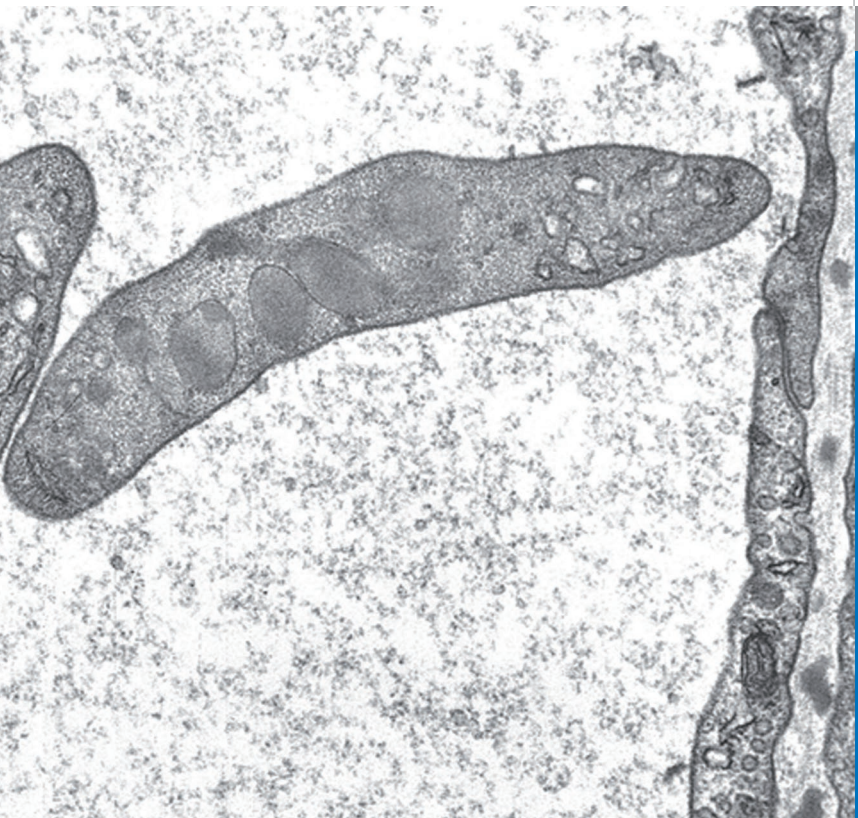
SWISS SOCIETY OF NEONATOLOGY

Neonatal autoimmune thrombocytopenia



November 2013

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This male infant was born to a 33-year-old G1/P1 mother at 38 3/7 weeks of gestation. The mother was known to have idiopathic thrombocytopenic purpura (ITP). No other family member was diagnosed with any hematological disorder. During her pregnancy, the mother had received oral prednisone from 35 weeks of gestation onwards until delivery. Her minimal platelet count was 61'000/µl, but increased to a maximum of 188'000/µl 10 days after prednisone treatment was started. On the day of the planned Caesarean section, her platelet count was 84'000/µl. Apart from thrombocytopenia, the pregnancy had been uneventful.

The infant was delivered by Caesarean section at another hospital. Intraoperatively, vacuum as well as forceps were required to deliver the infant. The infant was born nonreactive, bradycardic and showed no spontaneous respiration. After mask ventilation for 2 minutes, normal heart rate and spontaneous breathing were noted. Apgar scores were 2, 7, and 8 at 1, 5, and 10 minutes, respectively, and umbilical arterial cord-pH was 7.40. Due to respiratory distress, he was transferred to our hospital for further care. His birth weight was 3510 g, length 50 cm and his head circumference 36 cm (all between the P25 and P90). His platelet count was 7'000/µl.

On admission to our unit at the age of 7 hours, his respiratory distress was resolving. He showed multiple

and generalized petechiae, a forceps imprint with bruising, a cephalhematoma over the right occiput and bruises on the right earlobe and temple. Clinical examination was otherwise normal; no hepatosplenomegaly or dysmorphic signs were noted. Cranial ultrasound (cUS) on the first day of life showed bilateral frontoparietal (right > left) subarachnoid hemorrhage and intraparenchymal hemorrhage in the right frontal lobe (Fig. 1).

Given the history of maternal ITP and the clinical findings, we suspected neonatal autoimmune thrombocytopenia. The extensive bruising and intracerebral hemorrhages were thought to be consequences of the combination of traumatic instrumental delivery and low platelet count.

