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Case Report

Factor-V Deficiency: A Case Report

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Abstract: Coagulation factors are required for the blood to clot along with the platelets in case of injury to the vessel endothelium. Factor V is one of the coagulation factors which is found both in the plasma and the platelet granules. It has both anticoagulant and pro coagulant activities.

Deficiency of factor V either congenital or acquired leads to a bleeding tendency in the patient. We here report a patient who was a diagnosed case of factor V deficiency and presented with intra-peritoneal bleed.

Introduction

Coagulation Factor V is present both in the plasma and the platelets in the blood. It has a role as a main regulator of the coagulation process because of its interaction with other coagulation factors and the conversion of prothrombin to thrombin. This is the procoagulant function of the factor V. In addition to this it also has an anticoagulant function whereby it inactivates the activated factor VIII by the activated protein C protein S complex.[2]

Factor V was discovered for the very first time by Owren in a 3 years old female patient who had a prolonged history of nasal bleed and loss of vision. She also had symptoms of easy bruisability, prolonged bleeding after an injury and menorrhagia. He named the disorder as parahemophilia. The factor V gene is located on the long arm of chromosome 1.

Factor V is synthesized primarily by the liver and diseases that affect the synthetic function of the liver tend to decrease its blood concentration. It is found in the blood circulating as a 330 kDa (kilo Dalton) single chain polypeptide in the inactive procoagulant form. 20% of the blood factor V is found in the alpha granules of the platelets. It is known that the megakaryocytes take in the plasma derived factor V which is then stored in the alpha granules of the platelets.

In addition to the mutations that affect the factor V gene or the genes involved in its processing and storage(**Congenital factor V deficiency**), deficiencies can also develop due to inhibitor production **Acquired factor V deficiency**) in the effected individual as well as due to processing and storage defects.

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(Mutations that cause the deficiency of the factor include mis-sense, nonsense and splicing mutations along with insertions and deletions in the factor V gene. Severity of the disease can be graded as mild, moderate and severe with factor V levels >5%, 1-5% and <1% respectively.

Inhibitors have been seen mostly in patients been given factor derived from cattle but have also been found in patients treated with certain antibiotics or those having underlying rheumatological diseases or malignancies. The factor V inhibitors tend to produce more severe bleeding. Some cases of factor V inhibitors are associated with thrombosis rather than bleeding. This happens when the inhibitors affect the anticoagulant function of the factor. If the patient has inhibitors only to the plasma derived factor V and not to the platelet derived factor V they might not even have the bleeding complications and the patients with inhibitors to factor V from both sources will have a greater tendency to bleed[1–11]

The prevalence of factor V deficiency is approximately 1 in 1000,000 persons with no predilection for a specific race. Only 150 cases of the disease have been reported since 1943.[4]It is an autosomal recessive disorder. The patients usually present with bleeding episodes in the skin and mucosal surface, joints, muscles, urinary tract, gastrointestinal tract and central nervous system. Females typically present with menorrhagia and postpartum bleeding.

Patients with factor V deficiency are expected to present at an early age. Some do present early whereas others are diagnosed only after screening due to a positive family history. The diagnosis is made after both Prothrombin time (PT) and Activated Partial Thromboplastin Time (APTT) are prolonged. Factor VIII levels are also required to differentiate a combined deficiency of the two factors from only Factor V deficiency. If the facilities are available along

with the DNA sequencing of both the parents, antenatal diagnosis is possible.

Fresh frozen plasma (FFPs) are the main treatment option because of the non-availability of the factor concentrates. Patients are treated episodically though there have been reports where the effected individuals were given regular prophylactic transfusions of FFPs. The frequency and dosing should be enough to maintain hemostasis. In addition to the risk of infection and allergic reaction, volume overload is a disadvantage of the transfusion of FFPs. It can be dealt with by plasma exchange or transfusion under cover of a diuretic. Patients who develop inhibitors to factor V are given factor VIII inhibitor bypassing agents(FEIBA) can be used or platelet transfusion can be of help.[1–3,7]

Case Presentation

A 17 years old female presented with pain in the abdomen for two weeks and difficulty in retaining solid food. Pain was generalized and increased after micturition. Her appetite was decreased and she vomited after intake of solid food. She could tolerate fluids only. At the time of her birth, umbilical cord was detached with excessive bleeding post–delivery. She was normal until menarche which was around 13 years of age. Cycle was 7/30 days with change of one pad per day and heavy discharge of clots. She had been transfused 4 fresh frozen plasma and one unit of red cell concentrate per month till now. She also complained of febrile non-hemolytic reaction after blood transfusion. History of allergy was not significant. She underwent laparotomy due to ruptured appendix 3 years back. Her elder sister had Thalassemia major and factor V deficiency, with regular blood transfusion for Thalassemia major; and additional transfusion of fresh frozen plasma and blood after any episode of trauma. She died at 22 years of age.

