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Cerebral Hemorrhage With Edema in A Five-week-old: A Case of Late-onset Vitamin K Eficiency Bleeding, Rare Diagnosis in Resource-Limited Settings

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ABSTRACT

Introduction: Vitamin K deficiency bleeding (VKDB) is a term that describes the condition of hemorrhagic disorders in newborns. Late-onset VKDB occurs between the second week and sixth month of life. Intracranial hemorrhage often occurs in cases of late-onset VKDB and can cause 14-20% mortality and 40% long-term neurological morbidity, so it is important to treat patients until they are stable, especially with limited health facilities.

Case Report: A baby boy aged 1 month 8 days was brought by his parents to RSUD Deli Serdang Lubuk Pakam with the chief complaint of an enlarged stomach, accompanied by paleness, weakness, convulsions, and altered consciousness. A midwife assisted the delivery with unknown history of immediate vitamin K injection after birth. We diagnosed the patient with VKDB according to the clinical symptoms. The head CT scan showed subdural and subarachnoid hemorrhage with cerebral edema. We transfused the patient Packed Red Cells and Fresh Frozen Plasma 20 cc/12 hours 5 times, administered Vitamin K injection 3 mg/IM for 3 days, and other supportive therapy. The patient's condition improved within the third day of hospitalization with recovered consciousness and transferred to the referral hospital.

Discussion: The key feature of late-onset VKDB is the incidence of ICH in 30-88% of patients, leading to a high incidence of mortality. This study highlights the importance of prompt, and early treatment of VKDB with proper history taking, clinical examination, and relevant investigations to reduce morbidity and mortality.

Conclusion: In conclusion, secondary late-onset PDVC is more common than the primary subtype, and late-onset PDVC is still an important cause of morbidity and mortality in developing countries including Indonesia, where vitamin K prophylaxis is not routinely performed

Keywords: vitamin K deficiency bleeding, late-onset, subdural hemorrhage

1. Introduction

Vitamin K deficiency bleeding (VKDB) is a term that describes the condition of hemorrhagic disorders in newborns. VKDB can be caused by primary or secondary etiologies such as drugs, breastfeeding, secondary malabsorption in gastrointestinal and hepatobiliary disease, poor vitamin K intake, or a history of taking vitamin K antagonist drugs. PDVC is categorized into three main types: early, classical, and late with different pathophysiologies indicating the use of vitamin K prophylaxis. Early-onset PDVC occurs at <24 hours of age; Classical PDVC begins in the first week excluding the first 24 hours, and late-onset PDVC occurs between the second week and sixth month of life.[1,2]

The incidence of late-onset PDVC without vitamin K prophylaxis ranges from 10.5 to 80 per 100,000 live births. When prophylactic intramuscular vitamin K is given at birth, the incidence of late-onset PDVC ranges from 0.24 to 3.2 cases per 100,000 live births. In late-onset PDVC, the hemorrhagic manifestations are severe and involve mainly the gastrointestinal tract and skin, but also the central nervous system. Intracranial

hemorrhage (ICH) is common in cases of late-onset PDVC and can cause significant morbidity and mortality. In one study that looked at ICH cases in 30-63% of late-onset PDVC, with 14-20% mortality and 40% long-term neurologic morbidity among survivors.[3]

In the clinical criteria for the diagnosis of late-onset PDVC in primary PDVC, no cause other than breastfeeding could be found, whereas, in the secondary type, external factors such as malabsorption secondary to gastro-hepatobiliary disease or history of antibiotic use, and certain cases must meet laboratory criteria. of prolonged prothrombin time (PT) or International Normalized Ratio (INR) >3.5, activated prolonged partial thromboplastin time (APTT) with normal fibrinogen levels and platelet counts with changes in these values (PT and APTT), and cessation of bleeding after administration vitamin K.[4]

Late-onset PDVK is one of the important health problems with high morbidity, mortality, and socio-economic problem in the country, which can be prevented by vitamin K prophylaxis. There are several reported case reports related to this case from various regions in Indonesia. Good and appropriate early treatment is an option to reduce the number of deaths that can occur in this case. Researchers report the case of a male patient aged 1 month 8 days who came with complaints of decreased consciousness and enlarged abdomen who was diagnosed with PDVK and stabilized with limited health facilities.[3]

