

Case report

Severe subgaleal hemorrhage is the first clinical manifestation of neonatal hemophilia A: report of two cases

Bunchoo Pongtanakul and Nattee Narkbunnam

Division of Hematology and Oncology, Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Mahidol University

Abstract:

Subgaleal hemorrhage (SGH) usually occurs after instrumental delivery, while hemorrhage in neonatal hemophiliacs is rarely seen. We report two newborns diagnosed with severe hemophilia A with no family history of bleeding disorders, uneventful pregnancy or uncomplicated delivery without instrument, presenting life-threatening SGH. If SGH occurs during the neonatal period without perinatal risk factors, uncomplicated delivery and no instrumental assisted delivery, bleeding disorders should be evaluated to find the cause of this severe bleeding.

Keywords : ● Hemophilia ● Neonates ● Subgaleal hemorrhage

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Correspondence should be addressed to Bunchoo Pongtanakul, MD, Division of Hematology and Oncology, Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok 10700

รายงานผู้ป่วย

ภาวะเลือดออกใต้หนังศีรษะเป็นอาการนำของผู้ป่วยฮีโมฟีเลียเอชชนิดรุนแรง ในทารกแรกเกิด: รายงานผู้ป่วย 2 ราย

บุญชู พงศ์ธนากุล และ นัทธี นาคบุญนำ

สาขาวิชาโลหิตวิทยาและอองโคโลยี ภาควิชากุมารเวชศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล

บทคัดย่อ

ภาวะเลือดออกใต้หนังศีรษะ (subgaleal hemorrhage) ในทารก มักเกิดหลังจากการคลอดที่มีการใช้เครื่องมือในการช่วยคลอด เช่น การช่วยคลอดโดยใช้คีมหรือเครื่องดูดสุญญากาศ อาการเลือดออกรุนแรงในทารกที่เป็นโรคเลือดออกง่ายฮีโมฟีเลียพบได้ไม่บ่อย รายงานนี้เป็น การรายงานผู้ป่วยทารกแรกเกิด 2 ราย ได้รับการวินิจฉัยว่าเป็นโรคเลือดออกง่ายฮีโมฟีเลียเอชชนิดรุนแรง ที่มีอาการภาวะเลือดออกใต้หนังศีรษะ โดยไม่มีประวัติเลือดออกง่ายในครอบครัว การคลอดไม่มีภาวะแทรกซ้อนและไม่ได้ใช้เครื่องมือในการช่วยคลอด ถ้าพบผู้ป่วยทารกแรกเกิดที่มีภาวะเลือดออกใต้หนังศีรษะ โดยที่ไม่มีปัจจัยเสี่ยงใดๆ ในการคลอด ไม่ได้ใช้อุปกรณ์ในการช่วยคลอด การตรวจหาสาเหตุของโรคเลือดออกง่ายหายาก เป็นสิ่งจำเป็นที่ต้องได้รับการตรวจหาสาเหตุภาวะเลือดออกนี้

คำสำคัญ : ● ฮีโมฟีเลีย ● ภาวะเลือดออกใต้หนังศีรษะ ● ทารกแรกเกิด

วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต. 2565;32:253-7.

Introduction

Hemophilia is the most common inherited bleeding disorder, involving a x-linked recessive transmission, occurring mainly in males. This disease leads to decreased coagulation factor VIII or IX activity resulting in uncontrolled bleeding. During the neonatal period, diagnosis of hemophilia is made after postpartum bleeding complication or unexpected bleeding after medical procedures. Hemorrhage among people with neonatal hemophilia is rarely seen. The prevalence of subgaleal hemorrhages (SGH) involves 0.04 to 0.15% of all deliveries, with mortality ranging from 12 to 25%^{1,2}. They are caused by the rupture of emissary veins (connections between the dural sinuses and scalp veins), followed by separation of the epicranial aponeurosis from the underlying periosteum. SGH usually occurs after instrumental delivery (vacuum extraction or forceps). This can lead to the loss of up to 50 to 75% of the blood volume, resulting in shock or anemia. We report two newborns who were newly diagnosed with severe hemophilia A with no family history of bleeding disorders, uneventful pregnancy and uncomplicated delivery without instrument, presenting life-threatening SGH.

