Factor V Deficiency Associated with Congenital Cardiac Disorder and Intracranial Hemorrhage

Halit Özkaya · A. Baris Akcan · Gökhan Aydemir ·
Mediha Akcan · Mustafa Kul

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Abstract Factor V deficiency is an inherited disorder, in which the clotting factor V is low. The disorder is very rare, occurring in only one in one million people. It is inherited as an autosomal recessive disorder. The results of coagulation studies include a prolonged prothrombin time and partial thromboplastin time associated with reduced plasma factor V content. Patients with factor V deficiency have a hemophiliac like hemorrhagic disorder. Epistaxis, bruising, and menorrhagia are some of the common features. If treatment is needed, fresh frozen plasma is typically given. In this report we present a 12 year old girl who was admitted to our clinic with recurrent nosebleeds and intracranial hemorrhage after head trauma. After examination, factor V deficiency was diagnosed. She also had congenital cardiac disorder (VSD), probably a co-incident finding.

Keywords Factor V deficiency · Intracranial hemorrhage · Bleeding disorder

Introduction

Factor V (FV) was first identified by Owren in Norway during World War II. Patients with factor V deficiency have a hemophiliac like hemorrhagic disorder [1]. Epistaxis, bruising and menorrhagia are some of the common

features. FV is synthesized primarily by the liver and levels can decrease when liver synthetic function is impaired. The source of platelet FV has not been definitively established, but evidence indicates that platelets or megakaryocytes can synthesize FV [2]. The normal range of factor V concentration is 80–120%. Bleeding usually occurs when the factor V level is below 20% of normal [3].

It is activated by both factor Xa and thrombin to form factor Va. Activated factor V serves as an essential protein in the coagulation pathway and acts as a cofactor for the conversion of prothrombin to thrombin by factor Xa. Factor Va is inactivated by activated protein C. At the same time, factor V has been reported to act as a cofactor of APC in the proteolytic degradation of both factor VIII and factor VIIIa [4]. Factor V has a dual function in coagulation both procoagulant and anticoagulant. FV deficiency can be caused by mutations in the FV gene or in genes encoding components of a putative cargo receptor that transports FV and factor VIII from the endoplasmic reticulum to the Golgi. Congenital factor V deficiency is inherited in an autosomal recessive manner and the patients suffer a moderate to severe bleeding disorder. No clear ethnic predisposition is apparent. Most factor V-deficient patients have low factor V activity and antigen level. More than 200 factor V-deficient cases have been reported in the literature, but the molecular basis for factor V deficiency has been established in only a few cases [5, 6]. Hereditary factor V deficiency is a relatively uncommon disorder characterized by a variable course but with a uniformly favorable response to transfusion with fresh plasma or freshly frozen plasma.

Affected patients become symptomatic in early childhood with spontaneous or post-traumatic bleeding complications [7]. As there is no specific concentrate available, the mainstay of treatment for severe factor V deficiency is

H. Özkaya · A. B. Akcan (✉) · G. Aydemir · M. Kul
Department of Pediatrics, GATA Haydarpaşa Teaching
Hospital, Uskudar, 34668 Istanbul, Turkey
e-mail: barisakc@hotmail.com

M. Akcan
Department of Pediatrics, Division of Pediatric Hematology
and Oncology, Akdeniz University, Antalya, Turkey

FFP. Platelets also contain factor V, though their use should be reserved for life threatening bleeding and prior to surgery. There is a considerable variation in the volume of fresh frozen plasma (FFP) and frequency of its administration needed to achieve hemostasis for a particular bleeding episode in the individual patient [8].

Case Report

Twelve year old girl admitted to our pediatric outpatient clinics with recurrent nosebleeds for 3 years and a history of head trauma 2 days before. She was followed in clinic and demonstrated some easy bruisability, manifested by frequent formation of hematomas with surrounding ecchymoses and by recurrent nosebleeds. She was unconscious. The Glasgow Coma Score was 5. CT Scan was done and showed a large subdural hematoma (Fig. 1). The hematoma was drained. In her laboratory investigation; prothrombin time (PT) and activated partial thromboplastin time (APTT) prolonged. In her blood examination, Hb was 6 gr/dl, MCV: 70 fl, bleeding time 5 min, clotting time 15 min, prothrombin time 32 s (control 15 s), INR: 2.3, APTT 130 s (control 40 s), platelet count 150,000/mm³. All other blood tests and chemistry were normal. Factor V level 1%. Factor VIII level 65%. In order to exclude evidence of inhibitor we did mixing test. After mixing test corrected PT was 14.5 s and APTT was 46 s. Her coagulogram repeatedly confirmed the diagnosis of factor V deficiency. The factor V level was measured with Elisa KIT (E90675Hu). There was a history of first degree consanguinity. The father and mother have both been investigated and all tests including PT and APTT were normal.