2. Case Report

A baby boy aged 1 month 8 days was brought by his parents to the Deli Serdang Lubuk Pakam Hospital with the main complaint of an enlarged stomach. The patient's parents complained of an enlarged stomach that was experienced for approximately 1 day before entering the hospital. Complaints accompanied by not wanting to drink since one day. The patient's parents said the patient looked weak, and the face looked pale. The patient's parents also complained that their child vomited twice before eating. The frequency of stool is once per day. Stool consistency is normal. The patient's parents said their child was in a normal state of defecation with a frequency of 3 times a day. There is no history of being given food. So far, the patient has only been given breast milk, and only one day before entering Deli Serdang Lubuk Pakam General Hospital then was given formula milk. Regarding the history of childbirth, the patient was delivered vaginally with the help of a midwife and was full term.

The patient had never had a similar complaint before. There was no history of trauma, the patient was born with the help of a midwife and did not know whether to receive a vitamin K injection after birth. No history of allergies was found, and a family history of illness related to the patient's condition was also denied. Prenatal history in patients with a gestation period of 9 months and no maternal complications and problems were found. The patient was born spontaneously and without complications. The postnatal history of the patient was born at term, according to gestational age. History Immunization in the patient is hepatitis B0 once given.

On physical examination, the patient's consciousness is sober with GCS 5 E2M2V1, pulse 136 times/minute, temperature 36oC, breathing 48 times/minute, body weight 3500 grams, and body length 57 cm. On investigation, hemoglobin was 4.27 g/dL (reference value: 11.5 – 14.5 g/dL), hematocrit 11.5% (reference value: 33–43%), leukocytes 9.18 thousand/uL (reference value: 4.0 – 12.0 thousand/ L), platelets 332,500 cells/uL (reference value: 150,000–450,000 cells/uL), erythrocytes 1.19 million/uL (reference value: 4–5.3 million/uL), MCV 96.4 fL (reference value: 76–90 fL), MCH 35.9 fL (reference value: 28 – 31fL) and MCHC 37.1 g/dL (reference value: 31.5 – 35 g/dL).

On radiological examination of head CT scan, the frontoparietal hyperdense lesion appeared and filled the sulcus and cisternae, sulcus, gyri, and ventricle appeared prominent, midline shift did not appear, paranasal sinus and mastoid did not show abnormalities. There is an impression of subdural and subarachnoid hemorrhage with cerebral edema, as shown in Figure 1. The patient was differentially diagnosed with Bleeding Due to Vitamin K Deficiency, Hemophilia, and Von Willebrand disease and with a working diagnosis of Bleeding Due to Vitamin K Deficiency Regarding this condition, the patient was treated with transfusion of 20 cc/12 hours for 5 times Packed Red Cells and Fresh Frozen Plasma, Cefotaxime injection 175 mg/12 hours, Gentamycin injection 15 mg/24 hours, Vitamin K injection 3 mg/IM for 3 hours. day, diet 30 cc/2 hours of breast milk via OGT, IVFD RL 20 gtt/min, O2 0.5-1 lpm, 3% NaCl 15 cc/12 hours given for 30 minutes. On the first day of monitoring, after insertion of the OGT, it looked dirty. This explains the bleeding that occurs in the upper gastrointestinal tract and causes the patient's stomach to bloat. On the third day of treatment,

October 12, 2019, the patient's condition improved with reduced clinical pallor and consciousness that became E4M6V5.