Treatment with intravenous immunoglobulins (IVIG) 0.5 g/kg was started shortly after admission and a single dose of intravenous hydrocortisone 0.5 mg/kg was given. On the second day of life, a single platelet transfusion (15 ml/kg) was given with a subsequent platelet count of 23’000/µl that dropped again rapidly. Until the fourth day of life, IVIG was administered repeatedly 3 times (total dose of 2 g/kg). Until discharge on the tenth day of life, no new petechiae appeared and existing petechiae and bruises were decreasing. Platelet counts were fluctuating between 5’000/µl and 9’000/µl (Fig. 2).

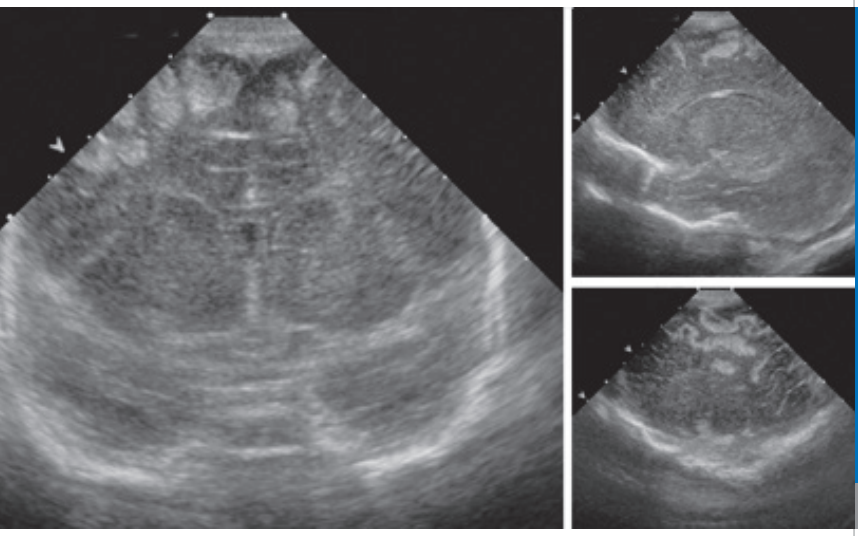

Fig. 1

Coronal and right sagittal cUS images on admission showing bilateral frontoparietal (right > left) subarachnoid hemorrhage and intraparenchymal hemorrhage in the right frontal lobe.

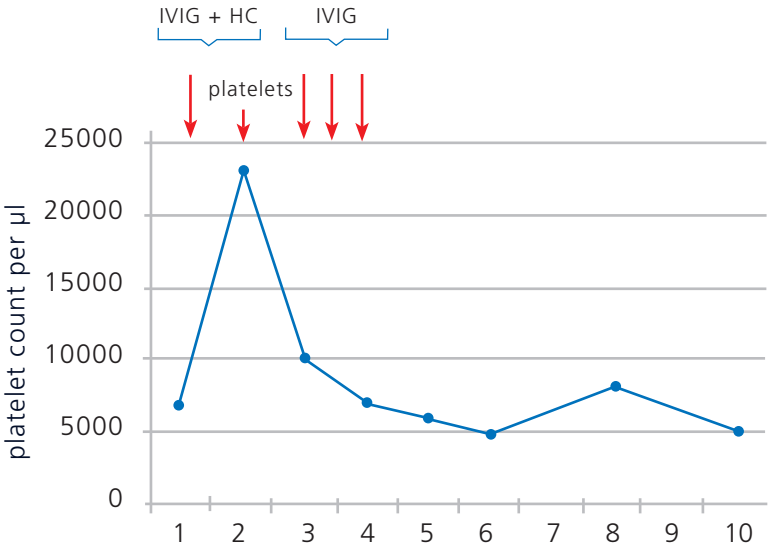

Fig. 2

Interventions and platelet counts over the first 10 days of life.

A cranial CT scan performed on the second day of life showed bilateral subarachnoid hemorrhages and bilateral petechial hemorrhages in the fronto-temporo-parietal white matter, with both findings being more pronounced on the right side (Fig. 3). Furthermore, a right-sided parietal skull fracture with an overlying galeal hematoma and an underlying epidural hematoma was found (Fig. 4). There was no sign of intraventricular bleeding, no ventricular dilatation and no midline-shift.