Fig. 1 CAT scan of the patient showing subdural hematoma

There was no bleeding history in her family. FFP with an initial dose of 20 ml/kg was used for 2 days after than FFP with a dose of 3–4 ml/kg was continued for 1 week. The factor V level increased to 25% on the second day. The conscious of the patient returned back on the second day. During following period after 4 days; the patient was unconscious. We thought that the factor V inhibitor was developed, but we did not represent the inhibitor, then we did platelet transfusion and also because intracranial hemorrhage is a life threatening bleeding, we gave to patient active factor VII concentrate. The patient survived with a little sequela in 2 weeks time. In echocardiographic examination ventricular septal defect observed.

Discussion

Factor V deficiency, also called parahemophilia or Owren's disease, is a very rare coagulation disorder. It was first identified in 1943 in Norway by Owren. In the case of factor V deficiency, the PT and PTT will be prolonged. Clinically significant hemorrhage may occur in patients with factor V deficiency, and this is usually amenable to treatment with plasma [9]. Many reported cases of severe factor V deficiency did not have such severe bleeds and only needed treatment at times of surgical challenge [10].

FV is synthesized primarily by the liver, and levels can decrease when liver synthetic function is impaired. Deficiencies of FV can also arise because of acquired inhibitors to FV and defects that affect the storage and processing of FV. FV-specific inhibitors most often develop after exposure to preparations of bovine thrombin but have also been reported in patients who have underlying rheumatologic conditions, malignancies or who were being treated with antibiotics [2]. If a low FV activity is discovered, then FV deficiency must be distinguished from consumptive coagulopathy, liver disease, combined FV and FVIII deficiencies, and an acquired FV inhibitor. Importantly, the clinical history is also useful for distinguishing between congenital FV deficiency and an acquired inhibitor to FV.

The age at presentation indirectly varies with the severity of disease. Bleeding is a major risk in patients with factor V deficiency undergoing surgery. Heterozygous deficiency states are generally unrecognized because of a lack of significant clotting time prolongation or bleeding risk. The presence of a mild prolongation of PT and aPTT may be the first clue for factor V deficiency. Bleeding time can be prolonged in severe cases. APTT and PT prolonged, thrombin time is normal and Russell viper venom time (RVVT) is prolonged.

The severity of bleeding symptoms was only partially related to the degree of factor V deficiency in plasma. In most patients bleeding symptoms first developed during the

first 6 years of life [11, 12]. A case of severe factor V deficiency associated with multiple episodes of intracranial bleeding which presented at birth was reported. The case's plasma levels of factor V was 10%. The majority of cases reported have low plasma FV antigen and activity levels (1–10%). It can be difficult to predict a clinical bleeding phenotype from FV activity levels alone [8].

Fresh plasma or FFP infusions are used to correct the deficiency temporarily and should be given daily during a bleeding episode. The loading dose of FFP is 15–20 mL/kg and then 3–6 mL/kg daily. The half-life ranges from 24 to 36 h, with the aim being a factor V level of 25%. Subsequent dosages depend upon monitoring the factor V level by obtaining the peak and trough levels, with the aim having a factor V level of 25% before surgery. Postoperatively, FFP should be administered daily for 3–10 days, with careful observation of bleeding. Fluid overload and viral transmission may be a complication of plasma therapy. A potential complication of the therapy of any coagulation deficiency disorder is immunization to the transfused component and development of an acquired anticoagulant. Some patients with inhibitors may also require immunosuppression. The treatment of factor V inhibitors involves plasma and platelet transfusions to cover bleeding episodes and immunosuppressive measures to remove the antibodies. The administration of immunoglobulin has also proved helpful in the elimination of the antibody.

It is also important to check the blood level of factor VIII. Be careful not to confuse factor V deficiency with factor V Leiden nor with the combined deficiency of factor V and factor VIII. This is because another inherited bleeding disorder combines factor V and factor VIII deficiencies. The two disorders must be distinguished before appropriate treatment can be administered. By comparison with some other coagulation factor deficiencies, the bleeding that accompanies factor V deficiency is generally harmless. Factor levels are generally between 5 and 30%. A factor V blood level between 10 and 20% of normal is enough to prevent bleeding, even after surgery. The most common symptoms of factor V deficiency are: nosebleeds; internal hemorrhaging at the slightest trauma; abundant or prolonged menstruations; bleeding after a trauma wound; bleeding after surgery; occasional post-partum hemorrhaging; hemarthrosis, rarely; a few cases of gastrointestinal bleeding and central nervous system bleeding. The severity of the

symptoms may vary within a single family. There appears to be no correlation between the severity of symptoms and the level of factor V [1, 2, 13].

We also wanted to take note after neonatal period, a patient with factor V deficiency can be seen. In this report we present an adolescent case with factor V deficiency and co-incidental congenital cardiac disorder.

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