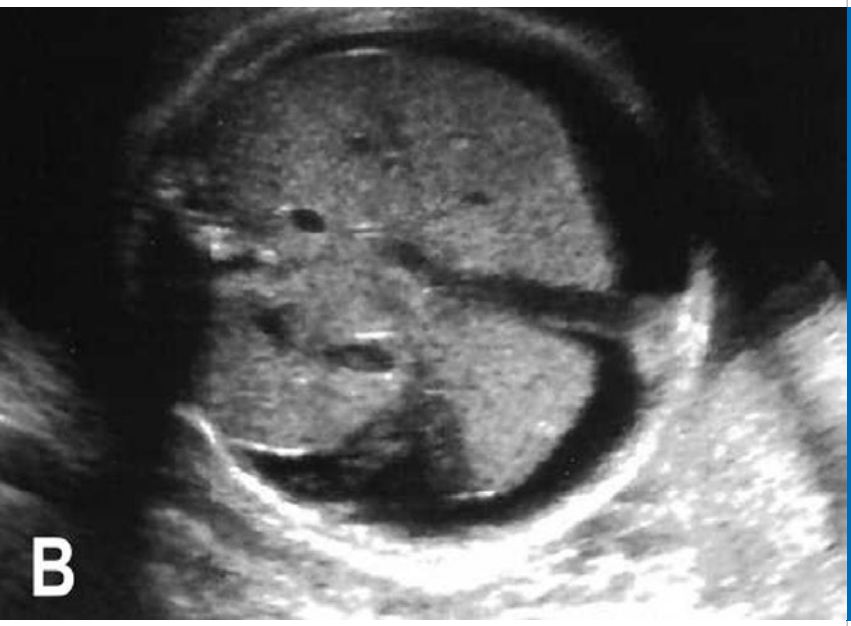


Fig. 1

Dectection of fetal ascites at 28 weeks of gestation.
A) sagital view; B) transverse view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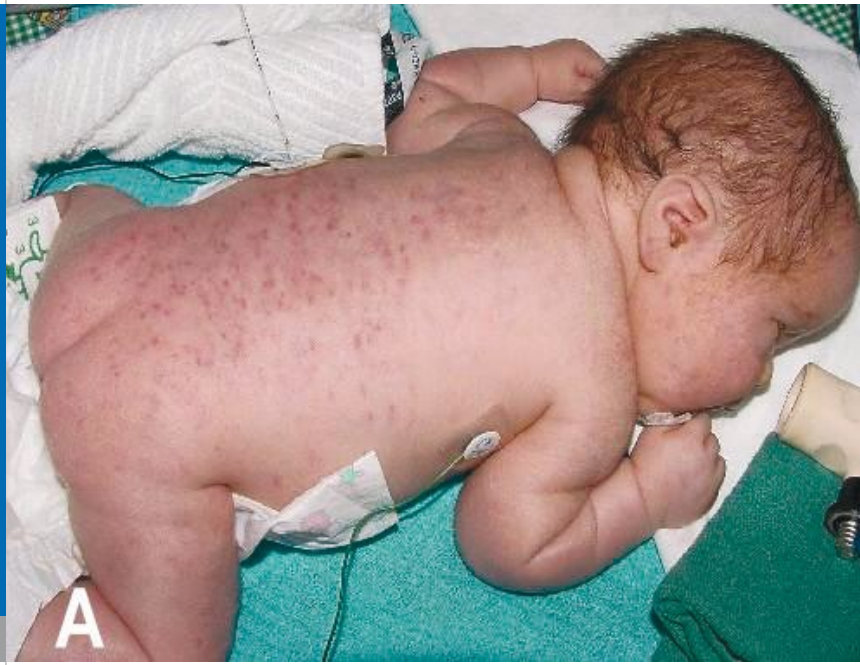
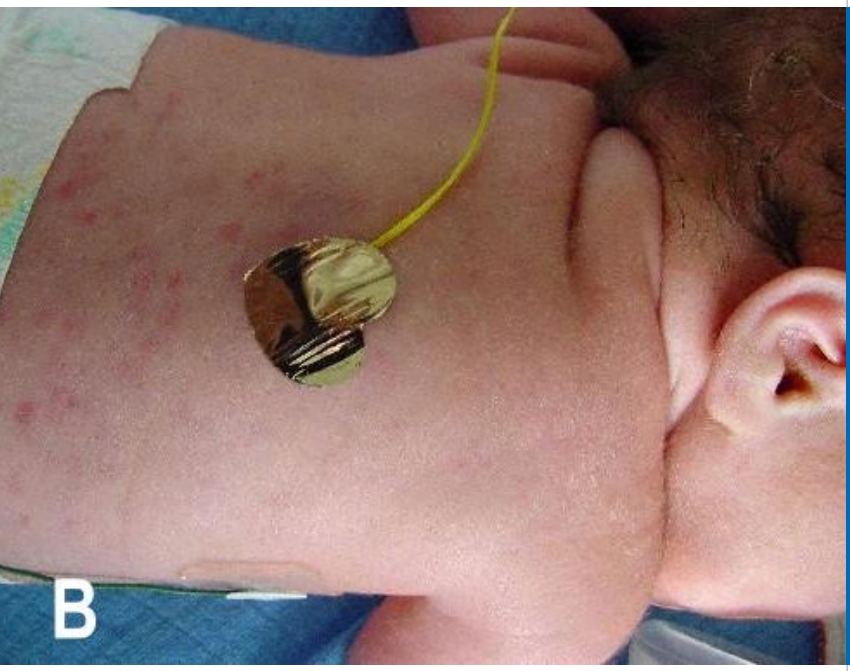


