Original Research Paper

Volume - 12 | Issue - 04 | April - 2022 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Obstetrics & Gynaecology

A CASE REPORT ON ANTENATAL MOTHER – THE HEMOPHILIA CARRIER

Dr.Shery Angel Rajakumar

Consultant Obstetrician and Gynaecologist Supreme speciality Hospital Padur, Chennai Tamilnadu India-603103

ABSTRACT **BACKGROUND** Hemophilia is a rare bleeding disorder which is due to the deficiency of a coagulation protein- the most important factor VIII.The incidence of Hemophilia- A is 1 in 5000 male births. This is a case report on an antenatal mother, who is a known case of Hemophilia-A, carrier admitted for safe confinement. **CASE PRESENTATION :** We report a case of 37-year-old G4P2L1A1 at 38 weeks and 4 days period of gestation, a Hemophilia- A carrier was admitted for safe confinement.She had family history of Hemophilia-A. All her three off-springs had Hemophilia-A. The patient was taken up for an Elective Caesarian section and she delivered an alive-term boy baby. The baby was advised by the Paediatric Hematologist to review at the age of 6 months for factor VIII assay. **CONCLUSION:** In some parts of developing countries like India reducing the mortality rate of Hemophilia is still a hindrance due to the scarce availability of healthcare facilities and poor follow-up. When we diagnose Hemophilia, we should include the family history, active carrier status, clinical manifestations as well as laboratory testing. There should be equal coordination between the Obstetrician, Hematologist, Immunologist, Genetics department, and Psychologist.

KEYWORDS : Hemophilia, Factor VIII, Bleeding, Genetics

INTRODUCTION:

Hemophilia, a rare bleeding disorder is caused due to the deficiency of a coagulation protein called factor VIII1. On the other hand, Hemophilia-B is due to the deficiency of factor IX, also known as the Christmas factor. The mode of inheritance of both diseases is X-linked recessive. The incidence of Hemophilia- A is around 1 in 5000 male births. On the other hand, Hemophilia-B occurs in 1 in 30,000 live births2. The affected ones will have an increased possibility to develop traumatic bleeding events. The following figure shows the normal coagulation cascade that takes place in our body:

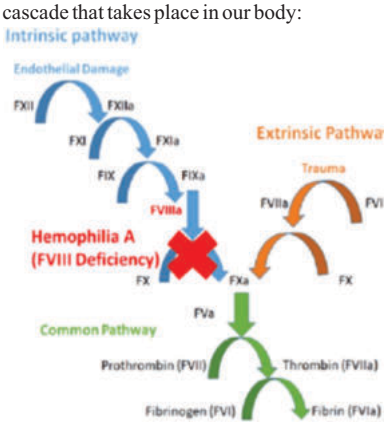

FIGURE 1: COAGULATION CASCADE

The factor VIII is synthesized in the liver and the Von-Willebrand factor is the carrier for factor VIII. It is a protein that regulates the activation of factor X, by proteases that are secreted in the intrinsic pathway. Hence, deficiency of factor VIII leads to defective coagulation and bleeding.

The gene coding for factor VIII is located on X-chromosome. Hemophilia can be classified as A)Mild Hemophilia(factor level 5-25 % of normal level), in which excessive bleeding occurs usually after surgery or dental procedures. B) Moderate Hemophilia(Factor VII level 1 to 5% of normal, in which bleeding is seen after minimal trauma. C)Severe hemophilia(factor VIII level < 1% of normal) which usually results in severe bleeding throughout life, which begins soon after birth(e.g. scalp hematoma after delivery or excessive bleeding). It is more common in deep tissues/joints/GIT/Hemarthrosis. Hemarthrosis is very common in Hemophilia-A and is almost diagnostic of the disorder. Recurrent bleeding into joints leads to joint destruction and joint deformities.

CASE REPORT

A 37-year-old G4P2L1A1 at 38 weeks and 4 days period of gestation, a known Hemophilia-A carrier was admitted for safe confinement. She was able to perceive fetal movements well. Her brothers and cousins were known cases of Hemophilia-A. Her mother was a known carrier of Hemophilia-A. Her pedigree chart is as follows:

