

INTRACEREBRAL HEMORRHAGE: A RARE LATE MANIFESTATION OF VITAMIN – K DEFICIENCY IN A BREASTFED INFANT*

A Case Report

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SUMMARY: Soylu H, Aslan Y, Sari A, Erduran E. (Departments of Pediatrics and Radiology, Karadeniz Technical University Faculty of Medicine, Trabzon, Turkey). Intracerebral hemorrhage: a rare late manifestation of vitamin-K deficiency in a breastfed infant. A case report. *Turk J Pediatr* 1997; 39: 265-269.

Late hemorrhagic disease of the newborn (HDN) is a rare complication of vitamin-K deficiency and is especially associated with intracranial hemorrhage. It may also occur in infants who received vitamin-K prophylaxis at birth. Here, we reported a case of late HDN with frontal lobe hemorrhage due to vitamin-K deficiency. This form of intracranial hemorrhage of late HDN has been reported in the literature very rarely. We conclude that the efficiency of single-dose vitamin-K prophylaxis should be reevaluated. *Key words: intracerebral hemorrhage, vitamin-K deficiency.*

Hemorrhagic disease of the newborn (HDN) consists of hemorrhages from multiple sites in otherwise healthy infants in the absence of trauma, asphyxia or infection¹. The link between vitamin-K deficiency and spontaneous hemorrhaging was first made by Dam in 1929^{1,2}. Hemorrhagic disease of the newborn due to vitamin-K deficiency may occur at three different times:

1. On the first day of life: Drugs taken by the mother may play a part-notably, anticonvulsants (e.g., phenobarbital and phenytoin), rifampicin, isoniazid, anticoagulants (e.g., warfarin) and phenylbutazone^{1,2}.
2. Between the second and fifth days: This is defined as classic HDN and is characterized by gastrointestinal bleeding, mostly from the stomach, intestine, umbilical stump and needle or operation sites, widespread ecchymoses and, rarely, intracranial bleeding.

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3. Beyond the second week: This form is called late HDN and is particularly associated with intracranial hemorrhage. Mortality and morbidity rates are higher in this group than others⁴.

Severe intracranial hemorrhage due to vitamin-K deficiency in young infants may occur suddenly and result in death or severe central nervous system dysfunction. Therefore, it is an extremely serious event³.

HDN may be associated with a variety of disorders compromising the supply of vitamin-K, including chronic diarrhea, diarrhea of breastfed infants, cystic fibrosis, α -1-antitrypsin deficiency, hepatitis, celiac disease and others^{1,5}. Because of maternal milk's low vitamin-K content and inhibition to colonization of the intestinal microbial flora capable of synthesizing vitamin-K, it has been accused of causing HDN¹⁻³.

Since the 1970s, through the oral administration of vitamin-K, the incidence of intracranial hemorrhage has markedly decreased from 34.3/100,000 to 10.1/100,000 live births⁶. Also, in our country, 1 mg vitamin-K₁ has been administered routinely via intramuscular injection at birth. However, late HDN has still occurred rarely.

Here, we report a case of late HDN with intracranial bleeding in an infant who had received vitamin-K prophylaxis at birth.

Case Report

A 37-day-old boy was admitted to our pediatric emergency ward with the complaint of seizures. He had no history of diarrhea or drug use. He had been born at term following a healthy labor and delivery. The patient's mother had not used any medicine during the prenatal or postnatal period. The baby was breastfed. There was not any hemorrhagic diathesis disorder in his family. Vitamin-K₁ (1 mg) had been injected intramuscularly within the first 24 hours following delivery.

Physical examination revealed a temperature of 36 °C, pulse of 152 beats per minute, respirations 44 per minute, and a blood pressure of 64/39 mmHg. Pallor, generalized tonic-clonic seizures with a left predominance, fontanel bulging and grade I papillary stasis of both eyes were observed. The deep tendon reflexes were more active on the left side. The seizures were stopped by intravenous diazepam, and phenobarbital prophylaxis was commenced.

Laboratory findings included hemoglobin 7.4 g/dl, leukocytes $14.1 \times 10^9/L$, thrombocytes $186 \times 10^9/L$, bleeding time 4.5 minutes, prothrombin time (PT) 22 sec, activated partial thromboplastin time (aPTT) 34.6 sec, and fibrinogen level 264 g/L. The results of liver function tests were in the normal range. Intracerebral hemorrhage due to vitamin-K deficiency was diagnosed, and vitamin-K₁ (2 mg) was administered intravenously.

Cranial tomography (CT) originally revealed a large hemorrhage surrounded by edema in the right frontal region (Fig. 1). Two weeks later, magnetic resonance imaging (MRI) was done, and the same hemorrhagic lesion was seen in the subacute period (Figs. 2a,b). After observation for 15 days, PT and aPTT were within normal limits and the previous clinical findings had improved. Moreover, the results of both the sweat test for cystic fibrosis and the α -1-antitrypsin level were found in normal ranges. Therefore, the patient was discharged on phenobarbital prophylaxis. He has been followed for six months as an outpatient with no complaints.

