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Factor V Deficiency in an Adolescent: A Case Report

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Abstract— Factor V is a major part of coagulation system and maintains a balance in pro-coagulant and anti-coagulant pathways. Any deficiency or mutation can lead to the disequilibrium. Factor V deficiency presents with bleeding while Factor V Leiden leads to a hypercoagulable state. Factor V deficiency can be congenital or acquired. The clinical findings range from asymptomatic to life threatening hemorrhage. Prothrombin time and Activated partial thromboplastin time are elevated. The management includes Fresh frozen plasma infusion. This is a case of 14-years-old female presenting with menorrhagia and hemorrhagic ovarian cyst, diagnosed as congenital factor V deficiency after factor V assay. Initially it was considered as platelet functional defect. As seen in the current report, it is observed that patients with factor V deficiency presents early in life with mucocutaneous bleeding, so early diagnosis and prompt management plays an important role in order to avoid the severe symptoms in future.

Keywords— factor V, factor V deficiency, bleeding diathesis, prothrombin time, activated partial thromboplastin time, hemorrhagic cyst, procoagulant, anti-coagulant, ovarian cyst, menorrhagia.

1. INTRODUCTION

Factor V is a vital component of the procoagulant and anti-coagulant pathway. It interacts with Factor X to activate the prothrombin into thrombin. It also interacts with activated protein C (APC) to inactivate factor VIII. Factor V is synthesized in liver cells, megakaryocytes and bovine aortic endothelial cells [1]. The disequilibrium in coagulation pathway can be due to Factor V deficiency or Factor V Leiden. Factor V deficiency presents with bleeding diathesis when the Factor V activity level is < 5 %. [1] Whereas, Factor V Leiden presents with a hypercoagulable state due to the substitution of Arg 506 by Gln at APC cleavage position [2]. This mutation renders the APC resistant to cleavage, causing thrombosis. Factor V deficiency can be congenital or acquired. Congenital factor V deficiency is inherited through an autosomal recessive pattern with a prevalence of 1 in million [3,4]. The incidence is highly reported in areas of consanguinity like the Middle East and India [4]. Conversely, Acquired Factor V Deficiency (AFVD) develops due to autoantibodies against Factor V after the exposure of bovine thrombin through antibiotics, infection, autoimmune disease and malignancies [5]. The clinical presentation of factor V deficiency ranges from asymptomatic to life threatening hemorrhage. On work up, Prothrombin time (PT) and Activated partial thromboplastin time (APTT) are prolonged. The condition is treated with Fresh frozen plasma (FFP) infusion with the target Factor V level of 20-30% [3].

We report a case of congenital Factor V deficiency with unusual presentation of menorrhagia and hemorrhagic ovarian cyst in an adolescent girl. We will also review various clinical presentations, diagnostic challenges and management strategies.

2. CASE PRESENTATION

We present a case of 14-years-old female student, resident of Badin, Karachi, Pakistan, with no known co-morbids, presented to the emergency department of Jinnah Postgraduate Medical Centre (JPMC) with

complains of vaginal bleeding and abdominal pain for the last eight days.

She was in a usual state of health eight days back when heavy vaginal bleeding started. She had to change tampons five to six times per day and the bleeding continued for three days. After the three days, generalized abdominal pain started which was sudden in onset, colicky in nature, non-radiating, aggravated by walking and movement, but non-relieving. She was taken to the nearby clinic where some pain killers were prescribed and was referred to another hospital where she got treatment (undocumented) and abdominal pain was relieved. In the evening, she again started to have heavy vaginal bleeding for which she presented to JPMC.

Patient also complains of blood in stools for the last three days without any clots or tenesmus. She is passing stool once a day for the last three days which is less than usual. Upon systemic inquiry, there is no history of joint pain, redness of eyes, photosensitivity, mouth ulcers, hair loss, dry mouth or dry eyes. There is no history of heat or cold intolerance, change in voice, change in appetite or weight, change in size of hands and feet, or any abnormal hair growth. Gastrointestinal system was clear with no history of mouth ulcers, difficulty in swallowing, abdominal pain, loose motions, or black colored stools. Urinary system was clear with no increase in urgency, frequency, incontinence, pus or blood in urine, or flank pain. Central nervous system inquiry was unremarkable with no history of decreased vision, diplopia, difficulty in swallowing, neck stiffness, fits, any facial or limb weakness, or incontinence.