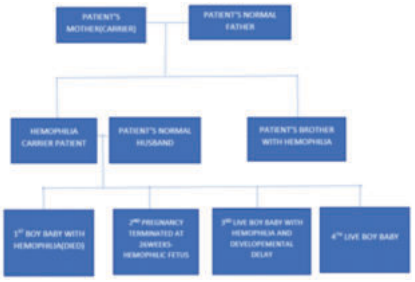

Figure 2: Pedigree Chart

Her 1st pregnancy was a full term vacuum-assisted delivery. She delivered an alive boy baby. After birth, the baby developed a massive cranial hematoma and passed away at 2 months of life. Her second pregnancy was terminated at 16 weeks of gestation since Hemophilia was evaluated for the fetus. In the 3rd pregnancy, she delivered a boy baby at home. The baby developed seizures on day 15 of life. The neonate was diagnosed to have alloantibodies against Factor VIII. The baby was hospitalized for 15 days and Factor VIII infusion was given. The baby had developmental delay. The baby developed bleeding manifestations at around 4 years of age, crippled for 1 month (since the site of bleed was thigh), and later 2 doses of factor VIII infusion were given (at a rate of 20-30 IU/Kg). In both 1st and 2nd pregnancy, the neonates were positive for the inhibitors(alloantibodies that develop against the factor). On examination, the patient's condition and vitals were stable. NST was reassuring. Investigations done are as follows:

Table 1: Lab Investigations

HEMOGLOBIN	9.1 g/dl
TOTAL COUNT	5100/mm^3
DIFFERENTIAL COUNT: N/L/E/B/M	61/26/5/8/0%
PLATELET COUNT	4.55 LAKHS
T3	160
T4	10.74
TSH	5.08
BLEEDING TIME	4 MIN 16 SECONDS
CLOTTING TIME	6 MIN 05 SECONDS
PROTHROMBIN TIME	11.8
APTT	26.9 SECONDS
INR	0.75
ISI	1.09
URINE ROUTINE	NORMAL
SEROLOGY	NON-REACTIVE

After obtaining high-risk consent regarding the chances of bleeding, poor perinatal outcome, need for blood and blood product transfusion, the patient was taken up for an Elective Caesarian section and she

delivered an alive-term boy baby. Intraoperatively bleeding was within normal limits. Intraoperative and postoperative periods were uneventful. The baby had no bleeding manifestations after birth. Gentle handling of the baby was advised. Injections to the baby were contraindicated. The baby was advised by the Pediatric Hematologist to review at the age of 6 months for factor VIII assay.

DISCUSSION:

When we diagnose Hemophilia, we should include the family history, active carrier status, clinical manifestations as well as laboratory testing. During pregnancy, the genetic testing to be done includes chorionic villous sampling or amniocentesis. Immediately after delivery, the factor VIII and Factor IX levels in cord blood sample plays an important role in diagnosing both Hemophilia-A and B. In a patient with Hemophilia, the complete blood count, Prothrombin time(PT), and bleeding time(BT) are usually found to be normal whereas activated Partial thromboplastin time(aPTT) is prolonged and factor VIII/IX are reduced. Molecular genotyping must be done to finalize the diagnosis and also to determine the severity of the disease. The most important complication of Hemophilia-A is the development of alloantibodies known as "inhibitors" against the exogenous factor VIII that we infuse 3 . These are IgG types of immunoglobulins produced against the factor VIII activity, and are calculated by using BETHESDA Units per ml. Prophylaxis with clotting factor concentrates is the standard treatment. TUROCTOCOG ALFA(NOVOEIGHT ®) is a 3rd generation, recombinant, B-Domain-truncated human coagulation Factor VIII molecule approved for Hemophilia-A in all age groups4-6. Performing factor VIII assay is mandatory to determine the severity and no. of infusions required. When we infuse recombinant factor VIII at a rate of 1U/dl/kg, the plasma activity rises by 2.5% of normal activity

Formula:

REQUIRED UNITS= BODY WEIGHT(Kg) x DESIRED FACTOR VIII RISE(%) or IU/dl x 0.5

Table 2: The following table gives the dose of Factor VIII according to the severity:

Degree of hemorrhage/ Surgery Type	Factor VIII level required (%)	Dose frequency (hours)/ Duration of therapy (days)
Hemorrhage		
Minimal Joint bleed, muscle bleeding, or oral bleeding	20-40	Every 12 - 24 hours / 1 day
Extensive joint bleed, muscle bleeding	30-60	Every 12 - 24 hours / 3 - 4 days
Life-threatening hemorrhage	60-100	Every 8 - 24 hours until the threat is resolved.
Surgery		
Minor Surgeries and dental procedures	30-60	Every 24 hours/ 1 day, until healing, is achieved.
Major	80-100 (pre-operative and post-operative)	Every 8 - 24 hours until adequate wound healing/ 7 days

Paediatric population
Dosage of 1.5 IU/dl/IU/kg

Formula :

Required units = body weight (kg) x desired factor VIII rise (%) (IU/dL) x 0.7

AVAILABLE FORMS:

250 IU or 500 IU VIALS IN POWDERED FORM.

The ultimate aim is to increase the factor VIII levels by more than 25% of the normal in mild and moderate Hemophilia. In case of any major surgeries, the factor VIII level should be raised to 100% and later should be maintained more than 50% of normal for 10 to 14 days. For mild Hemophiliacs, Desmopressin is enough for minor surgeries. It causes the release of stored factor VIII. Epsilon Amino Caproic Acid may be added if bleeding persists after treatment with factor VIII and Desmopressin. Fresh frozen plasma can be used in cases of unavailability of factor VIII concentrates. Emicizumab is a monoclonal antibody that binds to both factors 9 and 10, turns them into active complex, and precludes the need for factor VIII. Gene therapy is currently in the developmental phase.