General Physical Examination: She was a young female, well – oriented in time, place and person, calm and co-operative. She had pallor, no jaundice, cyanosis, nail clubbing etc. Lymph nodes were not palpable. Her respiratory rate was normal.

Systemic Examination: On abdominal examination, she had generalized tenderness. Her abdomen was distended. On palpation, painless mass was palpable in hypogastrium. Her bowel sounds were normal. There were no signs of scars, engorged veins, caput medusa, visible peristalsis etc. Her neurological, musculoskeletal, respiratory and cardiovascular examinations were normal.

Laboratory Test	Report
Complete Blood Picture	**Total Leucocyte Count** 15.8 x 10^3/µL **Hemoglobin**6g/dL **Red Cell Count** 2.12 million/µL **Hematocrit** 19.2% **Mean Corpuscular Volume** 90.6fL **Mean Cell Hemoglobin** 28.3pg **Mean Corpuscular Hemoglobin Concentration**31.3g/dL **Platelet Count**293000/µL
LIVER FUNCTION TESTS **Serum Amylase** **Serum Bilirubin** **Alanine Amino Transferase** **Alkaline Phosphatase**	 55U/L 3.11mg/dL 13U/L 97U/L
Renal Function Tests	Normal
Serum Albumin	3.6g/dL
Serum Total Protein	1.6g/dL
Serum Electrolytes	Normal
HbsAg	Negative
Anti HCV	Negative
Activated Partial Thromboplastin Time	81.4 seconds
Prothrombin Time	More than 120 seconds
International Normalized Ratio	More than 9
Correction of APTT with Normal Plasma	42.3 seconds
Correction of PT with Normal Plasma	22.1 seconds
Hemoglobin Electrophoresis	Normal Pattern
CA-125	16.26 U/mL
Factor V levels	Less than 1%
Factor VIII levels	116%
Factor XI levels	75%
Fibrinogen level	547mg/dL

Discussion and Conclusion

Similar cases of factor V deficiency with internal peritoneal bleeds have been reported. One of these was a 13 years old female at a hospital in Karachi, Pakistan who had bilateral ovarian cysts with left ovarian capsule ruptured leading to hemoperitoneum with 1000mL blood in the peritoneum. She was operated upon and discharged on oral contraceptives to avoid future episodes of menorrhagia.[4]

A case of acquired deficiency of the factor has been reported in China following use of Ceftazidime in a 59 years old male. The patient developed inhibitors after the drug was started and withdrawal of the drug along with the use of steroids helped improve his condition.[6]

Another case report has been seen with a 59 years old patient with isolated factor V deficiency and no history of any bleeding episode even on tooth extraction and an episode of road side accident. He was diagnosed pre operatively when his baseline lab investigations were done for his non obstructed inguinal hernia.[10]

Factor V deficiency is not very common. Few cases have been reported worldwide. Early diagnosis and management, which is required for saving the life, is important for the patient. Had our patient stayed in the hospital she could have survived with intervention to look for the source of bleed, its control and prevention.

Facilities for the early diagnosis and management of bleeding disorders should be available at all the hospitals in our region considering the increased prevalence of consanguineous marriages, at least at the tertiary care ones where people are referred to from the periphery, to reduce the mortality associated with them. Hemoperitoneum is a serious condition that can result due to factor V deficiency and it needs to be dealt with immediately. The identification of the drugs causing development of antibodies to the factor V is necessary in case of acquired deficiency following their administration.

Nation-wide epidemiological studies are required to identify the families at risk and adopt methods of early diagnosis, prevention and prophylaxis for the disease as have already been done in Iran and Korea which show that there is not a significant relation between the clinical picture and the level of factor V in the plasma.[7,11]

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