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CASE REPORT

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Late hemorrhagic disease of the newborn as a cause of intracerebral bleeding

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Abstract We report a case of a 4-week-old female who presented with late hemorrhagic disease of the newborn (HDN). The newborn was previously healthy, and she received 1 mg of intramuscular vitamin K at birth. She was exclusively breast-fed. At 4 weeks she began bleeding at the umbilicus and 4 days after she suffered an intracranial hemorrhage. Coagulation studies showed a deficiency of vitamin K-dependent coagulation factors, and the normalization of all clotting studies after administration of vitamin K confirmed the diagnosis of HDN. Our conclusions are that physicians must be alert to mild bleeding in newborns and that prophylaxis with 1 mg of intramuscular vitamin K at birth may be insufficient to prevent late HDN.

Key words Late HDN · Vitamin K · Intracranial hemorrhage

Introduction

Hemorrhagic disease of the newborn (HDN) is a bleeding disorder caused by a deficiency of vitamin K during early life. HDN has been classified into three syndromes according to the moment of appearence: early, classic, and late. Since the introduction of routine vitamin K prophylaxis for newborns, the incidence of the classic form has been decreased dramatically [3, 4]. Nevertheless, a concomitant increase in the late form has been observed in developed countries. We report a case of a 4-week-old newborn who received intramuscular vitamin K prophylaxis at birth and presented a typical late form of HDN, with cerebral hemorrhage and death.

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Case report

A 4-week-old female was seen at our hospital with a 4-day history of increased irritability, mild umbilical bleeding, poor feeding and vomiting. Her past medical history was that of a term vaginal delivery at hospital without incidence. According to the baby's clinical history, prophylaxis with 1 mg of parenteral vitamin K had been given within the first 2 h of life. The child had been exclusively breast-fed and received no vitamins or medications. There was no history of underlying disease, previous trauma, or poor weight gain. Family history was negative for bleeding diathesis.

Physical examination revealed intense pallor, cold, and anisocoria. She had a bulging anterior fontanela and bled at the umbilicus. A CT-scan showed intracerebral hemorrhage (Fig. 1). Initial stabilization included intravenous fluids, endotracheal intubation, blood transfusion, and phenobarbital to avoid seizures.

Initial laboratory data included hematocrit: 23%, hemoglobin: 76 g/l, platelet count: 406×10^9/l. WBC count was: 18.4×10^9/l with 50% segmented cells, 2% bands, 38% lymphocytes, and 10% monocytes. Blood biochemical studies were normal. The initial coagulation studies showed APTT ratio: 3.54, INR: 12.5, and TT: 29.5. Blood samples were drawn to determine multiple coagulation factors, and 3 mg of parenteral vitamin K and fresh-frozen plasma (15 ml/kg) were given. The coagulation studies performed

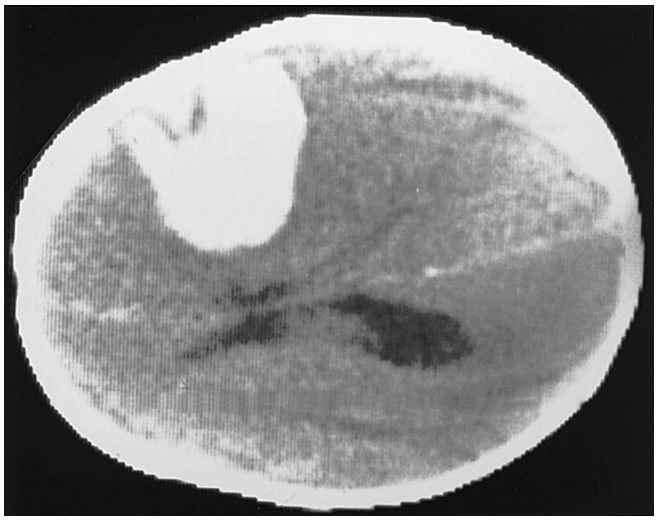

Fig. 1 CT-scan: large right intraparenchymal hematoma and marked deviation of the interhemispheric fissure

