Isolated acquired factor VII deficiency in a patient with cholecystolithiasis

Oyaert M(1), De Cooman L(2), Dujardin K(3), Devreese K(2), Van Haute I(1)

(1) Clinical Laboratory, AZ Delta Roeselare Menen, Roeselare, Belgium
(2) Coagulation Laboratory, Ghent University Hospital, Ghent, Belgium
(3) Department of Cardiology, AZ Delta Roeselare Menen, Roeselare, Belgium

Case-report: A 68-year-old man was admitted to AZ Delta Roeselare due to acute epigastric pain and vomiting. Relevant medical history included first-degree atrioventricular block for which a single chamber pacemaker was implanted in 2009 and aspirin 80 mg/d was initiated. Due to chronic persistent fibrillation, aspirin was changed for dabigatran (Pradaxa®) 2x150 mg/d in November 2012. There was no personal or family history of a bleeding diathesis. Computer tomography confirmed the diagnosis of acute calculous cholecystitis. Investigations at admission revealed a normal platelet count (195 x 10^3/µL) and leukocytosis (21.17 x 10^3/µL) with neutrophilia (18.68 x 10^3/µL). Biochemically, an elevated CRP (282 mg/L) was determined with normal renal and liver function tests. Coagulation test results revealed a prolonged prothrombin time (35%, reference interval 70-116%) and INR (2.21, reference interval 0.85-1.50) and a normal activated partial thromboplastin time (aPTT) (34.9 s, reference interval 28.0-39.0 s). The fibrinogen concentration was slightly elevated 516 mg/dL (reference interval 180-400 mg/dL) reflecting the patient’s inflammatory state. Urinalysis revealed no hematuria. Blood culture bottles taken at admission remained negative. Mixing tests with normal pool plasma showed correction of PT values (76.3%). To exclude vitamin K deficiency, factor IX was determined and found to be within normal range. Factors II, V, VII and X were measured in a one stage PT clotting assay with the standard predilution (1:10) of the plasma. Factor II and V were within the normal range, factor VII was 16%. The Bethesda assay could not demonstrate the presence of a neutralizing inhibitor.

Discussion: Laboratory tests (mixing tests and factor dosage) indicated an isolated acquired factor VII deficiency (FVIID). Acquired FVIID in the absence of vitamin K deficiency, liver dysfunction or DIC is rare. The majority of cases are associated with malignancy, sepsis, and/or bone marrow transplantation. Despite the elevated CRP and neutrophilia at admission, sepsis triggered by cholelithiasis could not be proved (negative blood cultures). There were no arguments for underlying malignancy. Before surgical evacuation of the gallstones, seven units of fresh frozen plasma were administered. No symptoms of bleeding were noticed during cholecystectomy. Factor VII concentrations continued fluctuating around 15-16% and correlated with the still increased CRP (range: 208-235 mg/L) during hospitalization. The mechanism of factor VII deficiency in these cases is frequently unclear, but two main explanations have been advanced, primarily based on mixing study results. One is that a transient inhibitor is formed that results in either inhibition of factor VII function or in accelerated factor VII clearance. In those cases where mixing studies were performed, several show an inhibitor pattern but others show a deficiency pattern, as in our case. Ten days after admission, INR normalization along with normal factor VII dosage (71%) and a decrease in CRP was noticed. Dabigatran 2 x 150 mg/d was restarted. This case describes the transient nature of a FVIID in a patient with cholecystolithiasis.