Bangabandhu Sheikh Mujib Medical University Journal 2023;16(1): 62-65 bsmmu.edu.bd

Case Report

Hemophilia in a newborn without family history: A case report

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ABSTRACT

Haemophilia is the most frequent diagnosed inborn clotting factor deficiency in newborn. Studies reveal that majority of hemophilia A cases are due to an inversion of the long arm of X-chromosome. Newborns with hemophilia are at risk of intracranial and extracranial hemorrhage, and other bleeding complications. Diagnostic criteria for haemophilia include confirmation of a factor activity level below 40% of normal (below 0.40 IU/mL), or a hemophilia gene mutation. Haemophilia typically result in an isolated prolongation of the activated partial thromboplastin time. However, the definitive diagnosis requires measurement of factors VIII and IX levels. Here, we describe a newborn with cephalhematoma gastrointestinal bleeding that is the manifestation of neonatal haemophilia with antenatally diagnosed duodenal atresia and there is no positive family history. This case shows a rare hemophilia presentation reflecting the importance of coagulation studies when faced with unexplained bleeding.

Keywords: haemophilia, cephalhematoma, gastrointestinal bleeding, dudenal atresia

INTRODUCTION

Hemophilia, a hereditary coagulopathy linked to X-chromosome, mainly affects male individuals with an prevalence of 1 per 5000 births. It can be either hemophilia A or B depending on the decrease of factor VIII or IX activity.[1] Hemophilia disorders with X-linked recessive inheritance often occur with a family history or in children born to mothers who are known carriers. However, hemophilia can occur as the result of new mutations in patients without family histories of the disorder. Newborns with hemophilia are at an increased risk of intracranial and extracranial haemorrhage and other bleeding complication.[2, 3]

After diagnosis of hemophilia, treatment for acute bleeding should be undertaken urgently with factors VIII or IX concentrates. Despite being a hereditary condition, it has a significant rate of de novo mutations which can go from 30-50%.[1, 4]

CASE DESCRIPTION

A newborn, the first issue of non-consanguineous parents, got admitted in neonatal intensive care unit (NICU) of Bangabandhu Sheikh Mujib Medical University with the complaints of antenatally diagnosed duodenal atresia and respiratory distress after birth. The 21 years old mother, para 1+0, was on irregular antenatal check-up. At 33 weeks of pregnancy, ultrasonography of pregnancy profile revealed increased amniotic fluid (amniotic fluid index 27 cm) and features of duodenal atresia. She developed prolonged rupture of membranes and suspected chorioamnionitis at 37 weeks of pregnancy, and treated accordingly.

The male baby weighing 2140 gm was born by vaginal delivery. Baby cried immediately after birth but developed respiratory distress and vomited soon after birth which was about 10 ml and bile stained. On examination, the baby was pink with acral cyanosis with 2L/min O_2, saturation of peripheral oxygen 95% in right upper limb and 93% in lower limb, well perfused, normothermic and euglycaemic.

Cephalhaematoma was present over the right parietal region measuring about 5x6 cm and anthropometrically appropriate for gestational age. Respiratory system

Received: 25 Aug 2022; Revised version receiving: 04 Mar 2023; Accepted: 05 Apr 2023; Published online: 18 April 2023
Supplemental file, and peer review and author response: available at DOI: https://doi.org/10.3329/bsmmuj.v16i1.65670

LEARNING POINTS

1. **Hemophilia in the newborn could be misdiagnosed, especially in the setting of negative family history due to different clinical presentation comparing to older children.**
2. **The newborn with cephalhematoma and gastrointestinal bleeding are manifestations of neonatal haemophilia with antenatally diagnosed duodenal atresia.**

examination revealed tachypnea and lower chest retraction. Downe's score was 4/10 and there was good and equal air entry in both lungs. Genitourinary system examination revealed left kidney palpable and ballotable.

The baby was initially diagnosed as term (37 weeks), low birth weight, appropriate for gestational age, antenatally diagnosed duodenal atresia, right sided cephalhaematoma, early onset neonatal sepsis (congenital pneumonia), and left sided renal mass.

CASE MANAGEMENT

The baby was managed by supportive and respiratory care by heated and humidified high flow nasal canula. Our plan was to do septic work up, plain x-ray abdomen, serum electrolyte, serum creatinine, urine routine examination and culture sensitivity, and ultrasonography of renal system and brain. Plain X-ray of abdomen showed double bubble shadow suggesting duodenal atresia **(FIGURE 1a)**. Serum creatinine was raised but gradually became normal at day 14.

Ultrasonography of whole abdomen done at seventh postnatal age showed distended pylorus and first part of duodenum, dialted stomach, and gallbladder sludge. Echocardiography showed normal findings. At postnatal age 24 hours, the baby had blood stained orogastic aspirate 50 ml, coffee ground color **(FIGURE 1b)**. Per rectal bleeding (bright red) was managed by 1-unit fresh frozen plasma (FFP). The following laboratory investigations were performed with prothrombin time, international normalized ratio (INR), activated partial thromboplastin time (APTT), D-dimer, and fibrinogen. All tests were normal.