Patient had a history of prolonged uncontrolled bleeding from umbilical cord at the time of birth for which she was transfused with blood. Patient's father reported that she also has the problem of gum bleeding since childhood. She also had a history of head injury for which sutures were applied on her head but big swelling formed at the suture site after which her wound was drained and restored. Sleep, appetite, bowel habits, and micturition was found to be normal. There is no history of addiction or weight loss. Family history was unremarkable. She belonged to poor socioeconomic status where seven people were living in a house with one room and unhygienic sanitary conditions. They used hand pump for drinking water.

On general physical examination, young female of average height, thin built, conscious, oriented with time, place and person, looking pale was lying on bed. Her vital signs on arrival were as follows: blood pressure, 110/70 mmHg (reference, 120/80 mmHg); pulse, 104 bpm (reference,70 to 100 bpm); respiratory rate, 24 breaths/minute (reference range, 18 to 22); and temperature, 98°F (reference, 98.6°F). There was no yellowish discoloration, clubbing, koilonychias, cyanosis, dehydration, or edema. Jugular venous pressure was not raised and thyroid was not enlarged. Gum hypertrophy and bony tenderness was negative.

On abdominal inspection, shape was normal, abdomen was moving normally with respiration, and umbilicus was central and inverted. There was no visible pulsation, scar, striae or any prominent veins. On palpation abdomen was soft but tender at lower quadrant. Spleen was palpable two fingers below the costal margin. Shifting dullness was positive and gut sounds were audible.

Examination of the cardiovascular, respiratory and central nervous system was unremarkable. Upon arrival we sent clinical laboratory testing of this patient. Her laboratory test results are presented in Table-1. Viral markers came out to be negative.

Analyte	**Patient Level on admission (18-11-2017)**	**Patient Level on 29-11-2017**	**Reference Range**
Hemoglobin	4.7 g/dL	13 g/dL	13.8–17.2 g/dL
Total leukocyte count	6 $\times 10^9$/L	6 $\times 10^9$/L	4.5–11.0 $\times 10^9$/L
Neutrophils	65%	75%	50-70%

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Lymphocytes	28%	18%	30-45%
Platelet count	374 $\times 10^9$/L	382 $\times 10^9$/L	150–400 $\times 10^9$/L
Hematocrit	13.6%	41.9%	37-47%
Mean corpuscular volume	72.7 fL	79 fL	80-98 fL
Blood urea nitrogen	19 mg/dL	28 mg/dL	7–20 mg/dL
Creatinine	0.8 mg/dL	1.0 mg/dL	0.6–1.2 mg/dL
Sodium	141 mEq/L	140 mEq/L	135–145 mEq/L
Potassium	3.2 mEq/L	4.0 mEq/L	3.5–5.5 mEq/L
Chloride	104 mEq/L	102 mEq/L	97–107 mEq/L
Total bilirubin	0.57 mg/dL	0.36 mg/dL	0.1–1.2 mg/dL
Direct bilirubin	0.14 mg/dL	0.08 mg/dL	0.1–1.2 mg/dL
SGPT	11 units/L	34 units/L	7–56 units/L
Gammq-glutaryl transpeptidase	19 units/L	22 units/L	8-40 units/L
Alkaline Phosphatase	279 units/L	450 units/L	150–480 units/L
Total Protein	6.67 g/dL	-	5.5-9.0 g/dL
Serum Albumin	3.68 g/dL	-	3.5-5.5 g/dL
Prothrombin time	57.6 seconds	25.1 seconds	9.1-13.1 seconds
Activated partial thromboplastin time	115.9 seconds	51.8 seconds	22.9-34.5 seconds
International normalized ratio	5.49	2.5	0.9-1.3
Factor II, Plasma	-	98%	70-146%
Factor V, Plasma	-	2%	62-150%
Factor VIII, Plasma	-	>143%	50-149%
Factor X, Plasma	-	87%	70-152%
Fibrinogen level	-	464 mg/dL	156-400 mg/dL

Table 1: Patient baseline laboratory values

Ultrasound whole abdomen and pelvis was done which showed fatty changes in the liver, splenomegaly, pelvic ascites, and right ovarian hemorrhagic cyst. Computed Tomography (CT) scan of abdomen and pelvis with contrast was also done which showed complex cystic lesion arising from right adnexa showing hyperdensity within it. This could be hemorrhagic cyst with possible active bleed (Figure 1A and 1B).

