Case Report

Management of pregnant female with Haemophilia-A: A case report

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Abstract

Haemophilia-A is a rare, X-linked recessive inherited disease affects males and females are carrier results in prolonged bleeding after minor injuries, procedures or surgery. Spontaneous or recurrent bleeding may occur in deep muscles, joints but intracranial haemorrhage can be dangerous. Women with a family history of bleeding disorder, personal history of bleeding (menorrhagia, mucous membrane, postoperative bleeding and PPH) or a prolonged activated partial thromboplastin time (aPTT) should be screened for haemophilia by measuring coagulation factor VIII level during hospital visits for these reason or antenatal care (ANC). Female heterozygote carriers may have variable presentation of bleeding due to reduced levels of clotting FVIII and may experience excessive bleeding due to gynaecologic issues, during spontaneous abortion, medical termination of pregnancy or invasive prenatal diagnostic techniques in first trimester of pregnancy, antepartum and postpartum haemorrhage in later part of gestation and after delivery.

Keywords: ANC, carrier, case report, delivery outcome, Haemophilia-A, pregnancy

Introduction

Hereditary bleeding disorders (HBD) in pregnant females can have devastating consequence for both the mother and neonate. Mother has haemostatic challenges of pregnancy and risk of bleeding complications during pregnancy, delivery, and postpartum period.[1] Haemophilia-A type (classic haemophilia) accounts for 80 to 85% of total cases. Female who inherits one affected X-chromosome becomes a "carrier" to pass the affected gene to next generations.[2] The carriers have factor VIII (FVIII) level approximately half of healthy individuals with adequate haemostasis.[3,4] The carrier women with symptomatic Haemophilia-A (FVIII activity <30 IU/dl) are approximately 1 per 100,000 needs prophylactic FVIII administration. Severe Haemophilia-A very rare (FVIII <1%), high risk for severe bleeding complications.[2] Haemophilia-A is a rare, known cause of life-threatening bleeding and cause of mortality and morbidity in mother and fetus. Very less known about standard treatment protocols and outcome of Haemophilia-A, during pregnancy management.

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Case History

Patient consented for publication as case report in Journal with promise to keep her identity undisclosed. She was aged 35 years, primigravida, spontaneous conception referred at 19 weeks gestation for safe confinement. Patient was investigated at 12 weeks of pregnancy for genetic mutation in Medical Genetics department of our institute in view of history of Haemophilia-A bleeding disorder in her siblings. Her brother was known case of Haemophilia-A whereas her sister was carrier of Haemophilia-A gene mutation, had received FVIII correction therapy various

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time since diagnosis. On genetic testing of patient had two gene mutations (compound heterozygote). One was mutation of single nucleotide change in F8 gene at Exon -14, same as her brother and second was mutation of single nucleotide change in F8 gene at Exon -22, both were pathogenic and have been reported in mild, moderate and severe haemophilia patients in literature.

Patient was advised for prenatal testing to know the gene mutation in fetus. She refused invasive prenatal testing in view of risk of haemorrhage. Anomaly USG scan at 19 weeks was normal. She opted for Non-Invasive Prenatal Testing (NIPT) for aneuploidy screening, result was low risk for aneuploidy. At 27 weeks gestation she had history of tooth extraction and was transfused FVIII (total 1250 IU twice a day up to 4 days) along with antibiotics. On follow up she was diagnosed as a case of gestational diabetes controlled on diabetic diet. At 36 weeks and 6 days of gestation patient was admitted with decreased foetal movements and itching all over body, diagnosed as a case of cholestasis of pregnancy and started on oral ursodeoxycholic acid. On USG liquor was reduced but growth parameters and doppler studies were normal.

She was planned for elective caesarean section at 37 weeks gestation in view of cephalopelvic disproportion, reduced liquor and off and on decreased fetal movement under spinal anaesthesia. The dose of FVIII (antihemophilic factor recombinant FVIII, ADVATE, Takeda Pharm. Co. Ltd.) is calculated by multiplying the patient's weight in kilograms by the desired rise in factor level in IU/dl, multiplied by 0.5 as per guidelines.[4,5] Preoperatively she was transfused with FVIII 2000 IU on one day before of surgery followed by 1500 IU on the day surgery. Serial activated partial thromboplastin time (aPTT) levels were measured. The half-life of FVIII is approximately 8-12 hours and infused by slow IV infusion at a rate not to exceed 3 ml/min. FVIII 1500 IU was given 8 hourly up to 3rd postoperative days, followed by 1000 IU 8 hourly from 4th to 6th days and 750 IU 8 hourly from 7th -14th postoperative days. FVIII infusion was given till 14th postoperative day in tapered doses and then stopped.