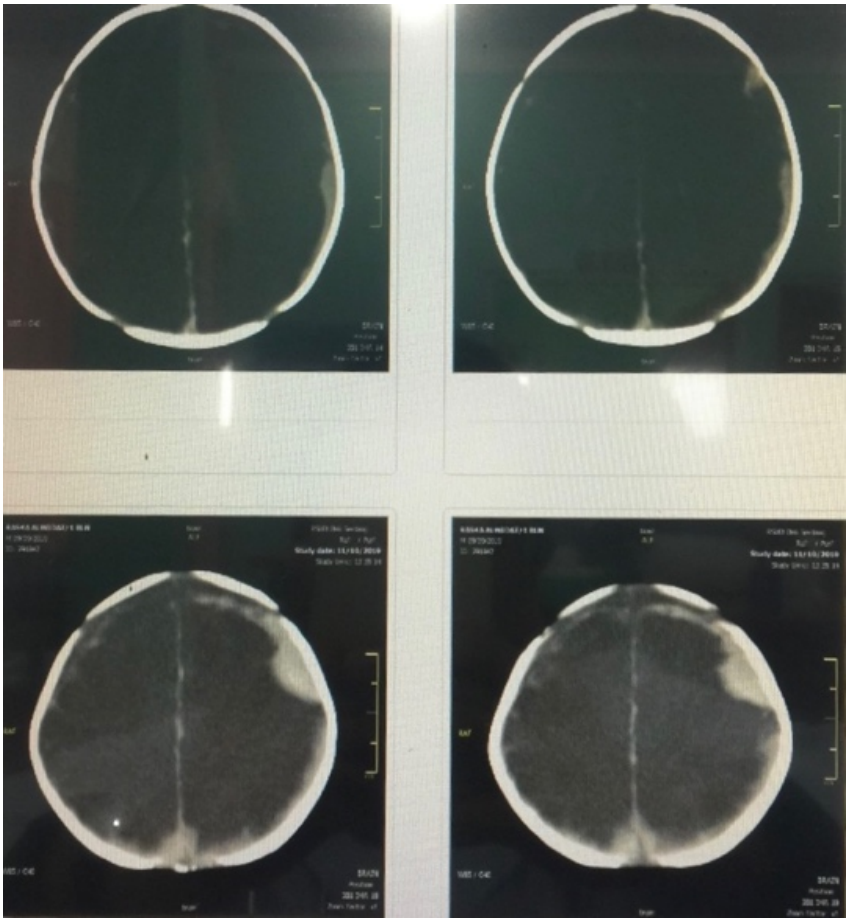

Fig. 1 Head CT scan results, This examination shows the impression of subdural and subarachnoid hemorrhage with cerebral edema.

The patient was then referred to the RSUP. H. Adam Malik Medan to undergo additional examinations, namely Prothrombin Time, International Normalized Ratio, APTT, and TT where after being referred, the PT value reported in the patient was 16.2 seconds (referral value 14 seconds), INR 1.23 (reference value 0.8-1.30), APTT is 53.6 seconds (reference value 32.9) and TT is 49.8 seconds (reference value 18).

3. Discussion

The bleeding tendency in infants, which is now classified as late-onset PDVC, should be taken into account that PDVC is more common in the Asian population than in the European population.[2] One study reported that infants with late-onset CVD (88.3%) often had signs and symptoms of predisposing disease; however, in a national survey in Japan of vitamin K deficiency in infants, it was found that 10.5% and 16% had bleeding episodes due to PDVC associated with an obvious pathological cause, respectively, and 3.7% of infants with bleeding were diagnosed with secondary PDVC.[2,5]

Late-onset PDVC is characterized by bleeding in infants between the eighth and sixth months of life and has a peak incidence between the third and eighth weeks of life.[6] According to the investigator's case, the mean age of infants with late-onset PDVC was 10.3 weeks (range, seven to 20 weeks). Other studies also reported that the median age was three to seven weeks, of which the peak age was 4 weeks, and the majority of 79% of infants were between three and seven weeks.[7]

Although prothrombin levels are lower than in term infants at birth, recent research does not support the notion that bleeding from vitamin deficiency is more common in premature infants.[8] Under the researcher's case, another study reported that all infants with PDVK were born late at term, which was 93%. Exclusive breastfeeding has become a concern in developing countries, where exclusive breastfeeding is highly recommended to promote optimal health in infants. However breastfed babies are at risk because of their low concentrations in breast milk, whereas bottle-fed babies are hardly at risk because almost all infant milk is artificially fortified.[9]

Under the case that the investigators reported, another study also reported that the most common sites of bleeding were the skin, gastrointestinal tract, and intracranial hemorrhage, especially in cases of late-onset PDVC. The main feature of late-onset PDVC is the much higher incidence of ICH of 30-88% in patients, leading to high morbidity and mortality. The investigator's case manifestations were similar to those reported in another study which observed that the most common site was intracerebral, followed by multiple ICH.[3] Subdural hemorrhage was the most commonly reported type of ICH, followed by intracerebral and subarachnoid hemorrhage. The late-onset PDVC subtype is associated with life-threatening bleeding, especially ICH resulting in low hemoglobin levels and anemia, as the investigators found in this case.[7]

