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Ovulation triggered hemoperitoneum in inherited Factor VII deficiency

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Abstract

Background: The most commonly prevalent inherited bleeding disorder, Factor VII deficiency presents with spontaneous or triggered bleeding manifestations of variable severity. In reproductive age women, menorrhagia is the commonest presentation followed by ovulation triggered bleeding.

Case presentation: We hereby present a young hypertensive woman with diagnosed factor VII deficiency and history of recurrent major bleeding manifestations. This time, she presented with acute pelvic pain and shock. Emergency laparotomy revealed massive hemoperitoneum due to bleeding from the rent on ovarian surface following ovulation.

Conclusion: Younger age at initial bleeding presentation and major bleeding episode increases risk of subsequent major bleeding in inherited factor VII deficiency. Acute pelvic pain and shock in reproductive aged women should warn the treating physician of ovulation triggered bleeding

Clinical significance: In the presence of risk factors for major bleeding in inherited bleeding disorders, acute pelvic pain with shock should direct the treating physician to ovulation triggered bleeding.

Keywords

Factor VII deficiency; acute pelvic pain; ovulation triggered; hemoperitoneum

Introduction

Inherited factor VII deficiency is the most common of the rare inherited bleeding disorders at a prevalence rate of 1 in 300000 to 1 in 500000 population [1]. It is inherited in autosomal recessive pattern but with variable penetrance. The European Association for Hemophilia and Allied Disorders (EAHAD) data-

base on F7 gene located on chromosome 13q34 has recorded 221mutation variants so far. Translating the genomic heterogeneity into quantitative or qualitative defect of factor VII, the clinical phenotype is highly variable. Homozygotes may remain asymptomatic and the compound heterozygotes or heterozygotes may have bleeding manifestations albeit not fatal [1,2]. Therefore the bleeding tendency do not correlate with the plasma level of the factor VII but its activity [3]. The risk of spontaneous, triggered and asymptomatic bleeding correlates with factor VII activity level <10, 10-20 and 20-50% respectively [4]. Reproductive aged women with inherited bleeding disorder are at risk of gynecological and obstetrical complications. The most common presentation is menorrhagia followed by ovulation related bleeding, adverse pregnancy outcome and postpartum hemorrhage [5-7].

Case Presentation

A 30 year old nulliparous woman diagnosed case of factor VII deficiency presented to the ER with acute pelvic pain and syncope. The sharp stabbing pain initially started on the left lower quadrant which became generalized. Her periods were irregular and the last menstrual period was 2-3 weeks ago. She gives a history of excessive bleeding during her periods lasting 4-5days. She underwent dacryocystorhinostomy for left nasolacrimal duct obstruction 15 years ago. Intractable intraoperative bleeding ensued during the procedure which lead to blindness of the left eye. Subsequent investigation revealed prolonged PT/INR, normal aPTT and low factor VII activity level (20-25%) leading to diagnosis of factor VII deficiency. She does not have a family history of any bleeding manifestations. Two years ago she was diagnosed as a young hypertensive for which no cause was found by the medical team except for the periodically symptomatic right ovarian dermoid of 8 x 5 centimeters. She was treated with oral Losartan 5 mg daily. Eight months ago she suffered a major left frontoparietal subdural hemorrhage necessitating burr hole drainage under fresh frozen plasma cover. She recovered without any residual neurological deficits.

Initial assessment at the ER revealed marked pallor. She was in shock with feeble pulse rate of 120 beats per minute and BP of 70/50 mm of Hg. The abdomen was distended with generalized tenderness, guarding and rigidity. Hematological investigation reports showed non pregnant βhcG level, normal total leucocyte and platelet count. Her hemoglobin level was 5 gm/dl. Her liver and renal function tests were within the normal range. PT/INR was markedly elevated. Transabdominal ultrasound of the abdomen revealed massive free fluid (Figure 1A) and the right ovarian dermoid which has remained the same. There was a ruptured anechoic cyst measuring 1.8 x 2.1 centimeters in the left ovary (Figure 1B). A presumptive diagnosis of intraperitoneal hemorrhage following ovulation was made. The patient was hemodynamically stabilized at the ER. 4 units of fresh frozen plasma and 2 units of packed red cells was transfused en route to OR for emergency laparotomy.