The surgery was uneventful and she delivered a male baby 2.92 kg weight with APGAR score of 7 at birth, 8 at 1 min and 8 at 5 min. Cord PH was 7.35 and placental weight of 600 grams. Neonate was examined for any apparent congenital malformations and investigated for Haemophilia (cord sample for FVIII levels and coagulation profile). Neonate FVIII level was 1%, hence a repeat venous sample was sent for coagulation, with values PT 15.7/12.5 sec, aPTT 77.7/30.0 sec, and INR 1.27, hence one unit Fresh frozen plasma was transfused slowly. After transfusion the repeat value of FVIII levels was 3%. USG cranium was done to rule out intracranial bleed which was normal and advised to repeat at every 3-4 weeks. The baby was given vitamin K shot at birth with other routine vaccines, he was discharged in stable condition. Parents were counselled for avoidance of any future IM injections and follow up in Medical Genetics for mutation analysis study.

Discussion

The diagnosis of Haemophilia-A is established in an individual with low FVIII. During pregnancy all clotting factor increases including FVIII, so if carrier status not known before pregnancy, it is difficult to confirm it only with FVIII levels because it can be within normal range. FVIII clotting activity is unreliable in the detection of heterozygous females (F8 pathogenic variant); only approximately 30% of Haemophilia-A heterozygous females have FVIII clotting activity lower than 40%.

Prenatal diagnosis (PND) of haemophilia by invasive methods such as chorionic villous sampling (11-14 weeks), amniocentesis (after 15 weeks), and cordocentesis (after 18 weeks) can be accurately determined as in worldwide but non-invasive prenatal diagnosis and preimplantation genetic diagnosis are predominantly considered beneficial.[3] If a woman has a low level of FVIII concentration of <50%, raise her FVIII concentration to 100% before any procedure.[4]

Women with haemophilia or HBD are at an increased risk of both primary and secondary PPH, especially if FVIII levels are <50 IU/dl at term.[5] The risk of PPH can be modified by prophylactic treatment to normalize their coagulation status and FVIII ≥50 IU/dl, and to be maintained for 24 hrs for vaginal delivery or caesarean section.[5,6] Obstetric measures to avoid uterine atony, and a method of delivery with minimal or less trauma and active management of the third stage of labour is important. The mode of delivery must be guided by obstetric indications. Any bleeding should be monitored and managed accordingly as per guidelines.[5-7]

Prophylactic use of Tranexamic acid in mild bleeding (1 gm IV stat then maintenance dose 1 gm over 8 hr) is to be done.[8] In selected cases desmopressin IV 0.3 μg/kg may increase FVIII concentrations and platelets, without any major side effects (mild facial flushing and headache). Mechanical thromboprophylaxis is sufficient for carriers undergoing surgeries, thromboprophylaxis with LMWH is not recommended.[9] There is no contraindication to regional analgesia (effective method for labour analgesia) or anaesthesia, when the FVIII concentration are ≥50 IU/dl. Regional anaesthesia can be given safely after correction of FVIII level, Platelets (>80,000) and normal range INR (<1.5) for caesarean delivery.[10]

Conclusions

Maternal hereditary coagulopathies during pregnancy are challenging. Identification by genetic testing prior to conception, proper counselling and determination of fetal gender for management of the child at delivery time is important. A multidisciplinary team approach with proper planning, coordination, timely communication, availability of FVIII (recombinant factor), and laboratory support are critical for the safe management of pregnancy with Haemophilia-A.

Research quality and ethics statement

The authors of this manuscript declare that this scientific work complies with reporting quality, formatting and reproducibility guidelines set forth by the EQUATOR Network. The authors also attest that this clinical investigation was determined to [not applicable] require Institutional Review Board/Ethics Committee review, and the corresponding protocol/approval number is [not applicable]. Finally, the authors have registered this clinical study with the following Clinical Trial Registry: [not applicable].

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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