Case Report

Case 1 comprised a 2,590 gm male infant born at 37 weeks' gestation by cesarean section due to prolonged premature rupture of the membrane. The Apgar scores were 8 and 10 at 1 and 5 minutes. His head circumference (HC) was 35 cm. His postpartum course was uneventful until three days of age. He developed pale complexion and lethargy with ecchymosis and diffused swelling of the scalp. HC increased to 37 cm and hemoglobin (Hb) was 6.5 g/dL, and head ultrasonography showed SGH. Prolonged bleeding was observed at the venipuncture site (Figure 1). A coagulogram revealed isolated prolonged activated partial thromboplastin time (aPTT): 100.8 seconds (normal 25 to 35 seconds) and prothrombin time (PT): 11 seconds (normal 10 to 13 seconds). FVIII:c, FIX:c and vWF:Ag were 0.8, 68 and 131.1%, respectively. He was treated with packed red

cell (PRC) transfusion and plasma derived FVIII concentrate 50 IU/kg for 10 days. SGH was resolved. He was started with factor VIII 20 IU/kg once weekly prophylaxis at the age of 1.6 years. His clinical course showed no breakthrough bleeding after starting prophylaxis treatment. Now, at 6 year old, he goes to kindergarten, his developmental milestone is up to date and his genetic mutation showed inversion intron 22 (Figure 2).

Case 2 involved a 3,350 gm male term infant born by vaginal delivery with no instrument. The Apgar scores were 5 and 10 at 1 and 5 minutes. His postnatal course was uneventful until five days of age. He developed pale complexion and poor feeding with fluctuant edema of the scalp and forehead (Figure 3). His HC increased 3 cm from birth and Hb was 7 g/dL. A computerized tomography scan of his brain confirmed SGH (Figure 4) and aPTT revealed 108.5 seconds (normal 25 to 35 seconds) with (PT): 10.5 seconds (normal 10 to 13 seconds). FVIII:c, FIX:c and vWF:Ag were 0.9, 55.8 and 105.6%, respectively. He received PRC transfusion and FVIII concentrate 50 IU/kg for 14 days and the SGH was resolved. His genetic mutation showed inversion intron 1. He was well until five months of age. Unfortunately, he experienced head injury and intracerebral hemorrhage. He received intensive FVIII replacement and craniotomy with clot removal. He developed high FVIII inhibitor with maximum titer of 365 BU. He was on immune tolerance therapy (ITI) one year after he developed factor VIII inhibitor. Factor VIII dose of ITI was 100 IU/kg three times weekly. ITI was continued for two years but factor VIII inhibitor did not decline



