Late vitamin K deficiency bleeding in an infant with choledochal cyst

Nada Krstovski[1], Dragana Janic[1], Lidija Dokmanovic[1], Jelena Lazic[1], Predrag Rodic[1], Zoran Krstic[2]

Departments of [1]Pediatric Hematology, and [2]Surgery, University Children's Hospital, Belgrade, Serbia

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Infantile choledochal cyst (CC) usually presents as jaundice, vomiting, acholic stools, and hepatomegaly, and it can resemble biliary atresia. Although bleeding tendency is a rare clinical presentation of CC, it can be the first symptom, especially in infants less than 12 months of age. We report a case of a two-month-old infant with choledochal cyst presenting as late vitamin K deficiency bleeding (VKDB). Early recognition of diseases predisposing to VKDB and immediate investigation and treatment of warning bleeds help to prevent the worst consequences. Late VKDB is often the presenting feature of a serious underlying disease that may be recognized early. The sudden onset of bleeding tendency in infants with congenital liver or biliary tract disease may suggest not only biliary atresia but also, although extremely rare, CC. Early vitamin K administration leads to rapid normalization of hemostatic parameters, which enables major liver surgery.

Key words: bleeding tendency, vitamin K deficiency, infant, choledochal cyst.

Late vitamin K deficiency bleeding (VKDB), peaking at 3-8 weeks, typically presents with intracranial hemorrhage in breast-feeding infants. Apart from breast-feeding, there is a lot of evidence of an association of late VKDB and hepatobiliary dysfunction[1,2]. The most common causes of neonatal cholestasis are biliary atresia, sepsis, idiopathic neonatal hepatitis, alpha-1 antitrypsin deficiency, and intrahepatic cholestasis syndromes. Infantile choledochal cyst (CC) usually presents as jaundice, vomiting, acholic stools, and hepatomegaly, and it can resemble biliary atresia[3,4]. Although bleeding tendency is a rare clinical presentation of CC, it may be the first symptom, especially in infants less than 12 months of age[5]. We report a case of a two-month-old infant with CC presenting as late VKDB.

Case Report

A two-month-old female, breast-fed infant was presented to the emergency room due to prolonged bleeding after capillary blood sampling for complete blood count, performed due to suspected anemia. There was a history of urgent delivery in the 36th gestational week due to suspected fetal distress, intrauterine growth retardation, maternal hypertension, and uterine myoma. Apgar score was 8 and birth weight was 1650 g. Due to asphyxia, admission to the neonatal intensive care unit (NICU) was required, where the child had been treated for eight days. One milligram of vitamin K was routinely administered on the first day of life. Unconjugated hyperbilirubinemia, with maximal total bilirubin value of 188 μmol/L, was recorded, with subsequent normalization during hospitalization. No abdominal ultrasound was performed. The child was discharged from the hospital at 36 days of age in a good general condition, weighing 2300 g.

On admission, the patient was slightly pale and jaundiced; otherwise, physical findings were normal including normal stool color. Laboratory studies on admission revealed the following: hemoglobin 9.3 g/dl, hematocrit 27.4%, mean corpuscular volume (MCV) 93 fl, platelet count 263 000/μl, white blood cell count 14 700/μl, and reticulocyte count 9.8%. Urinalysis was also normal. Biochemistry

analyses revealed conjugated hyperbilirubinemia and slightly elevated transaminases: total bilirubin 146 μmol/L, direct bilirubin 97 μmol/L, alanine aminotransferase 77 U/L (normal <61), aspartate aminotransferase 149 U/L (normal <61), and serum gamma-glutamyl transferase (sγGT) 412 U/L (normal <200). Other routine chemistry analyses including blood sugar, blood urea nitrogen (BUN), lactate dehydrogenase (LDH), alkaline phosphatase, and ammonia were normal. Coagulation tests were markedly abnormal: prothrombin time (PT) was prolonged >1000 seconds (s) and partial thromboplastin time (PTT) was 788.2 s. Detailed coagulation examination showed low values of vitamin K-dependent coagulation factors: FII <12.5%, FVII <12.5%, FIX 14.1%, and FX <12.5%.

Ultrasonography: Early diagnosis of CC was based on the finding of cyst in the liver hilum, measuring 53 x 35 mm (Fig. 1). Vitamin K 1 mg for two days and fresh frozen plasma (FFP) 5 ml/kg continuously for 24 hours (h), including 6 h after the end of surgery, enabled normalization of coagulation tests 12 h later. Urgent surgical treatment (portoenterostomy, Kasai operation) with liver biopsy was performed with no bleeding or other complications. Stool remained normal after the surgery. Choledochal fusiform type I cyst with normal liver tissue was confirmed by histology. Normalization of liver tests was confirmed during the follow-up of six months.