During days 3-8, the baby was hemodynamically stable, weaned from high flow nasal canula at 50 hours of age. Bleeding through orogastic aspirate continued. At day eight, we repeated prothrombin time, INR, APTT, D-dimer, fibrinogen, and platelet level. All tests were normal except D-dimer 6.8 µgm/ml and factor VIII 1% **(TABLE 1)**. So, the baby was diagnosed as hemophilia A. Factor VIII was given at a dose of 100 IU/Kg, 12 hourly at day 10 and 12. Repeat factor VIII level was 150%.

TABLE 1 Coagulation screen results of the newborn

Postnatal age	Factor VIII	D-dimer	FDP
Day 2	-	5.0	6.5
Day 8	1%	6.8	25
Day 10	150%	-	-
Day 13	150%	4.5	-
Day 16	-	6.9	3.8
Day 20	-	3.5	8.8

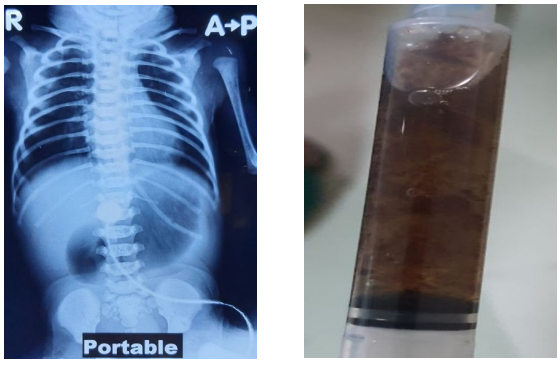
Normal value for factor VIII is 50-150%, D-dimer is 0.0-0.5 µg/ml, and FDP is 0.00-5.0 mg/dl

At day 12, the baby developed convulsion in the form of lip smacking and eye staring persisted for two minutes, provisionally diagnosed as intracranial hemorrhage due to hemophilia, managed by injection phenobarbitone. Laboratory investigations for septic screening, serum electrolyte, serum creatinine, serum calcium, serum magnesium and ultrasonography of brain were done which showed normal findings.

During days 13–30, the baby had orogastic aspirate bleeding on and off, disseminated intravascular coagulation (DIC) persisting, and two episodes of septic event needed mechanical ventilator care. Therefore, surgery was not possible. At day 30, the baby died due to DIC with shock. During hospital stay, the baby got 4-unit packed red blood cell, 10-unit FFP, 4-unit platelet and 3-times factor VIII.

DISCUSSION

Hemophilia has a worldwide distribution and occurs either in the form of familial disease or as a sporadic disease due to de novo mutations. Moderate and mild haemophilia are defined as factor 8 levels >1% to <5% and >5% to <40%, respectively.[5,6] Severe hemophilia occurs when circulating level of a factor is <1% of



a b

FIGURE 1 a. Chest and abdomen x-ray showing double bubble appearance, b. Altered blood staining orogastic aspirate

normal activity in the blood and is typically diagnosed in the first two years of life.[7] Absent or reduced activity of factors VIII and IX affects thrombin formation and consequently the conversion of fibrinogen into fibrin, i.e., clots do not form which leads to bleeding.[8]

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 newborn vary from adult values. The exception to this is factor VIII which is at the normal adult range or mildly increased at birth. Adult levels are also achieved in preterm infants; thus, it is possible to diagnose most cases of hemophilia A at birth.[9]

In newborns with hemophilia, intracranial hemorrhage is the most life-threatening complication. Newborns with mild hemophilia can have intracranial haemorrhage. After diagnosis, treatment for acute bleeding should be undertaken urgently with factor VIII or IX concentrates.[6]

The cranial ultrasound should be undertaken before discharge in all neonates with severe or moderate haemophilia but it fails to reliably detect small to moderate extra-crainal hemorrhages along the lateral surfaces of the brain or in the posterior fossa.[10] When present, disseminated intravascular coagulopathy seems to represent a sign of poor prognosis.[6] Diagnosis of sporadic cases of hemophilia in the newborns is underestimated, especially in children with moderate and mild forms of factor VIII or IX deficiency.

Conclusion

Abnormal bleeding in newborns should rise the suspicion of hemophilia. A blood coagulation disorder must be considered along with immediate aggressive support measures when a neonate has significant bleeding with no risk factors. Through our experience, we report on the atypical presentation of undiagnosed haemophilia A with antenatally diagnosed duodenal atresia, highlight the importance of timely investigation of a normal partial thromboplastin time in a neonate with early surgical intervention.

Acknowledgments

I would like to acknowledge and thank the medical, nursing and support staff of NICU of Bangabandhu Sheikh Mujib Medical University and the parents of the patient.

Funding

This study did not receive any funding.

Conflict of Interest

The author has no conflict of interest to declare.

Ethical approval

The study does not have any ethical approval from any review board but consent was taken from the parents of the patient.

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