

## CLINICAL OBSERVATIONS

# Intracranial hemorrhage associated with vitamin K deficiency in a breastfed infant after intramuscular vitamin K prophylaxis at birth. Follow-up at 18 months

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Hemorrhagic disease of the newborn or, more precisely, vitamin K deficiency bleeding (VKDB) in infancy, according to the Committee of the International Society on Thrombosis and Hemostasis (1), is a bleeding disorder due to vitamin K deficiency. It generally occurs during the neonatal period, but it is occasionally seen in infants several months old (2–4). The postnatal administration of vitamin K has dramatically reduced the incidence of VKDB during the first weeks of life, although sporadic cases with late-onset hemorrhage are described among exclusively breastfed infants who did not receive additional prophylaxis (5–7). In Italy, vitamin K prophylaxis at birth is routinely administered by a single injection of 1 mg of intramuscular vitamin K, or a 2-mg dose of oral vitamin K, but additional supplementation to exclusively breastfed infants is not consistent. We observed an exclusively breastfed infant who was treated appropriately with vitamin K at delivery but received no additional exogenous vitamin K thereafter, and subsequently developed a severe intraparenchymal and intraventricular hemorrhage.

### Case report

A 7-wk-old female infant was admitted to the Division of Pediatrics, Azienda Ospedaliera "A. Di Summa", Brindisi, Italy, with a 2-d history of vomiting, poor feeding, irritability and a bulging anterior fontanel. There were no ecchymoses, petechiae or signs of abuse. The history given by parents was consistent and no suspicion of non-accidental injury was raised.

She was born at term in a district general hospital by spontaneous vaginal delivery, with a birthweight of 3400 g. She received 1 mg of vitamin K intramuscularly shortly after delivery, as is routine practice at that hospital. The infant was exclusively breastfed, and no further vitamin supplementation was provided. She regained her birthweight rapidly and then grew regularly at 75th percentile of weight for age. Family history was unremarkable for hemorrhagic diathesis, and the mother was not taking any medications.

At the time of admission a generalized tonic clonic seizure occurred. A lumbar puncture was performed to

exclude bacterial meningitis and showed hemorrhagic liquor. Cranial ultrasonography through the anterior fontanel showed a large left intraventricular hemorrhage with ipsilateral involvement of the parenchyma in the frontal and parietal regions; a smaller parenchymal hemorrhage was also detectable in the right frontal area (Fig. 1). No mild bleeding or signs of cholestasis occurred before intracranial hemorrhage. Laboratory data indicated anemia (hemoglobin 5.8 g/dL) and a marked prolongation of the prothrombin time (PT) and the activated partial thromboplastin time (aPTT), but a normal platelet count, a normal fibrinogen concentration and a normal level of fibrin degradation products (FDP). She was treated with a packed erythrocyte transfusion (10 mL/kg), fresh frozen plasma (10 mL/kg) and 4 mg of intravenous vitamin K. Antibiotic treatment was discontinued after 48 h because the cerebrospinal fluid culture was sterile. Microscopic examination of stool for fat was normal as well as transferrin serum level. Liver function was evaluated by measurement of serum transaminases level, alkaline phosphatase level and serum albumin level. Liver and biliary ultrasound was also performed to rule out cholestasis. The laboratory values before and after vitamin K adminis-



Fig. 1. Coronal cranial ultrasonogram: left intraventricular hemorrhage with ipsilateral frontal and parietal parenchymal hemorrhage.

Table 1. Values for coagulation tests before and after vitamin K administration.

	12 h before treatment	48 h after treatment	3 d after treatment	Reference ranges at 30–90 d of age (*)
PT (sec)	>30	15.1	13.7	10.0–14.3
APTT (sec)	240	31.1	20.4	29.0–50.1
AT (%)	49	96	ND	80–120
FDP (µg/mL)	<0.5	<0.5	ND	0–0.5
Fibrinogen (mg/dL)	235	183	183	150–379
Platelet count (×10 <sup>3</sup> /µL)	362	270	368	150–400

PT, prothrombin time; APTT, activated partial thromboplastin time; AT, antithrombin; FDP, fibrin-degradation products; ND, not done.