Discussion

Most children with CC usually have jaundice as the universal presenting feature[3]. Bleeding tendency due to vitamin K deficiency is uncommon as the first symptom in infants with CC[5,6]. Bleeding tendency in a newborn with CC is rare and resembles late VKDB. Although diagnosis of CC in the prenatal period is not unusual, early surgical treatment usually prevents complications due to vitamin K deficiency and bleeding[7]. Thus far, only one infant with CC, aged one month, presenting with subdural hematoma and macrohematuria, was described in the literature[5]. Therefore, in infants with late VKDB, CC should also be considered together with biliary atresia and other congenital liver diseases.

There are reports of a connection between prematurity, low birth weight and coagulopathy due to antenatal hypoxia associated with liver dysfunction[8]. As our case was a low birth weight premature infant, we believe that early postnatal routine abdominal ultrasound could have shown CC before the appearance of bleeding disorders. Thus, routine abdominal ultrasound in all premature infants might be of benefit for any reason.

Early surgical treatment in infants with CC offers the best results in terms of outcome. Delay results in progression to end stage liver disease. It is well known that liver fibrosis of varying grade could be present at as early as four weeks of life, and that intra-operative liver biopsy has became an essential part of CC surgery protocol[3,7]. According to this recommendation, we performed surgery as early as possible, immediately after normalization of coagulation parameters. The majority of recommendations for treatment of late VKDB include single intravenous 1-2 mg dose of vitamin K and for severe bleeding episodes, FFP 10-15 ml/kg[1,9]. It seems that after a single dose of vitamin K and normalization of hemostasis parameters, even neurosurgery could be performed safely. However, the best strategy for vitamin K supplementation in

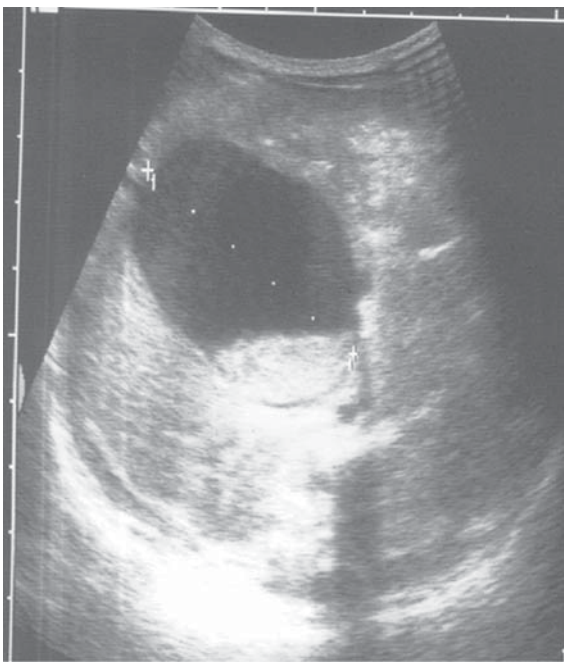

Fig. 1. Abdominal ultrasound of choledochal cyst.

chronic childhood cholestasis remains a critical issue[1]. There is also no clear recommendation with respect to the postoperative vitamin K regimen after major liver surgery. Repeated oral doses might be as effective as parenteral but the optimal dose regimen remains to be established[9]. Some authors recommend 50 mg of vitamin K from birth until 13 weeks in infants with underlying liver disease in order to prevent bleeding. However, it is also an important finding that some authors revealed that despite vitamin K supplementation, there is elevation in plasma PIVKA II, suggesting that ongoing vitamin K deficiency is common in cholestatic liver disease[10]. Since there is no registered oral vitamin K in our country, we adopted a regimen of 1 mg intramuscular vitamin K once a week.

Early recognition of diseases predisposing to VKDB and immediate investigation and treatment of warning bleeds help to prevent the worst consequences. Late VKDB is often the presenting feature of a serious underlying disease, which may be recognized early. The sudden onset of bleeding tendency in infants with congenital liver or biliary tract disease may suggest not only biliary atresia but also, although extremely rare, CC. Early vitamin K administration leads to rapid normalization of hemostatic parameters, which enables major liver surgery.

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