Discussion

Intracranial hemorrhage due to vitamin-K deficiency is the most common form of late HDN and accounts for approximately 50 percent of the bleeding episodes at presentation^{4,7}. It often occurs in the first to third months of life⁴. In our case, the episode occurred on the 37th day of life. The majority of these infants are breastfed⁸⁻¹⁰; the importance of breastfeeding as a risk factor seems to lie in the low concentrations of vitamin-K in human milk^{2,3,7}.

Gobel et al¹⁰ found that the serum prothrombin time of infants who were solely breastfed was longer on the fifth day of life than in infants fed formula. Furthermore, in early HDN, drugs taken by the mother during pregnancy, and

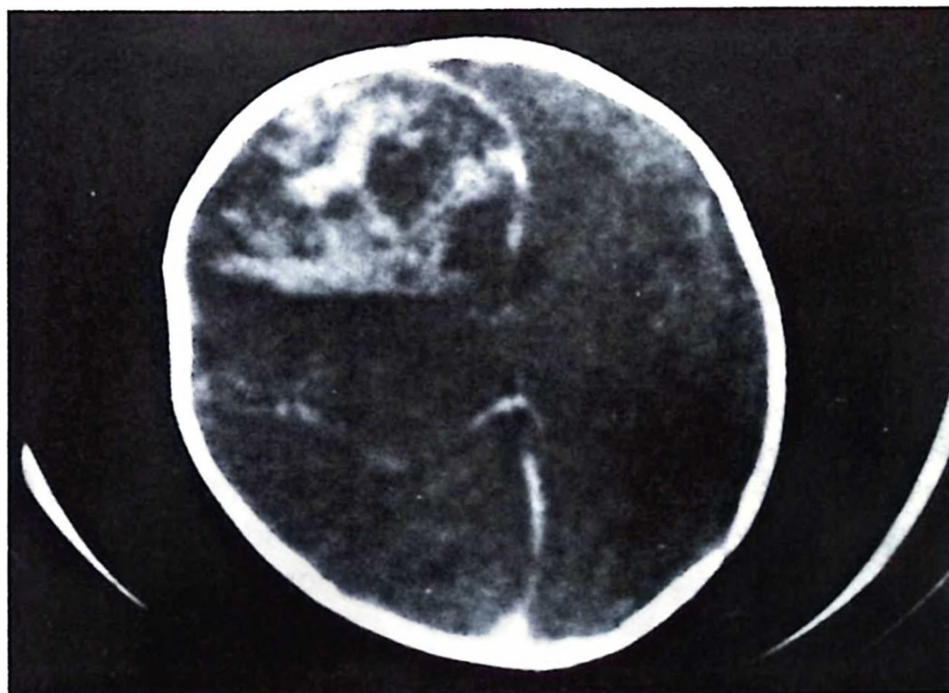


Fig. 1: CT showed a large heterogeneous hyperdensity in the right frontal lobe, indicating intracerebral hemorrhage in the acute-subacute period and shift of interhemispheric fissure to the left side.



Fig. 2a: T1 sagittal MRI on the 15th day of the hemorrhage, showing the late subacute hematoma in the right frontal lobe surrounded by a hypointense rim.



Fig. 2b: Axial proton density image revealed the presence of left lateral ventricle dilatation.

in late HDN, chronic diarrhea, hepatitis, α -1-antitrypsin deficiency and cystic fibrosis may also play roles^{1,2,5}. In our case, the patient had no history of gastrointestinal disorder or antibiotic use that might cause vitamin-K deficiency, and the results of α -1-antitrypsin measurement, liver function and the sweat tests were within normal limits. The patient had been solely breastfed.

Sutor et al¹¹ reported a sudden-onset and severe hemorrhage with prompt improvement after administration of vitamin-K, blood or blood derivatives. Similar findings were noted in our case.

The administration of vitamin-K prophylactically in the newborn period has been used widely in many countries. In the past, some clinicians suggested that vitamin-K prophylaxis was not needed for all full-term infants¹². Consequently, vitamin-K prophylaxis was suspended in some countries^{1,7}. This approach resulted in a recurrence of HDN in these countries and proved the effectiveness of vitamin-K statistically, thus advocating the need for vitamin-K prophylaxis^{4,6,8,10}. However, the advantage of this prophylaxis for late HDN has been controversial until now. Single-dose intramuscular vitamin-K prophylaxis (1 mg) may not be sufficient to prevent intracranial hemorrhage. A few cases of late-stage intracranial hemorrhage have been reported, despite receiving single-dose vitamin-K prophylaxis at birth, as in our case.

Late HDN occurs most often in the subarachnoid and/or subdural regions (90% and 37.5%, respectively)¹³. In our case, however, the hemorrhage occurred in the patient's frontal lobe, a rarely reported location^{13,14}.

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