\*Source: Andrew M, Paes B, Johnston M. Development of the hemostatic system in the neonate and young infant. *Am J Pediatr Hematol Oncol* 1990; 12: 95.

tration suggested late onset haemorrhagic disease due to vitamin K deficiency (Table 1).

Cranial tomography confirmed the intraventricular and parenchymal hemorrhages (Fig. 2), and magnetic resonance imaging was performed to better delineate the parenchymal lesion (Fig. 3). Neurosurgical drainage was not performed due to stabilization of the ventricular size and persistently normal Doppler Resistance Index. Serial cranial ultrasonography was used for outpatient monitoring. Psychomotor assessments (Brunet Lezine Index) and neurological examinations at 8, 12 and 18 mo of age were all in the normal range.

Discussion

Late hemorrhagic disease of the newborn is a form of VKDB, and occurs in neonates 4 wk to 6 mo after birth



Fig. 2. Computed tomography scan: tri-ventricular post-hemorrhagic hydrocephalus; left frontal and parietal parenchymal hemorrhage.



Fig. 3. Magnetic resonance imaging scan: tri-ventricular post-hemorrhagic hydrocephalus; left frontal and parietal parenchymal hemorrhage.

in association with inadequate vitamin K intake (low vitamin K content in breast milk) or with malabsorption of vitamin K due to hepatobiliary disease or to broad-spectrum antibiotics treatment. The incidence of intracranial hemorrhage in the late form of VKDB is greater than 59% (5–10). In the present case, malabsorption was not identified and our laboratory findings indicated that the cause of the intracranial hemorrhage was probably related to the low vitamin K intake in an exclusively breastfed infant receiving no additional vitamin K supplementation.

Healthy neonates have relatively low circulating vitamin K concentrations, and even prophylactic vitamin K administration at birth is not always sufficient. In fact, the vitamin K content of human milk is very low compared with standard infant formulas (around 7,000 pg/mL) (11). Commercial infant formulas are supplemented with vitamin K and, consequently, formula-fed infants are at lower risk for developing VKDB than are breastfed neonates. Although there are no national guidelines from the Italian College of Pediatrics on the timing of vitamin K supplementation to exclusively breastfed infants, it seems that some form of late prophylactic treatment is warranted. However, it is unclear how such supplementation should be provided (12). Recent reports indicate that a weekly dose of a new oral preparation of vitamin K (Konaktion MM) for the first 8 wk has equivalent effects to intramuscular administration of vitamin K at birth (13). Other reports illustrate that maternal supplementation with 5 mg of

phylloquinone daily, over the 12 wk following delivery, will increase the serum concentration of vitamin K in the babies who received a single dose of intramuscular vitamin K at birth (14, 15). On the basis of this and the few other similar reports, we speculate that, in addition to vitamin K prophylaxis at birth, vitamin K supplementation for exclusively breastfed neonates should be considered to prevent the late form of VKDB.

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## Infantile form G<sub>M1</sub> gangliosidosis with dilated cardiomyopathy: a case report

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G<sub>M1</sub> gangliosidosis is a rare disease in children caused by congenital deficiency of lysosomal acid  $\beta$ -galactosidase, resulting in accumulation of ganglioside G<sub>M1</sub> and the asialo derivatives in the brain and viscera (1–4). This disease is divided into three types in accordance with age of onset and clinical manifestation. Type 1 (infantile type) is characterized by neurologic deterioration and visceromegaly before the age of 6 mo. Type 2 (late infantile/juvenile type) usually occurs between ages 7 mo and 3 y, with less prominent dysmorphism. Type 3 (chronic/adult type) is characterized by later onset (7–30 y) and extrapyramidal signs. The mode of inheritance is autosomal-

recessive in all types. There is no known sexual or ethnic predilection.

The infantile form, G<sub>M1</sub> gangliosidosis, usually presents as a developmental delay or arrest in developmental milestones. In severe cases, weak sucking power, poor appetite and failure to thrive occur during the neonatal period. During the physical examination the patient usually presents with hypotonia, facial dysmorphism, generalized skeletal dysplasia, hepatosplenomegaly, hyperactive deep tendon reflexes and macular cherry-red spots (1). The diagnosis is confirmed by the finding of deficient  $\beta$ -galactosidase activity in leukocytes and skin fibroblasts.

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