Regular cUS examinations were performed and did not reveal signs of new hemorrhages (Fig. 5). A cranial MRI on day 10 of life showed multiple hemorrhages consistent with the cranial CT scan on day 2 of life. In addition, a hemorrhage in the left occipital white matter was seen (Fig. 6).

At the age of three weeks, the boy appeared healthy with minimal residual petechiae. The boy's platelet count was 3'000/µl. Cranial US showed multiple bilateral frontoparietal porencephalic cysts; ventricular size and extracerebral spaces were normal (Fig. 7). One week later, he was seen at the Pediatric Hematology Department. His platelet count was 6'000/µl and he received another dose of IVIG 0.8 g/kg. At 7 weeks of age, his platelet count was 68'000/µl but decreased again to 17.000/µl at the age of 9 weeks and a fourth dose of IVIG 0.7 g/kg was given. Since then his platelet counts remained >100'000/µl. Apart

from intermittently increased muscle tone with some fisting, neurological examinations at 9 and 15 weeks of life were normal and his development was within normal range.

There is no specific diagnostic test to confirm our presumptive diagnosis of neonatal autoimmune thrombocytopenia, but ITP in the mother makes it very likely. Furthermore, neonatal alloimmune thrombocytopenia (NAIT) was excluded by ELISA testing for HPA-1a/5b antibodies. Both parents showed antigen patterns of platelet glycoproteins that are not associated with NAIT. Finally, human platelet antigen (HPA) antibodies could not be detected in the mother.

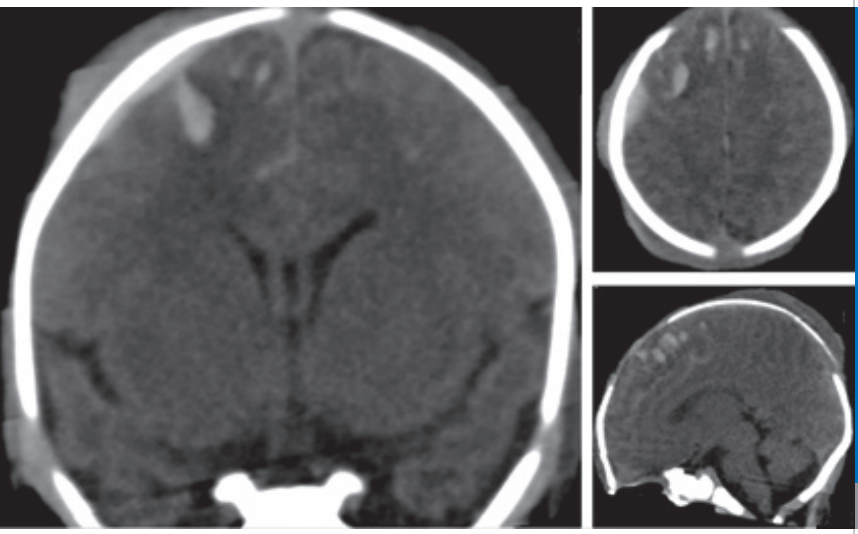

Fig. 3

CT images on day 2 of life: bilateral frontoparietal subarachnoid hemorrhages and bilateral petechial hemorrhages in the frontotemporoparietal white matter.

