

INTRACRANIAL HEMORRHAGE IN A NEWBORN WITH HEMOPHILIA

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Intracranial hemorrhage (ICH) in the newborn is an uncommon presenting manifestation of hemophilia, occurring with an incidence of 1%-4%,¹⁻³ however, because of its dramatic consequences, this complication raises serious concern. Apart from its high mortality rate, over 50% of survivors are left with psychoneurological sequelae, especially seizures and motor impairment.⁴ Only 18 cases of neonatal ICH occurring during the first week of life among hemophiliac infants have previously been reported.^{1,5-10} Here we present a one-week-old infant born in a family with positive history of hemophilia. With prompt replacement therapy and ventriculoperitoneal shunt inserted for progressive hydrocephalus, the child survived, but was left with gross motor retardation.

Case Report

A male full-term infant with birth weight of 3.5 kg was born into a family with a known hemophiliac male child aged nine years. The parents were nonconsanguineous. They had four other children, two females and two males. The patient was screened for hemophilia on the second day after birth. Activated partial thromboplastin time (aPTT) was raised (111 seconds, control 34 seconds) and factor VIII was 1 U/mL. As the patient was asymptomatic, he was discharged on the fourth day. He showed no unusual bleeding even when the umbilical cord fell off on the fifth day. But soon after, the child became irritable and difficult to feed. Three days later at the age of one week, he was brought to hospital for evaluation. On examination, he was found to be hypoactive with full anterior fontanelle and cyanosis, which improved on suction and oxygenation. The patient's head circumference (HC) was 37.6 cm, heart rate was 150/min, respiratory rate was 60/min, and BP was 87/55 mm Hg. He was immediately transferred to ICU for close observation, but he deteriorated and became

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FIGURE 1. CT scan of head showing intracranial hemorrhage.



FIGURE 2. CT scan of head showing intraventricular hemorrhage, dilated ventricles and the inserted ventriculoperitoneal shunt.

semiconscious, with shallow breathing. Arterial blood gas analysis showed respiratory acidosis that was managed with assisted ventilation. ICH was highly suspected and confirmed by CT scan of the head (Figure 1). Appropriate doses of cryoprecipitate were infused every 12 hours to raise factor VIII level to more than 50 units/mL. He also received top-up 45 mL of packed RBC. As the child developed progressive hydrocephalus, serial ventricular taps were performed initially, followed by insertion of ventriculoperitoneal shunt on the 20th day of age (Figure 2). Infusion of cryoprecipitate was continued for 16 days. A few days later, the patient regained consciousness, was

crying for feeds and suckling well, and was moving all the limbs, though with slight increase in the tone and an exaggerated deep tendon reflexes. He was, therefore, extubated from the ventilator. HC was 39.5 cm with normal tension of anterior fontanelle. Presently, the patient is three years old. Neurodevelopmental assessment shows gross motor developmental delay with normal vision and hearing. HC is 46.5 cm (below 5th percentile for age). Apart from non-paralytic convergent squint, CNS examination is normal.

Discussion

Hemophilia A is an X-linked coagulation disorder affecting 1 in 10,000 males with varying severity based on circulating concentration of plasma factor VIII (severe 0%-1%, moderate 2%-5%, or mild >5%-25%). Two-thirds of newly diagnosed patients have a positive family history.¹¹ Although estimated incidence of ICH in all hemophilia patients is reported as 2.6% to 13.8%,^{1,4,7} its occurrence in the neonatal period is considered lower, estimated as 1%-4%.^{1,8} Kletzel et al.¹⁰ suggested that this estimate might be falsely low, as it is mostly based on retrospective studies of infants who survived until the diagnosis was made. In most of these studies, the diagnosis of hemophilia in fatal ICH was often not considered immediately, probably because of the negative family history.

Among hemophiliacs, 18 cases of neonatal ICH occurring during the first week of life have previously been reported.^{1,3,7,8,10,12} All had severe or moderate disease. ICH was almost always related to mild or moderate head trauma, unlike in adult hemophiliac patients, in whom it occurs spontaneously in more than half the cases.¹³ Since birth trauma, especially related to a prolonged second stage of labor or use of forceps, can be a precipitating event for ICH, optimal mode of delivery for a hemophilia carrier gravidae has been a matter of debate. After reviewing 117 deliveries of children with hemophilia, Ljung et al.³ considered the risk of serious bleeding through normal vaginal delivery to be small, but the application of vacuum extraction had resulted in subgaleal or cephalic hematoma in 10 out of 12 cases. However, spontaneous CNS bleeding during the perinatal period is always a possibility.¹⁴ Thus, irrespective of the mode of delivery, the timing of the onset of ICH remains uncertain.

As the occurrence of CNS bleeding in hemophiliacs is attended with high mortality and at least 50% morbidity among the survivors, immediate diagnosis in a suspected case and treatment with replacement therapy is urgently warranted. Following an initial bolus dose of F-VIII, clotting factor should be given by continuous infusion to maintain a level of >0.50 U/mL (>50%).¹² Such protective levels of plasma factor-VIII concentration need to be maintained for several weeks. The importance of shortening the interval between injury and factor replacement is well established. Andes et al.¹⁵ have

emphasized that factor replacement within 6 hours of injury considerably reduces the risk of ICH. They attributed their lower mortality rates to early and aggressive factor replacement. In infants strongly suspected or confirmed to have hemophilia, a prophylactic F-VIII or F-IX shortly after birth could be administered to offset labor trauma. Recently, an intrauterine infusion of recombinant F-VIII during early labor to a fetus with proven hemophilia proved successful.¹⁶ However, neither of the latter two approaches is recommended.¹⁷

Although rare, ICH in a hemophiliac newborn, with its high mortality rates and disabling morbidity, requires urgent attention. Since it may largely be related to birth trauma, cesarean section delivery of a male fetus in mothers with positive family history is preferred. Estimation of plasma factor VIII levels, close clinical watch for any neurological features, and use of imaging technology for prompt diagnosis of ICH throughout the first week of life, if possible, are recommended. Immediate, aggressive treatment should be given for any suspected ICH. This approach can potentially limit the neurological damage in affected infants.

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