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Case Report

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A rare case of excessive bleeding after tonsillectomy; a diagnostic challenge

Abstract

Hemophilia C is a rare inherited clotting disorder caused by deficiency of factor XI with an incidence of 1 per million. It is an autosomal recessive disorder hence, male and female both are equally affected. This paper reports a 34 year old mother and her 14 year old son, residents of Sialkot Pakistan with a history of an unknown type of bleeding disorder.

Keywords: tonsillectomy, bleeding, hemophilia, platelet function

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Introduction

Factor XI deficiency is also known as Hemophilia C or Rosthental syndrome[1]. It was first identified in 1953 in patients who developed excessive bleeding after tooth extraction and surgical procedures[2]. In communities where consanguinity is common the prevalence of factor XI deficiency is higher, as Ashkenazi Jews descendants are more frequently affected (heterozygote frequency approximately 8%)[3] .Calculated prevalence of FXI deficiency in south Asia is $20.3x10^6$,however not a single case has been reported in national registry of Pakistan. It was observed that plasma obtained from these patients clotted slowly with prolonged aPTT mimicking hemophilia A and B. Nevertheless when mixing studies were performed, clotting defects in patient plasma were corrected upon adding hemophiliac plasma, signifying absence of a different clotting factor. Hence the missing factor was named plasma thromboplastin antecedent by Robert Rosthental[4]. Unlike hemophilia A and hemophilia B, deficiency of factor XI has a poor correlation between factor levels and symptoms. Patients with FXI levels as low as <20-25 IU /dL may be asymptomatic, whereas some may develop profuse bleeding after trauma[5]. Bleeding is more significant at the sites with high fibrinolytic activity such as oral cavity, urinary tract etc.

Case report

A 34-year-old woman reported to the AFIP, for evaluation of post tonsillectomy bleed. One year back she had tonsillectomy and developed hemorrhage for which she was given 1 unit of RCC, 4 units of fresh frozen plasma (FFP),1 mega unit of platelets and tranexameic acid. Her past history was significant for one spontaneous miscarriage, associated with severe bleeding. At that time she was transfused 6 units of FFPs and one unit of RCC. Rest of her past history was not significant. She has 3 sons born with normal vaginal delivery and no problem occurred during their delivery. There was no history of menorrhagia. Family history was not contributory. As she presented to our facility, initial laboratory results were notable for prothrombin time (PT) at 14 sec (reference range: 11.8-14.3 sec) and activated plasma thromboplastin time (aPTT) was 38 sec (reference range: 29-34 sec). Immediate mixing studies were performed, PT was normalized, showing no inhibitors. Then samples were incubated at 37ºC for 2 hours which showed correction revealing no delayed inhibitors. Bleeding time was normal. Taking into consideration a significant bleeding history after tonsillectomy, vonWillebrand factor antigen was performed which was 104% (ref; 50-150%) indicating normal vWF levels. Keeping in view, presence of hemophilia in females FVIII levels were done, which showed levels of 60% (50-150%). Urea clot solubility test was also normal. Further workup showed normal factor IX (65%) levels and XIII (80%) activity. Platelet function studies were also performed, which were normal.

Patient was given vitamin K replacement therapy and was called again after a few days. Detailed history was taken again, this time she gave history of prolonged bleeding and easy bruisibility in 14 year old son, who had been investigated in past but no diagnosis was made, while the other two children have no history of bleeding and are normal. Her laboratory tests were repeated again. this time PT and aPTT were normal. No inhibitor was found. Other tests were also repeated which showed; vWF antigen 93%, factor VIII assay 98%, factor XIII assay 133%, coagulation profile was in normal limits. Fibrinogen levels were also done, which were 1.5g/dl (0.5-4g/dl). D-Dimers were also normal. As FXII is not associated with bleeding and leads to significant prolongation in aPTT therefore; factor XI assay was performed which showed 19.4 % activity. Therefore, a final diagnosis of hemophilia C was made. She was educated on increased risk of bleeding and potential need for fresh frozen plasma (FFP) infusions or factor XI infusions (so far it's not available in Pakistan) prior to future surgical procedures, and was asked to follow-up with the local hemophilia center to create a plan for any future surgery that she may undergo.

Factor assay of her son was also carried out, which showed FXI level as 18.1%.

Discussion

Hemophilia C is associated with mutation in factor XI gene, located on chromosome 4 which contains 15 exons and 14 introns spanning a genomic region of 23 kb. About 253 mutations are narrated in studies[6]. Role of factor XI in coagulation is enhancing thrombin production and prevention of premature clot dissolution by inhibiting fibrinolysis. Absence of conventional symptoms results in underestimation of actual prevalence of factor XI deficiency, studies indicate that calculated prevalence was 2-20 times higher than expected[7]. Moreover, risk of bleeding may not always correspond with factor levels, prolonged bleeding post-surgery and easy bruisibility are the commonest manifestations as mentioned in our patient[8, 9] Initial investigations include platelet count, platelet function test, bleeding time, PT and

aPTT. The results indicated mildly prolonged aPTT. Final diagnosis is made after performing factor XI assay. APTT may be prolonged in Factor XI deficiency, however normal aPTT levels do not rule out mild to moderate deficiency[10]. It has also been reported that children with factor XI deficiency have normal aPTT[11] which is also evident in our case as the child had mildly prolonged aPTT. Hemophilia C patients require vigilant preoperative planning. Sites with high fibrinolytic activity bleeds more such as oral cavity. Mild bleed can be controlled by tranexameic acid. Factor XI activity should be monitored in major surgeries with replenishment using factor XI concentrates or FFP[4]. Recombinant factor VIIa along with antifibrinolytic therapy has also proven to be an effective hemostatic agent in patients with factor XI deficiency undergoing surgery.[12] Minor procedures such as tooth extraction, root canal and skin biopsy can be managed with amino caproic acid or tranexameic acid[4]. Patients should be advised to avoid contact sports and injuries.

Conclusion

Factor XI deficiency is an under recognized entity, it remains a rare bleeding disorder with poor correlation with bleeding tendencies and wide variability in clinical presentation. Factor XI concentrates and FFPs are the main modalities for managing patients with factor XI deficiency undergoing procedures or labor, and treatment should be based on individual presentation.

Acknowledgments

None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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