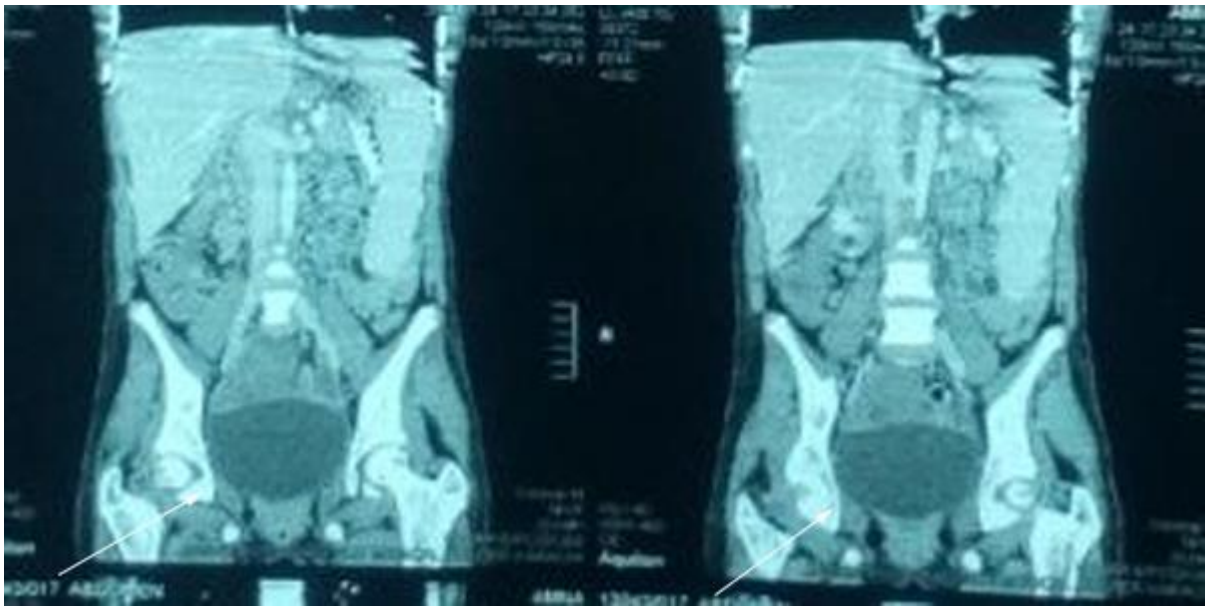

Figure 1A: Computed tomography scan of abdomen and pelvis (Coronal view) showing complex cystic lesion with hyperdensity

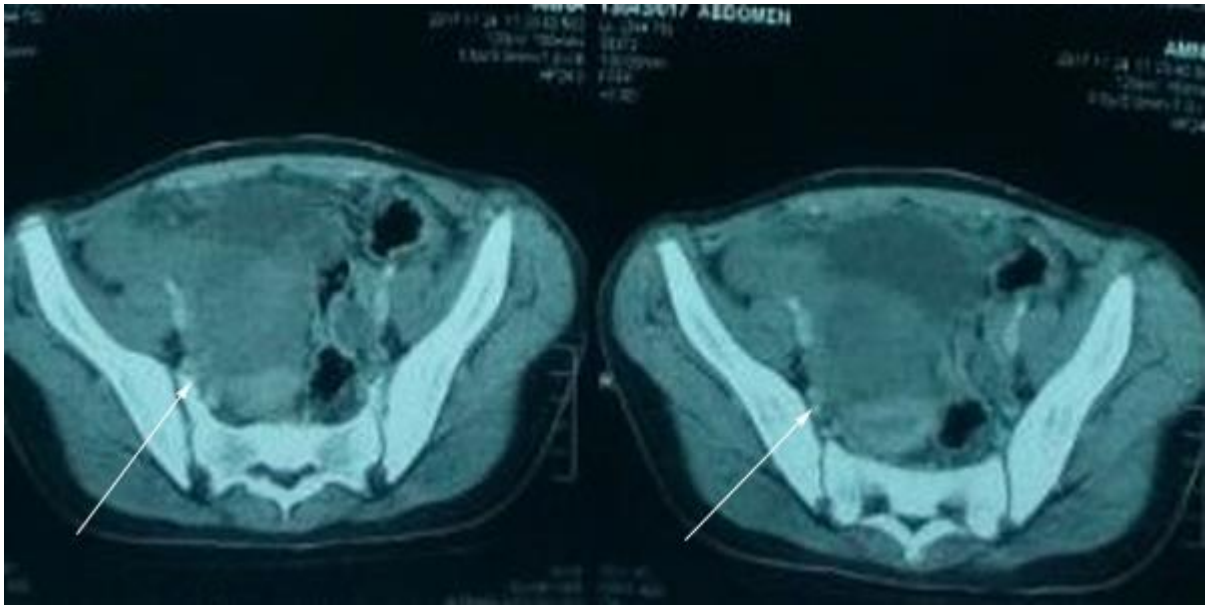

Figure 1B: Computed tomography scan of pelvis (Axial view) showing complex cystic lesion with hyperdensity

Initially on the basis of history, all the seniors in the department diagnosed this case as a platelet functional defect, but then factor V deficiency was diagnosed after seeing the laboratory investigations done on 29th November 2017.

