Serendipitous Discovery of Factor VII Deficiency and the Ensuing Dilemma

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ABSTRACT

Congenital factor VII deficiency is a challenging disorder to manage, as it is associated with varied genotypes that do not clinically correlate with a bleeding phenotype. Individuals with severe factor VII deficiency (FVII: c <1%) might be asymptomatic, while patients with moderate deficiency (FVII: c level >5%) may experience severe hemorrhages. In modern medicine, due to extensive routine pre-operative laboratory testing, clinically asymptomatic patients without any bleeding history might be incidentally discovered, raising clinical dilemmas. Careful consideration of bleeding versus thrombosis risk has to be made in such cases, especially in the elderly. Clinical history of no prior bleeding complications may be a reassuring factor. Minimal required replacement dosing of recombinant activated factor VII can be given peri-operatively in such situations, with close monitoring.

Keywords: Factor VII deficiency, Factor VII replacement, bleeding.

INTRODUCTION

Congenital factor VII deficiency, a rare autosomal hemorrhagic disorder, can have varied clinical presentations, which do not always correlate with the level of factor VII coagulant activity in plasma (1). Asymptomatic patients without any bleeding history might be incidentally discovered, raising clinical dilemmas espe-

cially during circumstances such as major surgery (1). Here we describe an elderly woman with incidental diagnosis of congenital factor VII deficiency before an orthopedic surgery.

CASE REPORT

A 93-year-old woman was admitted after a fall resulting in a left femoral neck fracture. Her past medical history included metabolic syndrome,

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atrial fibrillation, appendectomy, cholecystectomy and pacemaker implantation without bleeding complications. There was no personal or family history of bleeding disorders. She was evaluated by orthopedics for surgical fixation with arthroplasty. Pre-operative workup showed unremarkable complete blood count with normal chemistry and liver function panels. Interestingly, coagulation studies showed isolated prolongation of prothrombin time (PT) to 32 seconds (s) (reference range: 10.4 - 13.4 s) with International Normalized Ratio (INR) of 2.8. Activated partial thromboplastin time was normal at 28 s. Disseminated intravascular coagulation (DIC) evaluation was unremarkable, with fibrinogen level of 172 mg/dL. The primary care physician who took care of the patient for over two decades reported no bleeding issues. Due to suspected vitamin K deficiency, she received 10 mg of intravenous vitamin K for three days, which did not correct the PT; rather it became further prolonged to 48.8 s, with an INR of 3.9. A 1:1 plasma mixing study showed correction of the PT without any inhibitor activity. Lupus anticoagulant was negative. Factor VII coagulant activity (FVII: c) measured (recombinant human tissue factor – HemosIL® ReadiPlasTin® on ACLTOP500® analyzer) was low at 10%. Factor VII antigen level was low at < 28 (Reference range: 60-175). Other factors were not decreased with activities of Factor V at 83%, Factor VIII at 286%, and Factor X at 71%.

The patient had no known liver disorders and was not on anticoagulation therapy. Mixing study showed correction of PT without inhibitor effect to suspect acquired factor VII inhibitors. Vitamin K deficiency was felt to be unlikely due to normal levels of other vitamin K dependent factors and failure of response to empiric vitamin K therapy. Disseminated intravascular coagulation (DIC) was also ruled out. Hence, she was diagnosed with an occult congenital factor VII deficiency with an asymptomatic phenotype that might have resulted in undiagnosed biochemical defect through her lifetime. Given potential for significant bleeding with hip arthroplasty, orthopedics requested correction of her coagulopathy. Considering patient's advanced age and atrial fibrillation, large volume thawed plasma infusions were avoided. She instead received perioperative recombinant activated factor VII infusion at a dose of 10 mcg/kg prior to incision and on post-operative days 1

and 3. Surgery and post-operative course were uneventful, without bleeding or thrombosis in the available 60 days follow up period. □

DISCUSSION

Congenital factor VII deficiency is a challenging disorder to manage, associated with varied genotypes that do not correlate clinically with a bleeding phenotype (1). Individuals with severe factor VII deficiency (FVII: c < 1%) might be asymptomatic, while patients with moderate deficiency (FVII: c level >5%) might experience severe hemorrhages (2, 3). However, the risk of bleeding should not be underestimated during hemostatic challenges like major surgery, even in asymptomatic individuals (4). Minimal safe levels of FVII: c that guarantee hemostasis in different clinical scenarios have not been well defined (5). Furthermore, there are no standard guidelines for the management of congenital factor VII deficiency. Nonetheless, knowledge obtained from registries of STER (Seven Treatment Evaluation Registry) and IRF7 (International Registry of Factor VII deficiency) has helped enormously in providing clinical guidance (6, 7). The lack of predictable bleeding risk either from the genotype, measured factor activity levels or laboratory clotting assays pose a clinical dilemma in determining the necessity for administration of replacement therapy in an otherwise asymptomatic individual awaiting surgical intervention. The kaolin-based thromboelastography that is often used peri-operatively by surgeons and anesthesiologists would not likely detect this deficiency, as the extrinsic pathway is not interrogated by this method. Perhaps the lack of a clinical bleeding history might be the only reassuring indicator in these cases (8). Nevertheless, significantly prolonged coagulation assays especially prior to surgical procedures create anxiety among care providers. Expert opinion in these situations is to administer a minimal required dosing of replacement therapy to minimize the bleeding risk (6).

Our patient remained undiagnosed, asymptomatic and without any prior bleeding complications throughout her life, despite multiple prior surgeries, but given the significantly prolonged PT and INR prior to a planned major orthopedic procedure, we administered dose-reduced recombinant activated factor VII to correct her 'coagulopathy'. We did not encounter any throm-

botic complications, but one needs to be mindful of this even in patients with symptomatic factor VII deficiency (9). □

CONCLUSION

Our case is rare in the fact that a 93-year-old woman finally received a diagnosis for congenital factor VII deficiency, which went unno-

ticed for nearly a century. It also highlights the variable phenotypes that exist with this disorder, and the ensuing clinical dilemma it can generate during their perioperative management. □

Conflicts of Interest: none declared.

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