Fig. 2

Blueberry muffin spots.
A) overview; B) close-up view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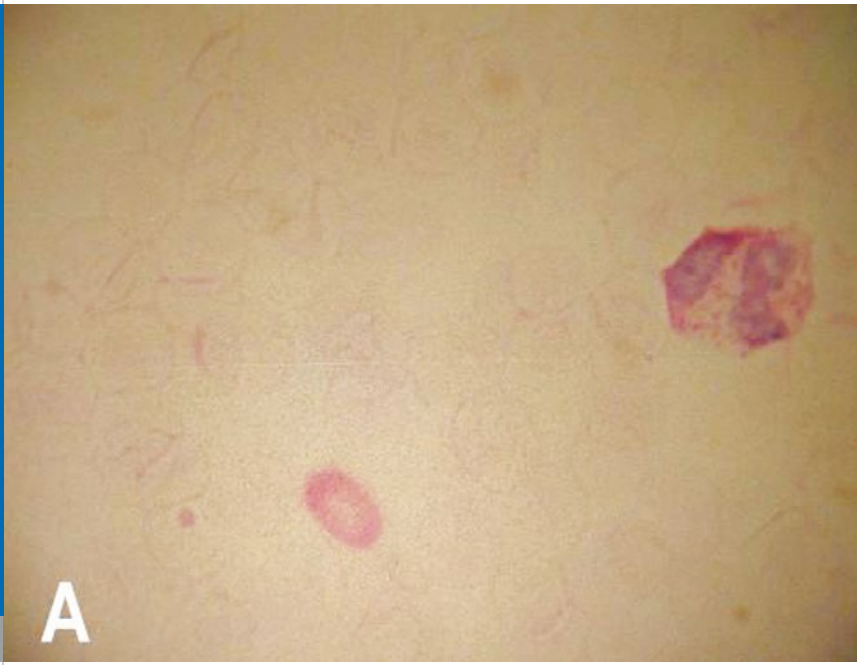

Fig. 3

HbF stains (Kleihauer-Betke acid elution test): A) very few HbF containing cells in the patient's blood smear (< 0.2% HbF-positive cells) with a predominance of "ghosts" (transfused adult erythrocytes); B) a normal HbF stain of a healthy term newborn (> 70% HbF-positive cells) is shown for comparison.

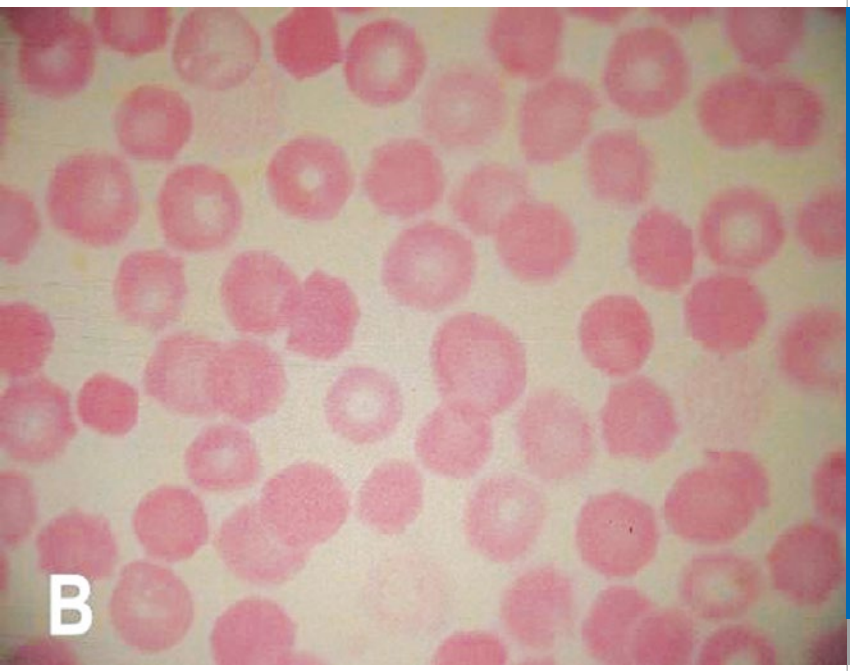

Fig. 3

DISCUSSION

Severe hemolytic disease of the newborn (HDN) is mostly due to Rh-incompatibility characterized by severe hemolysis and increased erythropoiesis with high erythroblast counts and erythropoietin levels (1-3).

The second most common cause of HDN is anti-Kell alloimmunization in which hemolysis is combined with suppression of erythropoiesis at the level of progenitor cells (non- or incompletely hemoglobinized erythroid precursors) (3-5). Therefore, in anti-Kell alloimmunization, bilirubin levels do not correlate with the severity of anemia in the fetus, and amniotic fluid analysis is not a reliable marker for anemia in affected fetuses. In contrast to Rh disease, the number of circulating erythroblasts is low (3,5). Interestingly, we found a highly elevated erythropoietin level in the patient's umbilical cord blood, suggesting that erythropoiesis was suppressed because of the known anti-Kell antibody mediated mechanism and not because of repetitive intrauterine transfusions.

Blueberry muffin spots are caused by dermal erythropoiesis in profound intrauterine anemia. They have been described in Rh disease, twin-to-twin transfusion syndrome and intrauterine infections (i.e. parvovirus B19, CMV, HSV, toxoplasmosis and lues) (6-8). It is not clear if circulating hematopoietic cells settle down in the skin or if dermal mesenchymal cells have the potency to differentiate in situ to blood producing cells (6). Lack of circulating erythroblasts in our patient seem to favor the latter mechanism.

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CONTACT

Swiss Society of Neonatology
www.neonet.ch
webmaster@neonet.ch