A Rare Case of an Acquired Isolated Factor VII Deficiency Discovered in a 23-Year-Old Female Patient

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Abstract

Background: Factor VII (FVII) deficiency, a rare bleeding disorder, can manifest as an autosomal recessive congenital or an acquired coagulopathy. Acquired FVII deficiency, although infrequently reported, presents unique challenges in understanding its mechanisms and identifying underlying causes.

Case presentation: We present a case of acquired FVII deficiency discovered in a 23-year-old female patient with no apparent underlying disease. The patient exhibited spontaneous ecchymosis and gingival hemorrhage, along with low FVII activity and isolated prolongation of prothrombin time. Extensive laboratory investigations excluded liver dysfunction, familial deficiency, vitamin K deficiency, and inhibitory antibodies. Prompt treatment with Fresh Frozen Plasma (FFP) and bypassing agents resulted in a favorable response and resolution of hematomas.

Conclusion: Acquired FVII deficiency has been associated with various conditions such as sepsis, aplastic anemia, stem cell transplantation, and neoplasms, although approximately 14% of cases remain idiopathic. Clinical outcomes remain generally poor, with limited complete remissions reported.

Introduction

Coagulation factors belong to a family of plasma glycosylated proteins that should be activated for appropriate blood coagulation. Factor VII (FVII) or proconvertin, when bound to tissue factor, initiates the clotting cascade [1. Factor VII deficiency is a rare disease that could be autosomal recessive congenital coagulopathy or acquired. The mechanisms of acquired FVII deficiency are still unclear, but multiple hypotheses were established. FVII deficiency is associated with clinical bleeding and isolated prolongation of the Prothrombin Time (PT). It may present with hemorrhages of Central Nervous (CNS) and Gastrointestinal (GIS) systems during infantile period or may be asymptomatic until adulthood [2. The severity of bleeding can be unpredictable and is not always linked with the measured levels of FVII [2. A variety of diseases are responsible for developing acquired FVII deficiency like sepsis, aplastic anemia, Stem Cell Transplantation (SCT), and in association with some neoplasms [2. In this report, we present a case of acquired FVII deficiency discovered in a 23-year-old female patient and developed with no underlying disease. We also explain the characteristics, the mechanisms, and the possible treatments for this disease.

Case Presentation

A 23-year-old female patient consulted the Emergency Department (ED) for recent onset ecchymosis and gingival hemorrhage appearing spontaneously with no context of trauma. She had no known personal medical history and did not report any previous personal or familial history of bleeding.

The physical examination of the patient showed a 9 x 7 cm ecchymosis on the right forearm, a right knee hemarthrosis and a 10 x 3 cm hematoma on the right foot (Figure 1). The rest of the examination showed no further abnormalities.

The Complete Blood Count (CBC) showed normal white blood cells count at 9 500/mm², microcytic hypochromic anemia with a level of hemoglobin at 7.4 g/dl and platelet count at 642 000/mm². The determination of Prothrombin Time (PT) showed a level of 8,4% (normal>70%) and the Activated Partial Thromboplastin Time (APTT) of 35 sec (normal 25.2-35.9 sec). Coagulation screening performed by coagulation analyzer on ACL TOP revealed a PT of 13%. A 1:1 mixing study showed correction of PT to 92% immediately and after incubation for 2 hours at 37 Celsius degrees therefore the presence of an inhibitor which may have developed against coagulation factors was ruled out. Also, vitamin K deficiency due to insufficient intake or malabsorption was eliminated since APTT level was normal, so a FIX, FII, and FX deficiency was unlikely. Factor VII activity level was low at < 5% (normal 50-150) and the screening of an inhibitory antibody to FVII was negative.

Liver function tests and serum albumin level were normal so coagulation factor deficiency secondary to liver dysfunction was eliminated.

Giving our patient’s history, the clinical and biological findings, the diagnosis of acquired FVII deficiency was confirmed, and no underlying diagnosis was identified.

Our patient received a total of 4 Fresh Frozen Plasmas (FFP) units and was put under tranexamic acid, ethamsylate and iron therapy with a prompt response to the treatment and gradual resolution of the widespread hematomas.

The patient’s parents and siblings were screened for FVII deficiency, but all the coagulation tests were normal.

Seventeen days later, she presented hemarthrosis of the right elbow. Biology showed the same initial coagulation tests abnormalities. The patient was treated with bypassing agent on account of the function-threatening bleeding.

Discussion

Factor VII is a glycoprotein that engages in the coagulation process. It binds to the exposed tissue factor after endothelium damage to be activated and therefore it activates factor X which is necessary for blood clotting.

The protein FVII plays a crucial role in starting the extrinsic coagulation pathway. It works by binding to Tissue Factor (TF) at the site of a blood vessel injury. This binding then leads to the activation of Factor X, which triggers the production of thrombin.