In the hospital, symptomatic treatment was given, with intravenous Ceftriaxone 2g once daily, intravenous Risek 40mg once daily, intravenous Transamine 500mg thrice daily, and intravenous vitamin K once daily (for three days). Two pints of packed-cell volume and four pints of manual platelets were transfused at the time of admission. After 15 days of treatment, sufficient improvement was seen. Patient was discharged with proper counseling and was kept on regular follow-ups.

3. DISCUSSION

Factor V (FV) is a high molecular weight glycoprotein (330 kDa) coded by a gene mapped on 1q24.2 chromosomal region [4]. This coagulation protein is produced in HepG2 in liver and megakaryocytes. 80 % of factor V is found in the plasma as a single chain polypeptide (80%) and 20 % in platelet alpha granules [5]. It combines with Factor X to form a complex and activate the prothrombin into thrombin which further activates the fibrinogen into fibrin.

Congenital FV deficiency is also known as Owren's disease as Owren was the first to discover FV deficiency in a patient with bleeding diathesis [6]. The presentation of FV deficiency can vary widely from bleeding with minimal trauma and mucocutaneous bleeding to hemarthrosis and intracranial hemorrhage [3]. It is observed that these patients present early in life with mucocutaneous bleeding and later at menarche with an already established diagnosis. Our patient reported an increased episode of epistaxis and gum bleeding since early childhood however due to social circumstances, she remained neglected until the dramatic presentation of symptoms became evident. Mansouritorghabeh et al. reported that 68.7% of patients with Factor V Deficiency presents with epistaxis [7].

The functional factor V activity level is also important in predicting the symptomatic presentation. In 2012,

Viswabandya et al. grouped patients in two categories, the category of patients with FV activity <1% had minor bleeding whereas those with FV activity >1 % had hematoma and GI bleeding [8]. Hence, patients with minor bleeding episodes had underlying severe FV deficiency. Naderi et al and Peyvandi et al. observed poor association between factor V activity and bleeding severity. The Factor V activity level in our patient wass 2 % with clinical presentation of menorrhagia and spontaneous ovarian cystic hemorrhage [3]. Menometrorrhagia occurs in adolescents at a frequency of 2-5 % among which 20% cases are attributable to hemostasis disorders [9].

These females are predisposed to recurrent ovulation bleeding. The diagnosis can be established by ordering a coagulopathy workup which includes PT, APTT and Von Willebrand assay. (2) If the PT or APPT is prolonged, then factor assay is ordered. When FV deficiency is identified, it is important to find if the deficiency is congenital, acquired or associated with concomitant FV Leiden mutation. This information will further guide the management.

The role of strong management strategies in Factor V deficiency cases is pivotal. In this case, we administered intravenous Transamine followed by platelet and packed-cell transfusion at admission. However, after the confirmed diagnosis, FFP was administered. This helped in controlling the bleeding, correcting anemia and correcting the FV levels. It is recommended that single daily dosage of 15-20 ml/kg is required to control soft tissue and mucosal tract bleeding [10]. FV activity level should be monitored until a target level of 30% is achieved. Future strategies should be directed on education and giving prophylactic FFP before every menstrual period. Oral contraceptives, Depo-provera and Gonadotrophin releasing hormone agonist can also be given in females who are not actively desiring pregnancy [2]. These options will not only avoid menorrhagia but also minimize the chances of ovulation bleeding. Surgical intervention is advised when medical management fails. Gynecologic bleeding was well controlled in our patient and she is followed up at the out-patient clinic every three months.

4. CONCLUSION

It is observed that patients with factor V deficiency presents early in life with mucocutaneous bleeding. Similarly, our patient presented with gum bleeding and epistaxis since childhood. Early diagnosis and prompt management plays an important role in avoiding severe symptoms in the future like what we witnessed in this case. FFP remains the treatment of choice.

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