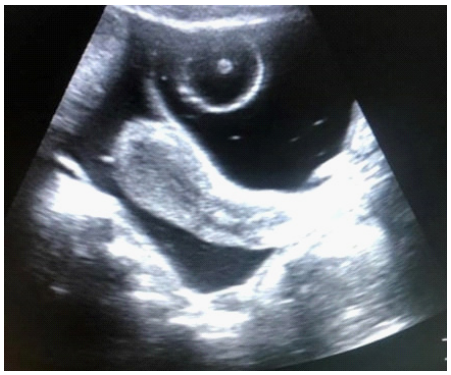

Figure 1A: Transabdominal sonography showing hemoperitoneum

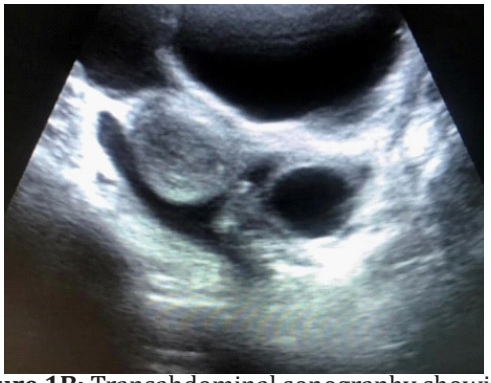

Figure 1B: Transabdominal sonography showing ruptured Graffian follicle

Intra operative finding was massive hemoperitoneum of 1.5 liters. Exploration of the whole abdomen revealed an untorsed right ovarian dermoid for which right ovariectomy was performed in view of periodic painful symptoms. The left ovary was enlarged and showed a coagulum on the surface with no active bleeding. The coagulum was left undisturbed. Cut section of the dermoid showed no focus of necrosis or hemorrhage. Post operatively, she was transfused 2 units of packed red cells. Her postoperative recovery was uneventful and discharged on 12th day.

Discussion

Hemoperitoneum in women with inherited or acquired bleeding disorder may result from ovulation or ruptured hemorrhagic corpus luteal cyst. Bleeding occurs from rent in the ovary following extrusion of ovum from the Graffian follicle or the subsequent rupture of hemorrhagic corpus luteal cyst as it regresses. Although, exact proportion of ovulation triggered hemoperitoneum is not known with factor VII deficiency, 4 out of 20 reproductive aged women with factor XIII deficiency had ovulation triggered hemoperitoneum as reported by Lak et al [7]. Our case had initial bleeding manifestation at a younger age and two episodes of life threatening hemorrhage. Therefore she remains at greater risk of subsequent major bleeding as per the age at initial manifestation and major bleeding episodes [8,9].

Hormonal contraceptives are known to inhibit ovulation thereby reducing the risk of ovulation triggered bleeding [10]. Combined oral contraceptives are known to increase the activity level of factor VII. Paradoxically, presence of iatrogenic risk factor such as hormonal contraceptives may cause thrombotic event in 3-4% of these cases [11]. However we could not start oral contraceptive to reduce the severity of menorrhagia and recurrence of ovulation triggered bleeding due to hypertension in this case. We planned to insert LNG intrauterine contraceptive device as an alternative [12]. The ovulation triggered bleeding may not be effectively mitigated due to its unreliable ovulation suppression especially in long term use [13]. However, our patient had a short uterine cavity as measured with uterine sound. We decided not to insert the IUCD in view of higher chance of expulsion. She was advised to stay close to health facility where blood transfusion facility is available.

In view of contraindication of hormonal contraceptives to mitigate ovulation triggered bleeding, we also tried to look at association of Factor VII deficiency and hypertension. Our patient is a young hyperten-

sive in whom no cause could be found. Sicker et al in their animal model study has shown the vasodilation effect of thrombin on vessels [14]. Clinical trial on humans by Gumundsdottir et al have demonstrated the vasoprotective and dilation effect of thrombin on endothelial cells [15]. Based on thrombin generation deficiency as the basic pathophysiology and extrapolating the results from these two studies, can we hypothesize the association of factor VII deficiency and hypertension in our case?