Figure 1 Bleeding at the venipuncture site

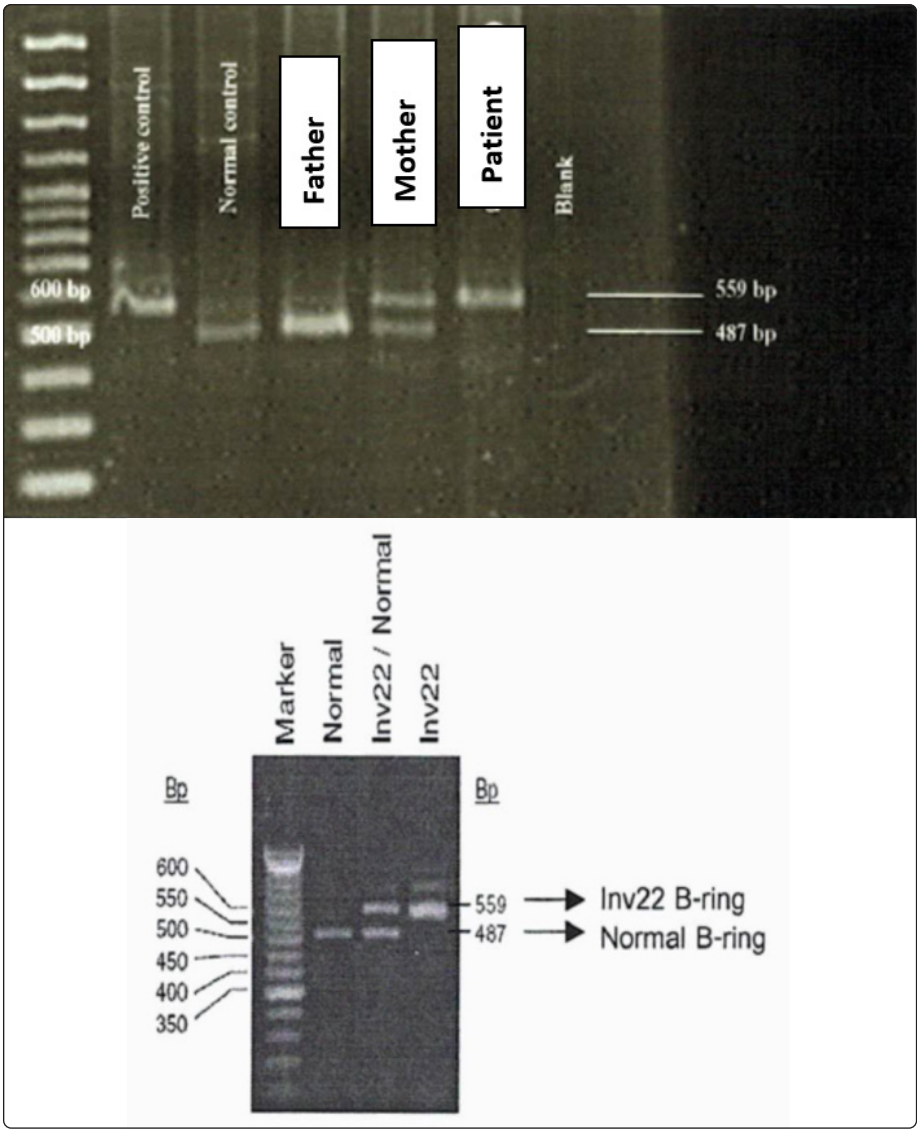


Figure 2 Genetic mutation: Inversion Intron 22



Figure 3 Edema of scalp and forehead

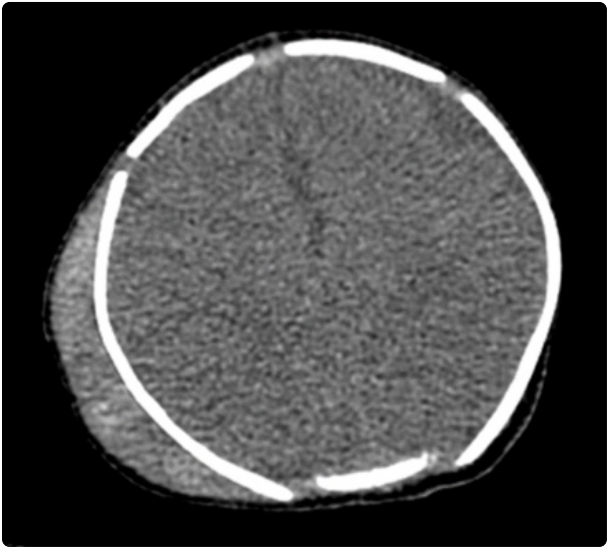


Figure 4 CT scan showed subgaleal hemorrhage

and ITI was stopped. He had head was injured again at the age of three years and presented to the hospital with intracerebral hemorrhage with brain death. Supportive care was initiated and he died at the hospital seven days after admission.

Discussion

Our two cases presented severe SGH as a first presentation of severe hemophilia A. Although hemophilia is a known risk factor for cranial bleeding, few investigations have reported a similar presentation after an uncomplicated vaginal delivery with no traumatic history or family history of bleeding disorders. Our patients presented anemia and lethargy, the most common presentation among patients with hemophilia with central nervous system (CNS) bleeding³. They presented severe SGH with an increase of 2 to 3 cm on HC and required PRC transfusion. Plauché et al. reported that 1 cm increase on head size can relate to at least 40 mL bleeding⁴. The total blood volume of a neonate is around 80 mL/kg, and 2 to 3 cm increase on head size represents at least a blood loss of 80 to 120 mL bleed (33 to 50% of total blood volume)⁵.

The coagulation system of the newborn is immature. The vitamin K-dependent coagulation factors (prothrombin; factors VII, IX, and X; proteins C and S) are lower levels than most of the coagulation factors during the neonatal period. However, the factor VIII level is normal among newborns, so hemophilia A with accurate severity can be made during the neonatal period. In contrast, diagnosis of severe hemophilia B is possible but factor IX levels in mild cases overlap with the normal newborn range, so definitive diagnosis may not be possible until around six months of age⁶.

Normally, hemophilia is an X-linked recessive inheritance but one third of all hemophilia cases can occur without a positive family history. Intra- and extracranial hemorrhage are major causes of morbidity and mortality among newborns with hemophilia^{7,8}. The overall incidence of CNS bleeding of hemophilia regardless of age is 2.2 to 7.5% and approximately 50% of cases

occur during the newborn period. The cumulative incidence of cranial hemorrhage in a retrospective study was 3.8%⁹. However, the true incidence of SGH among newborns with hemophilia remains unknown, mostly because of rare reporting of cases and the fact that SGH and cephalhematoma cases are usually combined in a single category of extracranial hemorrhage¹.

Conclusion

If SGH occurs during the neonatal period without perinatal risk factors, uncomplicated delivery and no instrumental assisted delivery, bleeding disorders should be evaluated to determine the cause of this severe bleeding. Hemophilia is the most common inherited bleeding disorder so definite and prompt diagnosis should be made for appropriate management.

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