Progressive Familial Intrahepatic Cholestasis Presenting With an Intracranial Bleed and Mimicking Abusive Head Trauma

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ABSTRACT

Introduction: Abusive head trauma is a serious, often fatal condition; early identification is important to prevent repeat episodes and/or injuries to siblings. This case emphasizes the importance of a thorough workup in cases of suspected abusive head trauma.

Case Presentation: A 4-month-old infant was found to have a severe subdural hematoma requiring surgical evacuation. Initially, abusive head trauma was considered as a diagnosis. Testing revealed vitamin K deficiency bleeding (VKDB) despite prophylactic vitamin K administration at birth. The infant eventually was diagnosed with progressive familial lintrahepatic cholestasis type 2 (PFIC2).

Discussion: Although VKDB is a known cause of infantile intracranial hemorrhage, PFIC has not been previously reported to cause severe VKDB resulting in an intracranial hemorrhage.

Conclusion: Our case illustrates the importance of a comprehensive systematic approach to investigate causes other than abusive head injury when intracranial bleeding is a significant finding.

CASE REPORT

A 4-month-old infant was admitted with concerns for altered mental status. Her parents related that 3 days prior to admission, they had been contacted at work by their in-home nanny. The nanny reported that the infant had vomited. The infant's mother contacted the primary physician and was given instructions on home care. The next day, the infant was seen by the primary physician for a sick visit and, at that time, it was noted that the patient had a bruise on her right chest and back. She was otherwise well and had a normal examination. She was sent home without intervention and did well that night. The next day, she was again in the care of her nanny, who reported more vomiting to the parents. The family tried oral rehydration solutions that night without significant improvement.

On the day of admission, the infant was taken to the primary physician and was noted to have a bulging fontanel. She was transferred to the Emergency Department where computed tomographic scan revealed a large left subdural hematoma with a significant left to right shift and early evidence of herniation. She was then transferred to the referral center where she had an emergent burr hole placed and evacuation of the subdural hematoma.Parents did not relate any history of falls, motor vehicle collisions, or other trauma. They had no history to account for the bruises or the subdural hematoma.

The patient was born at term in a hospital and received vitamin K after birth. She had been breastfed exclusively, and her mother reported that they had not been giving her multivitamin drops.

Family history initially was negative. A more detailed history later revealed that the infant's maternal uncle required vitamin K for treatment and that her father was a cystic fibrosis (CF) carrier. The mother was not a CF carrier.

Based on the patient's presentation with a large, surgical subdural hematoma and bruising without a historical explanation, nonaccidental trauma was considered in the differential diagnosis. A skeletal survey showed no fractures or bony abnormalities, and an ophthalmologic examination was normal without retinal hemorrhages. Law enforcement and child protective services were

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contacted because of the concern for nonaccidental trauma. They interviewed the family and the caregiver and found no further history to account for the injuries.

Coagulation studies performed in the operating room revealed a prothrombin test of >100, an international normalized ratio of >10, and a partial thromboplastin time of 74.7. Although this testing was performed as part of a routine evaluation for intracranial bleeding, the results were delayed due to multiple transfers of care and emergent neurosurgical intervention. Upon further testing, the patient also was found to have very low activity of all vitamin K dependent factors (II, Vii, IX, and X). Vitamin K levels were 0.04 ng/mL (normal 0.1-2.20) and protein induced by vitamin K absence-II (PIVKA-II) level was >36,20 ng/mL (normal < 6.3 ng/mL). She also was found to have mildly elevated total bilirubin of 2.4 mg/dL (normal <2.0 mg/dL) that remained elevated throughout her hospital stay. Her aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were initially normal, but her AST later ranged from 53 to 90 during the last days of her hospitalization (normal 15-41 U/L).

Based on her lab values, the patient was diagnosed with vitamin K deficiency bleeding (VKDB). Authorities were immediately informed as to her diagnosis and, given that there were no other concerns, they closed their investigations.

The patient was treated with intravenous vitamin K with improvement of her vitamin K level to 5.23 ng/mL. She recovered well from her surgery and appeared normal neurologically. She was discharged home after 8 days with oral vitamin K supplementation (2.5 mg of phytonadione/day) for 7 days. Eight days after stopping the oral vitamin K, her vitamin K level had dropped to 0.27 ng/mL. In addition, her AST and ALT were found to be mildly elevated at 108 U/L and 63 U/L, respectively (normal AST 15-41 U/L, ALT 14-54 U/L). This pattern prompted a more detailed workup of her cholestasis. Genetic testing revealed that she was heterozygous for a mutation in ABCB11, which is most associated with progressive familial intrahepatic cholestasis type 2 (PFIC2).

DISCUSSION

Late onset VKDB is a well-known, albeit rare condition where children will frequently present with intracranial bleeding.[1,2] This condition has become more rare since the use of newborn intramuscular vitamin K. Most cases reported now are when an infant does not receive vitamin K at birth or as a result of a malabsorptive condition from cholestasis.[2]

Common causes of cholestasis in an infant include biliary atresia, CF, and alpha-1-antitrypsin deficiency.[3,4] These cases are more likely to present with VKDB when the mother is breastfeeding, and there have been multiple reports of these cases either presenting with or being complicated by intracranial bleeding from VKDB.

Progressive familial intrahepatic cholestasis is a rare autosomal recessive condition; its incidence varies from 1/50,000 to 1/100,000 births.[5] There are 3 types of PFIC, all which result in hepatocellular cholestasis. They typically present in infancy with jaundice, pruritus, and other symptoms of cholestasis. Children with PFIC2 will commonly progress to liver failure in the first few years of life. PFIC2 has not previously been reported to present with vitamin K deficiency and a subdural bleed.

In this case, the combination of strict breastfeeding without vitamin supplementation and cholestasis from PFIC2 most likely contributed to her presentation with late-onset VKDB. Nonaccidental trauma was clearly considered in the differential and is one of the most common causes of subdural bleeding and unexplained bruising in this age group.[6] A recent clinical prediction rule would have placed this child in the high risk category,[7] but there were other aspects in this case that pointed away from a diagnosis of abusive head trauma. Retinal hemorrhages were not present in this case; and while retinal hemorrhages are not diagnostic for abuse, they are highly associated with abusive injury. In addition, the hematoma was unilateral and there was no significant brain injury noted. Bilateral subdural hematomas with deep brain injury are more likely to be seen in abusive head trauma.

Late onset VKDB previously has been mistaken for child abuse, but this is a rare occurrence and the search for a medical condition should not supersede a workup for suspected abuse.[8] The American Academy of Pediatrics has clear recommendations on how a bleeding disorder can be evaluated in cases of suspected abuse, which were followed with this patient.[9] In this case, the family was briefly interviewed by authorities who, with appropriate communication from the medical team, quickly closed their case when it was determined that a medical condition caused this infant's presentation.

Funding/Support: None declared.

Financial Disclosures: None declared.

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