Our case report is limited by lack of genetic studies to classify the genotype of factor VII deficiency in absence of positive family history and minimal reduction of factor VII activity level. We also could not initiate definite medical management to mitigate the problem of ovulation triggered bleeding in our case.

Conclusion

Younger age at initial bleeding presentation and major bleeding episode increases risk of subsequent major bleeding in inherited factor VII deficiency. Acute pelvic pain and shock in reproductive aged women should warn the treating physician of ovulation triggered bleeding.

Clinical significance

In the presence of risk factors for major bleeding in inherited bleeding disorders, acute pelvic pain with shock should direct the treating physician to ovulation triggered bleeding.

References

1. Robinson KS. An overview of inherited factor VII deficiency. Transfus Apher Sci. 2019; 58: 569-571.

2. Herrmann FH, Wulff K, Auerswald G, Schulman S, Astermark J, Batorova A, et al. Greifswald Factor FVII Deficiency Study Group. Factor VII deficiency: Clinical manifestation of 717 subjects from Europe and Latin America with mutations in the factor 7 gene. Haemophilia. 2009; 15: 267-80.

3. Sevenet PO, Kaczor DA, Depasse F. Factor VII Deficiency: From Basics to Clinical Laboratory Diagnosis and Patient Management. Clin Appl Thromb Hemost. 2017; 23: 703-710.

4. Jain S, Donkin J, Frey MJ, Peltier S, Gunawardena S, Cooper DL. Phenotypical variability in congenital FVII deficiency follows the ISTH-SSC severity classification guidelines: a review with illustrative examples from the clinic. J Blood Med. 2018; 19: 211-218.

5. Quintavalle G, Riccardi F, Rivolta GF, Martorana D, Di Perna C, Percesepe A et al.Ad-Hoc Study Group. F7 gene variants modulate protein levels in a large cohort of patients with factor VII deficiency. Results from a genotype-phenotype study. Thromb Haemost. 2017; 117: 1455-1464.

6. Sharief LA, Kadir RA. Congenital factor XIII deficiency in women: A systematic review of literature. Haemophilia. 2013; 19: 349-57.

7. Lak M, Peyvandi F, Ali Sharifian A, Karimi K, Mannucci PM. Pattern of symptoms in 93 Iranian patients with severe factor XIII deficiency. J Thromb Haemost. 2003; 1: 1852-3.

8. Di Minno MN, Dolce A, Mariani G; STER Study Group. Bleeding symptoms at disease presentation and prediction of ensuing bleeding in inherited FVII deficiency. Thromb Haemost. 2013; 109: 1051-9.

9. Mariani G, Herrmann FH, Dolce A, Batorova A, Etro D, Peyvandi F et al. International Factor VII Deficiency Study Group. Clinical phenotypes and factor VII genotype in congenital factor VII deficiency. Thromb Haemost. 2005; 93: 481-7.

10. Abbas I,Al-Rubaie, Haithem A, Alalsaidissa J. The Effect of Combined Oral Contraceptive Pills on Factor VII Activity and D-dimer Level in Healthy and Obese Women. Journal of the Faculty of Medicine, Baghdad. 2016; 58: 63-70.

11. Ruiz-Saez A. Occurrence of thrombosis in rare bleeding disorders. Semin Thromb Hemost. 2013; 39: 684-92.

12. Chi C, Huq FY, Kadir RA. Levonorgestrel-releasing intrauterine system for the management of heavy menstrual bleeding in women with inherited bleeding disorders: long-term follow-up. Contraception. 2011; 83: 242-7.

13. Xiao B, Zeng T, Wu S, Sun H, Xiao N. Effect of levonorgestrel-releasing intrauterine device on hormonal profile and menstrual pattern after long-term use. Contraception. 1995; 51: 359-65.

14. Sicker T, Wuchold F, Kaiser B, Glusa E. Systemic vascular effects of thrombin and thrombin receptor activating peptide in rats. Thromb Res. 2001; 101: 467–75.

15.Gumundsdottir IJ, Lang NN, Boon NA, Ludlam CA, Webb DJ, Fox KA, et al. Role of the Endothelium in the Vascular Effects of the Thrombin Receptor (Protease-Activated Receptor Type 1) in Humans. J Am Coll Cardiol. 2008; 51: 1749–56.

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