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General Medicine

A SILENT BITE : FACTOR XII DEFICIENCY UNMASKED IN THE WAKE OF A SNAKE ENCOUNTER

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ABSTRACT Factor 12 or the Hageman factor plays an essential role in the initiation of the intrinsic or the contact pathway of coagulation. The activation of the pathway occurs either due to direct contact with a negatively charged surface like glass or kaolin or proteolytic activation through prekallikrein and kallikrein system. Activated partial thromboplastin time or aPTT clotting assay is the test which is used to evaluate the status of the intrinsic pathway. Factor 12 deficiency is a rare genetic disorder which usually follows an autosomal recessive pattern of inheritance however an autosomal dominant inheritance has also been reported. There is no established data regarding the prevalence of Factor 12 deficiency in the normal population. Based on a study conducted on 300 healthy blood donors, an estimated prevalence of 2.3% has been reported according to Halbmayer WM, et al. The incidence of the condition is about 1 in 1,000,000 individuals. In patients with a deficiency of Factor 12, the aPTT is typically prolonged and there are no associated bleeding tendencies. More often there is an increased risk of arterial or venous thromboembolic events and the patient is usually asymptomatic according to Chaudhry LA, et al.

KEYWORDS :

INTRODUCTION

Factor 12 deficiency is a congenital condition often inherited as an autosomal recessive pattern. Patients are usually asymptomatic and abnormalities in activated partial thromboplastin time or undetected coagulopathies are frequently discovered by chance during coagulation screening. This may cause a delay in diagnosis. Surprisingly, it is hardly ever if ever linked to bleeding disorders, even the mildest ones like epistaxis or skin abrasions. Contrarily, although this is puzzling, factor XII deficiency is more frequently linked to life-threatening thromboembolic consequences if not treated. This article will discuss a case of an indolent Factor 12 deficiency that came to light as a result of an incidental snake bite.

Case Presentation

Herein we have a case of a 56 year old female who presented to the emergency with an alleged history of an unidentified snake bite associated with bleeding from bite site which then spontaneously resolved. There was no history of pain or necrosis at the bite site. No loss of consciousness or breathing difficulty was reported. She is a known case of hypertension for 10 years and coronary artery disease for 5 years. With regard to her menstrual history, she is post-menopausal with no history of menorrhagia or post-menopausal bleeds. At the time of presentation her bleeding time was 3 minutes and clotting time was 7 minutes and 30 seconds. Coagulation profile showed PT of 13.5, INR of 1.1 and a prolonged aPTT showing no coagulation. The snake venom was classified as hematotoxic based on the initial investigations and considering a possible hemotoxicity the patient was administered 10 units of Anti snake venom in 5% Dextrose and shifted to intensive care for monitoring. Thromboelastogram was deranged with high R time and low MA value, and she was administered 3 additional units of ASV. Coagulation parameters were repeated which showed improving bleeding and clotting time, but PTT continued to show no coagulation. Since she had persistent coagulopathy despite administration of ASV, an underlying factor deficiency was suspected. She had no past history suggestive of any overt bleeding manifestations like hemarthrosis, gum bleeding, epistaxis, easy bruising, hematuria or postpartum hemorrhage following her deliveries. Thrombin time, fibrinogen and D-dimer were evaluated and was normal. aPTT mixing study was done which showed correction of coagulation thus confirmed an underlying factor deficiency. The most probable factor deficiency suspected in this clinical scenario was a factor 12 deficiency and an assay was sent which showed severe deficiency with a value of 8.1%.

DISCUSSION

Patients with a Factor 12 deficiency usually do not have any well-defined clinical features which would raise the suspicion of the diagnosis. aPTT is a coagulation parameter which measures the amount of time blood takes to clot. Prolongation of this value is one of the indicators which would raise a suspicion of an underlying factor deficiency. It may also be seen in the presence of inhibitors of the intrinsic and final coagulation pathway. Some other common causes of prolonged aPTT include antiphospholipid antibodies, Vitamin K deficiency, liver disease, elevated hematocrit and laboratory errors like incomplete collection tube filling, line contamination by anticoagulants, prolonged time interval between blood sample collection, and assay performance[4]. In this case the subject did not have any signs of an autoimmune disease process or vitamin K deficiency. She did not have any typical bleeding manifestations in the past which also helped rule out the diagnosis of hemophilia.

An isolated prolongation of aPTT is often the only finding suggestive of a factor 12 deficiency as it is typically not associated with any bleeding tendencies. As in this case, the subject presented with an incidental snake bite which eventually revealed the underlying factor 12 deficiency.

An increased risk of thrombosis is found to be associated with factor 12 deficiency. In a 1983 study of 121 patients with Hageman phenotype ,10 of the individuals reported having experienced thrombosis, five had a myocardial infarction, and one had Moyamoya syndrome. None of these patients had ever experienced a tendency to bleed prior to these thrombotic events [4].

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