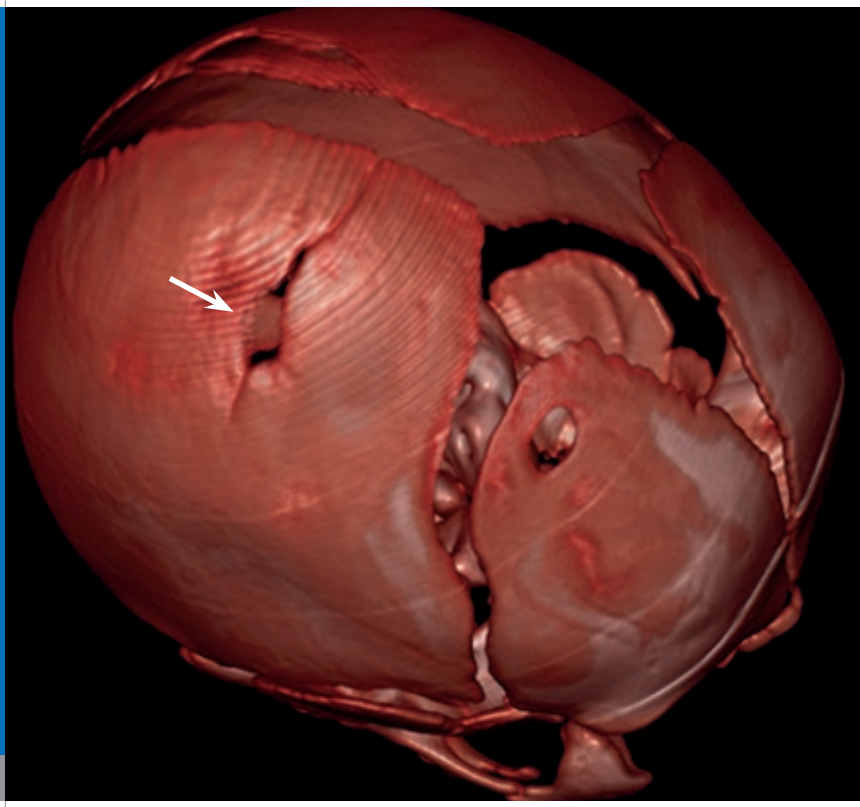

Fig. 4

CT with 3D reconstruction: parietal skull fracture (arrow).

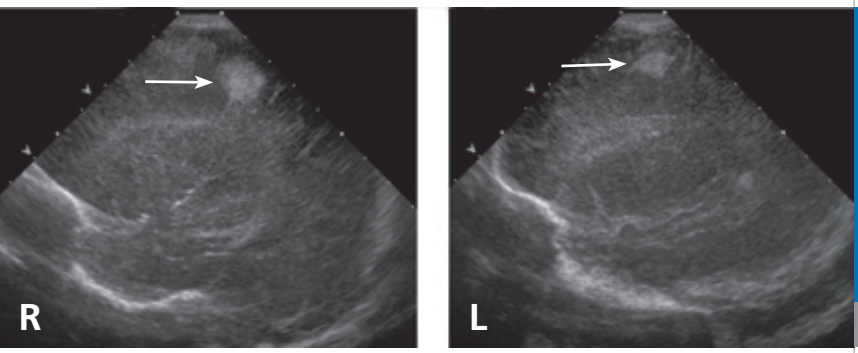

Fig. 5

Coronal and sagittal cUS images on day 10 of life: demarcated intraparenchymal bilateral frontoparietal hemorrhages (arrows); in addition, a focal hemorrhagic lesion is seen in the left temporal white matter (arrowhead).

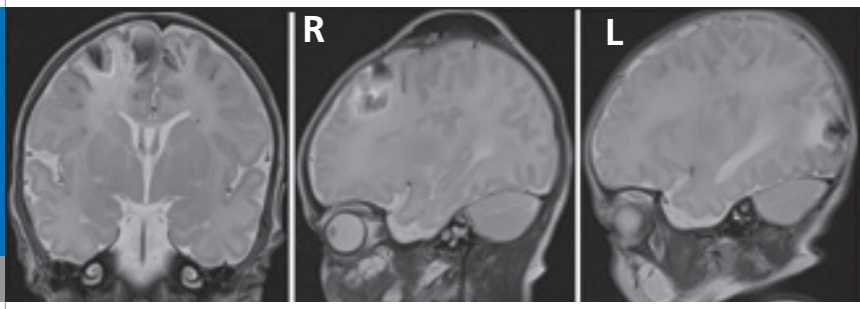

Fig. 6

Coronal and sagittal T2-weighted MR images on day 10 of life: parenchymal hemorrhagic lesions, subarachnoid hemorrhages, galeal and epidural hematomas.