Hemophilia is a disease that requires team effort at a higher level which when properly planned will provide a better prognosis, good quality of life, and life expectancy 7. Prenatal testing in a pregnant woman with a family history of Hemophilia or history of bleeding manifestations running in family is a must. It includes karyotyping, chorionic villi sampling, amniocentesis followed by genetic counseling. Though the incidence of Hemophilia is rare in pregnancy I.e, around 2.89%, genetic testing, factor VIII assay, coagulation profile, ruling out other bleeding disorders like Vonwillibrand factor deficiency are necessary for a carrier female. Pre-conceptional counseling is also a mandatory one. The life expectancy of patients with severe Hemophilia was only 11 years of age till the late 1960s and also the incidence of early neonatal death due to severe hemorrhage and intracranial hemorrhage was high. But, with the evidence of cryoprecipitate, lyophilized plasma concentrate of coagulation factors, Desmopressin, recombinant factors 8 and 9 production and increased awareness regarding vaccination against blood-borne viral diseases, the advancement in DNA technology and widespread availability of replacement therapy, the life expectancy of patients has increased.

CONCLUSION:

In some parts of developing countries like India reducing the mortality rate of Hemophilia is still a hindrance due to the scarce availability of healthcare facilities and poor follow-up. Both the carrier females and affected males should regularly visit the doctor. They should avoid the intake of unnecessary over-the-counter painkillers which will increase the risk of bleeding. There should be equal coordination between the Obstetrician, hematologist, Immunologist, Genetics department, and Psychologist.

Thus, the checklist to improve the prognosis of a Hemophiliac is as follows:

- Early detection
- Adequate and regular follow up
- Health education to the patient regarding symptomatology and complications
- Proper vaccination and dental care in the pediatric age group
- Non-contact activities8-10.
- Shared decision-making approach
- Compliance with the prophylactic treatment to decrease the incidence of joint space bleed.

CONSENT:

Informed consent was obtained from the patient for publication of this paper.

CONFLICT OF INTERESTS:

The authors declare that they have no competing interests.

FUNDING:

There is no external funding to declare for this publication.

AVAILABILITY OF DATA MATERIALS:

All relevant clinical data and images are included in this report.

REFERENCES:

1. Srivastava A, Santagostino E, Dougall A, et al. WFH guidelines for the management of hemophilia, 3rd edition. Haemophilia. 2020;26(Suppl6):1-158
2. Priyanka M, Ch. Saidatta, Shambu Ramesh. Case report on Hemophilia, International Journal of Science and Healthcare Research Vol.3; Issue: 3; July-September 2018.
3. Mariusz Flisinski, Jerzy Windyga, Ewa Stefanska, StawomirHuszcza, Rafat Donderski, Jacek Manitus. Acquired haemophilia: a case report. Polskie Archiwum Medycyny Wewnetrznej. 2008; 118(4): 228-31. [Internet]. 2008[Updated 2008; cited 2018 July 31]
4. Thim L, Vandal B, Karlsson J, et al. Purification and characterization of a new recombinant factor VIII (N8). Haemophilia. 2010;16(2):349-359.
5. Ahmadian H, Hansen EB, Faber JH, et al. Molecular design and downstream processing of turoctocog alfa (NovoEight), a B-domain truncated factor VIII molecule. Blood Coagul Fibrinolysis. 2016;27(5):568-575.
6. Novo Nordisk. NovoEight (turcotocog alfa) Summary of Product Characteristics. 2018.
7. Mehta P, Reddivari AKR. Hemophilia. [Updated 2021 Dec 31].
8. Cuesta-Barriuso R, Torres-Ortuño A, Pérez-Alenda S, José Carrasco J, Querol F, Nieto-Munuera J. Sporting Activities and Quality of Life in Children With Hemophilia: An Observational Study. Pediatr Phys Ther. 2016 winter;28(4):453-9
9. Manco-Johnson MJ. Collision sports and risk of bleeding in children with hemophilia. JAMA. 2012 Oct 10;308(14):1480-1.
10. Souza JC, Simoes HG, Campbell CS, Pontes FL, Boullosa DA, Prestes J. Haemophilia and exercise. Int J Sports Med. 2012 Feb;33(2):83-8.