

# A Case of Hemophilia A Presenting in a Neonate and a Review of the Literature

Global Pediatric Health  
Volume 4: 1–3  
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DOI: 10.1177/2333794X17693110  
journals.sagepub.com/home/gph



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Received December 23, 2016. Accepted for publication December 27, 2016.

## Introduction

Hemophilia A is an X-linked hereditary condition caused by decreased factor VIII activity, which predominately occurs in males.<sup>1</sup> Severe hemophilia occurs when circulating levels of a factor are less than 1% of normal activity in the blood and is typically diagnosed in the first 2 years of life.<sup>2</sup> Early identification of these patients is essential since they are at risk for spontaneous life- or limb-threatening bleeding and disability resulting from repeated joint bleeding.<sup>3</sup> Hemophilia A and B are X-linked recessive disorders, which explains their preponderance in males. Genetic studies reveal that majority of hemophilia A cases are due to an inversion of the long arm of chromosome X.<sup>4</sup> Hemophilia A, which is the deficiency of factor VIII, occurs with an incidence of 1 in 500 to 10000 males.<sup>5</sup> Diagnostic criteria for hemophilia include confirmation of a factor activity level below 40% of normal (below 0.40 IU/mL), or a hemophilia gene mutation. A normal von Willebrand factor antigen should also be documented in patients with reduced factor VIII activity levels, to eliminate the possibility of von Willebrand disease. Severe hemophilia is a relatively uncommon condition in the newborn period and usually manifests within the first year to 1½ years of life with easy bruising, hemarthrosis, bleeding due to oral injury, or after an invasive procedure.<sup>6</sup> Hemophilia can also be diagnosed in the absence of a family history with the initial presentation of bleeding in the neonatal period. Moderate and mild hemophilia, on the other hand, are defined as factor 8 levels >1% to <5% and >5% to <40%, respectively.<sup>7,8</sup>

## Final Diagnosis

We report a case of severe hemophilia presenting in a newborn after circumcision.

## Hospital Course

An African American male infant born via vaginal delivery to a 23-year-old gravida 3 para 1 woman at 40 weeks gestation. Pregnancy was unremarkable.

The infant's APGARs were 9 at 1 and 5 minutes, with no complications.

Birth parameters were birth weight of 2.94 kg, the birth length of 50 cm, and head circumference of 34 cm. Examination revealed a small for gestational age (SGA) baby with caput succedaneum and an extra digit on the right hand. The neonate was monitored in the newborn nursery. Baby received 1 mg of vitamin K with no feeding issues noted. Blood was drawn for complete blood count (due to SGA status) as well as blood typing.

Laboratory workup on day 1 revealed a white cell count of 11.5 k/mm<sup>3</sup>, hemoglobin of 21.7 gm/dL, hematocrit of 61.3%, with a platelet count of 32 k/mm<sup>3</sup>; on repeat, platelets were 183 k/mm<sup>3</sup>. The infant's blood type was B positive, and the antibody screen was negative.

On the second day of life, the patient was circumcised after which there was bleeding noted from postcircumcision frenulum tears. Pressure dressing was applied. Over the next 5 hours, the bleeding worsened with staff having to change 3 soaked pressure dressings. During that time the patient was also noted to have prolonged bleeding from prior heel sticks. The patient was transferred to the neonatal intensive care unit, and due to concerns of bleeding diathesis labs were sent for coagulation studies: factor VIII activity, factor IX activity, factor XIII activity, von Willebrand factor antigen/activity, platelet function assays along with a complete blood count. Hematology and urology were consulted.

Results were significant for a partial thromboplastin time of >200 seconds (23.1–33.1), D-dimer of >35.2 mg/L, and a fibrinogen level of 103 mg/dL (186–486 mg/dL). The patient was given cryoprecipitate for the presumed diagnosis of hemophilia as well as due to low fibrinogen while awaiting the remaining test results.

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Remaining lab work showed factor VIII level <1%, factor IX activity 9%, von Willebrand factor activity level 134% (43% to 138%), and von Willebrand antigen of 102% (60% to 153%). Platelet function testing with screening epinephrine was 119 seconds (100-163), and a platelet factor ADP of 78 seconds (57-114).

Once factor VIII deficiency was established, recombinant factor VIII was provided to the baby and bleeding subsided after replacement. Due to an increased risk of intracranial hemorrhage in patients with hemophilia, an ultrasound of the head was performed, which did not show any evidence of intracranial hemorrhage.

The clinical care team went back and elicited further history from the family. On further questioning of the family, it became apparent that the maternal grandfather had hemophilia, which the mother was unaware.

## Discussion

In any child with bleeding symptoms, initial evaluation should include a complete blood count, prothrombin time, and activated partial thromboplastin time. Testing factor levels, platelet function, and fibrinogen can also be considered based on the initial lab testing. Consultation with a hematologist should occur with the slightest concern for an inheritable coagulation defect. While interpreting the test results during the newborn period, it is important to remember that normal ranges for newborns vary from adult values. The exception to this is factor VIII, which is at the normal adult range or mildly increased at birth.<sup>9</sup> Adult levels are also achieved in preterm infants, thus it is therefore possible to diagnose most cases of hemophilia A at birth.<sup>10</sup> Prenatal diagnosis of hemophilia via chorionic villus sampling is the most widely used method,<sup>11</sup> but amniotic fluid, fetal blood, and pre-implantation genetic diagnostics can also be used in selected cases. Prenatal diagnosis must be preceded by adequate genetic counseling and risk assessment of the potential carrier and subsequent support during the diagnostic process.

As per the United Kingdom Hemophilia Centre Doctors' Organization Guideline approved by the British Committee for Standards in Hematology, the treatment of choice for both hemophilia A and B are recombinant factor VIII and recombinant factor IX concentrates, which carry the lowest risk of transmitting viral infection.<sup>12</sup> In a neonate with clinically significant ongoing hemorrhage, where hemophilia is suspected based on a prolonged activated partial thromboplastin time, it may be appropriate to administer fresh frozen plasma while the results of appropriate factor assays are awaited. In

the event of a low fibrinogen level, as in this case, cryoprecipitate is considered the best choice.

In newborns with hemophilia, intracranial hemorrhage is the most life-threatening complication.<sup>13</sup> The cranial ultrasound should be undertaken before discharge in all neonates with severe or moderate hemophilia.<sup>14</sup>

## Conclusion

Severe hemophilia is not an absolute contraindication to circumcision. However, there is a wide range of variation in approaching this clinical scenario among pediatric hematologist with the major concern of inhibitor development.<sup>15</sup> Circumcision has to be deferred in a male neonate of carrier mother until hemophilia A is confirmed or ruled out.

## Author Contributions

Esther Kisseih contributed to conception, design and drafting of the manuscript. Neeraja Yerrapotu contributed to data acquisition and drafting of the manuscript. Deepak Yadav and Melissa February reviewed and critically appraised the manuscript.

## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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