Factor XII Deficiency Discovered During Cardiac Catheterization

Jason L Rapaport DO, Edward Kaminski MD
Department of Anesthesia, Children’s Hospital of Michigan, Detroit, MI

Introduction
- Factor XII deficiency is an uncommon cause of prolonged PTT.
- Despite the profound abnormality in coagulation studies, these patients do not have significant bleeding complications.

Case Report
- A six-month old 6.8 kg female presented to the cardiac catheterization lab for closure of her PDA.
- After heparinization, her ACT was found to be greater than 1500 seconds. On recheck, the value was found to be greater than 1100 seconds.
- The patient had no active bleeding. After protamine reversal, her ACT was still found to be in excess of 600 seconds.
- After completion of the procedure there was a loss of pulses to the right (operative) leg. A subsequent vascular study revealed markedly diminished arterial flow to the right lower extremity.
- A coagulation workup was ordered including PT/INR, aPTT, aPTT with fibrinogen, factor activity levels for VIII, IX, and XII. The PT/INR was found to be normal, and factor activity levels for VIII, IX, and XII were slightly below normal, and factor XII level was found to be extremely low. The patient was subsequently diagnosed with factor XII deficiency.
- Postoperatively, the patient was administered heparin at a rate of 20 units/kg/hour for the diminished flow to the right leg.
- Adequacy of anticoagulation was followed using an unfractionated heparin assay rather than PTT.
- The following day, perfusion to the leg improved on clinical exam and Doppler.
- Heparin was discontinued and the patient was discharged home.

Discussion
- Factor XII, also known as Hageman factor, is an inactivated precursor to the active serine protease factor XIIa.
- The activity of factor XII is the basis for the aPTT test, as factor XII and the subsequent clotting cascade are activated by contact with silica, celite, or kaolin.
- Factor XII is called Hageman factor after the railroad worker John Hageman. He had been previously studied by Dr. Oscar Ratnoff after preop evaluation revealed prolonged clotting time.
- Paradoxically, he died from a pulmonary embolism after 3 weeks heparinization to his left ischium and ilium and subsequent immobilization.
- Several patients with factor XII deficiency have been found to have a stable platelet count, platelet aggregation, and bleeding time.
- The clinical relevance of factor XII deficiency is poorly understood, and evidence is contradictory.
- Renné et al. found that among individuals on oral anticoagulation, the prevalence of factor XII deficiency was higher than with healthy volunteers.

Conclusion
- Deficiency of factor XII is uncommon, but asymptomatic and typically found incidentally during laboratory studies such as PTT and ACT.
- Although some studies suggest patients with factor XII deficiency may be hypercoagulable, evidence for this is lacking.
- From a clinical standpoint, factor XII deficiency can be regarded as strictly a laboratory abnormality which should not affect routine intraoperative management.
- In cases where anticoagulation must be monitored, alternatives such as heparin concentration or normalization of values using FFP should be considered.

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