Late-onset PDVC may manifest as convulsions, poor sucking response, irritability, and pallor. In a study examining 120 cases, seizure and irritability rates were 50%; and feeding intolerance, poor sucking, vomiting were seen in 46% of patients.[10] Feeding intolerance, poor sucking ability were the most common findings in this study with rates of 61% and with lower rates of 46% for pallor and 42% for seizures. Although bleeding from the gastrointestinal system, mucous membranes and skin may accompany this disease, intracranial hemorrhage is a major cause of morbidity and mortality.[11]

The PDVC subtype was associated with morbidity and mortality among the studied patients, and patient outcomes did not have a statistically significant difference between the PDVC subtypes.[12] Another study found that mortality was 19% and neurologic sequelae 21% in infants who survived PDVK. Of the total 691 reported cases of advanced idiopathic PDVC, the mortality rate was 24%, and permanent neurologic deficits were found in 142/257 cases (55%); including seizure disorders (64%); muscle weakness (21%); mental retardation (15%); hemiparesis (13%); hydrocephalus (7%); and 5% microcephaly; however, neurologic sequelae in secondary late-onset PDVC were found in 7/25 (28%) who recovered, and the mortality rate was 26%.[13]

A recent study looked at a prophylactic regimen of 1 mg vitamin K orally at birth followed by 150 g daily for weeks 2 to 13 to adequately prevent PDVK in breastfed infants. The study concluded that a prophylactic regimen for breastfed infants consisting of 1 mg of vitamin K orally at birth, followed by 25 g or 150 g daily for weeks 2 to 13, was insufficient to prevent PDVK in breastfed infants with biliary atresia who had severe biliary atresia. still undiagnosed.[12,13] Cases of PDVK in healthy newborns who are exclusively breastfed, despite intramuscular prophylaxis at birth, suggest that prophylaxis with a single dose of intramuscular vitamin K may not be adequate to prevent all cases of late-onset PDVK.[14]

There are few studies discussing treatment for infants with PDVC. Infants with non-life-threatening bleeding should be treated with vitamin K1 by slow IV injection. A single IV dose of 250-300 g/kg body weight is generally recommended, and a dose of 1-2 mg to treat vitamin K deficiency in infants up to 6 months of age. The guidelines for vitamin K administration for vitamin K deficiency in infancy, proposed by the Japan Pediatric Society in 2011, recommend giving IV vitamin K2 (menaquinone-4, MK-4), in doses ranging from 0.3 to 1.0 mg according to age. birth weight. In cases of coagulation disorders caused by vitamin K antagonists, such as warfarin, high doses of vitamin K supplements may be effective. Time required for recovery from coagulopathy with vitamin K administration in four infants with severe PDVC. In all infants, PT rises by 30%-50% of normal values within 1 hour of IV vitamin K administration (1-3 mg phylloquinone), with bleeding cessation observed for 20 minutes.[2,15]

For severe bleeding events, it may be necessary to administer blood products, such as Fresh Frozen Plasma (FFP) or Prothrombin Complex Concentrate (PCC); where vitamin K should not be given. PCC, which contains all four vitamin K-dependent factors, can quickly restore coagulation function.[16] Although no studies have determined the dose of PCC in PDVC, one study conducted in adults suggested a dose of 50 units/kg. Infusions of FFP (10–15 mL/kg) or PCC (50–100 units/kg) should be considered in severe cases and for very low birth weight infants who are unable to take vitamin K adequately because of poor liver function.[15,16]

4. Conclusion

In conclusion, secondary late-onset PDVC is more common than the primary subtype, and late-onset PDVC is still an important cause of morbidity and mortality in developing countries including Indonesia, where vitamin K prophylaxis is not routinely performed. This study highlights the importance of prompt diagnosis, and good early management of this clinical condition with proper history taking, clinical examination, and relevant investigations. Vitamin K prophylaxis should be given to all exclusively breastfed newborns. Exclusive breastfeeding and cholestasis are closely associated with this deficiency and result in late-onset PDVC. Prophylactic intramuscular injection reduces the incidence of early-onset, classic, and late-onset PDVC.

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Conflict of Interest

The authors declare no conflicts of interest in preparing this article.

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