Acquired factor VII deficiency is a rare disorder, with only few cases published in literature. It is reported to affect more males than females [3]. It could be isolated or associated with other coagulation factors deficiency.

This pathology occurrence is reported to be associated with a context of infections, neoplasms and tumors and immune deficiency [3].

Acquired and isolated FVII deficiency is an extremely rare bleeding disorder, with only few cases published in literature, after eliminating the presence of a chronic liver disease, familial factor VII deficiency and vitamin K deficiency. Little is known about this disorder and its mechanisms are still unclear. The exact incidence of this disease is unknown, and it might be underestimated due to its rarity and being uncommonly diagnosed.

Acquired factor VII deficiency can appear in a variety of clinical symptoms ranging from cutaneous ecchymosis to gastrointestinal bleeding or central nervous system hemorrhages. It can also be asymptomatic. Besides, the severity of the bleeding is not correlated to the depth of the FVII activity deficiency. The clinical presentation of the acquired FVII deficiency is variable in bleeding severity and locations ranging from cutaneous ecchymosis to central nervous system hemorrhages [3]. Moreover Unlike most deficiencies in blood coagulation factors, FVII deficiency exhibits a distinct pattern where there is a weak correlation between FVII clotting activity and the likelihood of experiencing bleeding.

The CBC may show an anemia translating the severity of the bleeding and the absence of thrombocytopenia which excludes the probability of a Disseminated Intravascular Coagulation (DIC). The rest of the blood screening shows an isolated low PT and a normal APTT should eliminate a vitamin K deficiency. Other tests are necessary to eliminate an underlying liver disorder like albumin levels. The diagnosis is confirmed with a low level of FVII activity.

In literature, seventy nine cases have been documented so far [2-10]. The most common causes of acquired FVII deficiency described in literature were severe systemic sepsis, chronic packed cell transfusion, neoplasia (Solid tumors, acute myeloid leukemia, multiple myeloma) and stem cell transplantation. It is shown that no underlying disease was correlated to FVII deficiency which may lead to the conclusion that FVII deficiency can be idiopathic in some cases [2,3].
A number of hypotheses regarding the exact mechanisms for developing this disease were established, like the excessive consumption of FVII. This is caused by an increase of tissue factor exposure after an alteration of vascular endothelium as found in severe sepsis or intensive chemotherapy. Also, the accelerated catabolism of factor VII was described, resulting from proteases synthesized by leucocytes. Another described mechanism is the presence of a neutralizing antibody directed against FVII that decreases its activity. The presence of the inhibitor can be correlated to the underlying disease thus reappearing with the disease relapse [10-12].

In our case, the patient had isolated acquired FVII deficiency and none of the investigations underlined its cause. The mechanism of acquired FVII deficiency in our patient is unclear suggesting that either the cause preceded the clinical symptoms or that other factors are responsible for the disease development that are yet to be uncovered.

There are no standardized guidelines for the management and treatment of acquired FVII deficiency. The choice of initial treatment must be based on the bleeding severity. FFP is easily available and useful. However, due to the poor half-life of FVII, frequent infusions of FFP are required. Recombinant FVII is necessary to stop the bleeding, especially in a life-threatening bleeding, as well as securing hemostasis prior to invasive procedure which was the case in our patient and in literature. Whereas, no guidelines inform us of the adequate posology nor of the goals to be achieved in term of biological results [2]. The addition of antifibrinolytic drugs may be helpful to stop the bleeding [13]. Furthermore, finding and treating the underlying disease is necessary to stop the mechanism causing FVII deficiency and to prevent it from recurring again. The use of immunosuppressive agents is recommended in case of the presence of an inhibitor. Treatment with vitamin K is usually not effective [2].

The overall clinical outcome of acquired FVII deficiency described in literature is generally poor with complete remission seen in only 26 out of 79 patients (33%) [2,6,8,11,14,15]. Bleeding complications were the direct cause of death in four patients (intracranial, gastrointestinal and pulmonary hemorrhage) (5%) [2].

Conclusion
In conclusion we presented a rare case of isolated acquired FVII deficiency discovered in a 23-year-old female patient without inhibitor and where no underlying disease was found. Little is known about this disease. Plasma level does not correlate well with the hemorrhagic diathesis. Treatment includes replacement therapy and/or bypassing factors, antifibrinolytics as well as the treatment of underlying disease if exists. Clinical outcome is poor.

Abbreviations

Ethical Approval: Our institution does not demand ethical approbation for reporting individual cases or case series.

Informed Consent Obtained: Informed consent has been obtained from the patient.

Availability of supporting data: The dataset of the current study is available from the corresponding author upon motivated request.

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