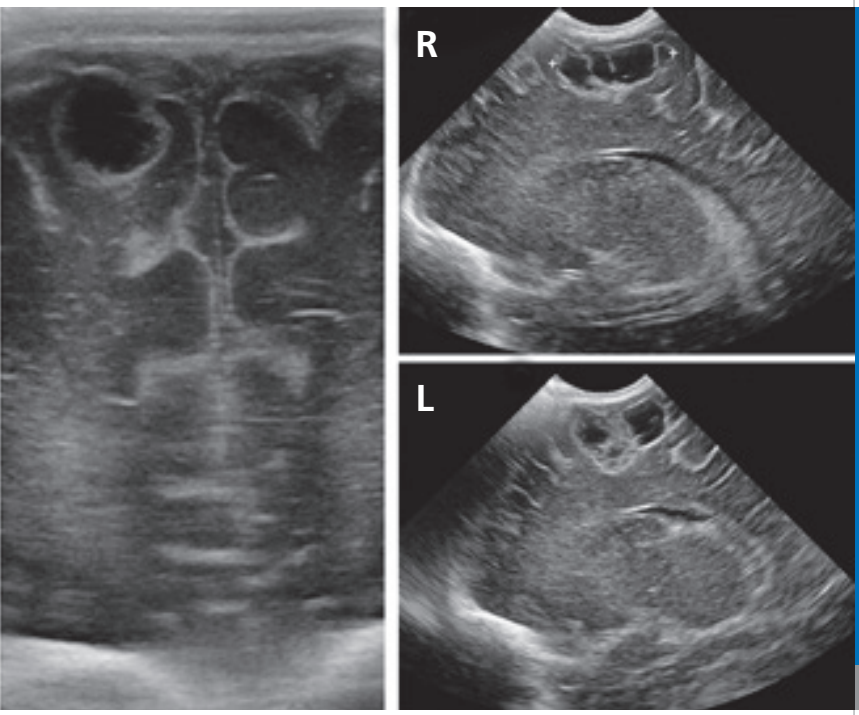

Fig. 7

Coronal and sagittal cUS images at the age of three weeks: cystic evolution of the hemorrhagic lesions bilaterally.

DISCUSSION

Thrombocytopenia is defined as a platelet count below 150'000/µl. It occurs in less than 1% of neonates, but it is one of the most common hematologic problems in the neonatal age group. Usually, a bleeding tendency is only observed if the platelet counts drop below 50'000/µl.

The causes of thrombocytopenia in neonates are diverse and include immune, inherited and acquired disorders and evaluation is challenging (1). Neonatal autoimmune thrombocytopenia accounts for only 3% of all cases of thrombocytopenia at delivery (2) and is present in about 10–15% of infants born to mothers with ITP (3). Maternal platelet counts do not correlate with neonatal platelet counts, and there are no serological tests or clinical characteristics in the mother, which reliably predict a low neonatal platelet count (2). There is a strong correlation between first and second siblings regarding the occurrence of autoimmune thrombocytopenia, and the severity and pattern of thrombocytopenia are similar among siblings (4).

Severe thrombocytopenia with platelet counts less than 50'000/µl is uncommon in babies born to mothers with ITP and intracranial hemorrhage (ICH) is rare with an estimated incidence of less than 1% (5). ICH is unlikely to be affected by the mode of delivery; therefore, ITP in the mother is not an indication for Caesarean section and the mode of delivery is based on obstetric indications (5). Nevertheless, current

guidelines recommend avoiding procedures during labor associated with increased fetal hemorrhage risk including the use of fetal scalp electrodes, fetal blood sampling, vacuum delivery and rotational forceps. In cases of maternal ITP, it might be prudent to discuss the transfer of the mother to a tertiary obstetric center to allow urgent transfer of the newborn to a neonatal ward if complications occur.

The international consensus report on the investigation and management of primary immune thrombocytopenia recommends the following procedure for infants born to mothers with ITP (6): a cord blood platelet count should be determined and intramuscular injections, such as vitamin K, should be avoided until the platelet count is known. Infants with subnormal counts should be observed clinically and hematologically, as platelet counts tend to nadir between days 2 and 5 after birth. Cranial ultrasonography should be performed in neonates with platelet counts less than 50'000/µl at delivery. If the extent and localization of any hemorrhages are unclear, further imaging such as MRI should be considered. Treatment of the neonate is rarely required. However, in infants with clinical hemorrhage or platelet counts of less than 20'000/µl, treatment with IVIG 1 g/kg is indicated. Life-threatening hemorrhage should be treated by platelet transfusions combined with IVIG. Since severe thrombocytopenia and clinical hemorrhage in neonates are rarely due to maternal ITP, NAIT should be excluded by laboratory te-

sting for alloimmune antiplatelet antibodies in maternal serum and platelet alloantigen incompatibility between the parents.

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concept & design by mesch.ch

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