Table 1 Coagulation studies performed before and after vitamin K administration

	Before vit. K	6 h after vit. K	12 h after vit. K
APTT (ratio)	3.5	1.03	0.84
PT (ratio)	12.5	1.06	0.91
TT (s)	30	26	24
Fibrinogen (g/l)	360	–	–
Platelets ($\times 10^9$/l)	407	305	379
Factor IIc (%)	2	–	–
Factor Vc (%)	106	–	–
Factor VIIc (%)	5	–	–
Factor IXc (%)	2	–	–
Factor Xc (%)	1	–	–
Factor XIII (%)	126	–	–

afterwards showed normal values. The results of the clotting factor functional studies were diagnostic for HDN (Table 1).

The infant was submitted to neurosurgery to drain the cerebral hematoma. However, despite surgery and intensive support, her condition deteriored and she died 12 days after admission. Coagulation studies remained normal until death. Postmortem examination excluded any underlying disease.

Discussion

This newborn was admitted with a 4-day history of mild bleeding at the umbilicus and a sudden intracranial hemorrhage. This clinical picture suggested three diagnostic posibilities: HDN, liver disease, and congenital factor XIII deficiency. The low levels of vitamin K-dependent factors were highly suggestive of HDN. Normal levels of factor V and XIII excluded liver disease and factor XIII congenital deficiency, respectively. Finally, the normalization of blood coagulation studies after vitamin K administration confirmed the diagnosis of HDN. The administration of plasma might explain an initial normalization of blood coagulation parameters but not the persistence of normal values until death.

This patient presented a typical case of late HDN. This form of HDN appears between 3 and 6 weeks of life, and intracranial hemorrhage accounts for 50% of the bleeding episodes at presentation [7]. Many cases have been reported, some of them associated with lack of vitamin K prophylaxis at birth [5] or with underlying diseases such as cystic fibrosis, jaundice, and diarrhea [1]. However, most cases are idiopatic and they occur even after the administration of prophylactic vitamin K [9].

There are probably more than one cause of late HDN. It has been demonstrated that normal newborns have a precariously low vitamin K status [8], and this makes them especially susceptible to developing a vitamin K deficiency and bleeding. Excluding underlying diseases, two main risk factors have been implicated in late HDN: the absence of vitamin K prophylaxis at birth and breast-feeding exclusively [6]. This newborn was previously healthy and had no hepatic or other underlying disease. She received intramuscular vitamin K (1 mg) at birth and was exclusively breast-fed. It has been reported that some infants with late HDN have mild and self-correcting disorders of liver function that lead to a degree of cholestasis and impairment of vitamin K absorption. There was no objective evidence that our patient suffered such liver dysfunctions. Moreover, no hepatic disease was detected at postmortem examination. Likewise, she had not received antibiotics or any other drugs.

It has also been reported that there is a higher incidence of late HDN in babies who received oral vitamin K prophylaxis at birth, and it has been suggested that intramuscular vitamin K prophylaxis may be a better way to prevent late HDN [10]. In this case, despite intramuscular vitamin K administration, the patient suffered a deficiency of vitamin K and intracranial hemorrhage. It seems clear that prophylaxis with 1 mg of parenteral vitamin K at birth was not enough, and she developed a severe deficiency that produced fatal intracranial bleeding. The main cause or causes of the vitamin K deficiency remain unknown, but breast-feeding probably played an important role. To prevent the appearence of late HDN, some authors have proposed that vitamin K prophylaxis at birth should be followed by further doses of oral vitamin K during the first months of life, not only for high-risk patients but also for healthy newborns [2]. Our case and another previously reported case support this proposal [9].

Initial symptoms in this child were irritability and umbilical bleeding. The persistence of mild bleeding can be a warning sign of HDN. Because of the risk of developing severe hemorrhagic symptoms and the bad prognosis, physicians should be alert to the possibility of vitamin K deficiency and bleeding in older infants.

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