Factor XII deficiency - A rare coagulation disorder

Rajesh Kumar, Ashok Gupta, Priyanshu Mathur, Manisha Garg

From Department of Paediatrics, SMS Medical College, Jaipur, Rajasthan, India

Correspondence to: Rajesh Kumar, Department of Paediatrics, SMS Medical College, Jaipur - 302 004, Rajasthan, India.

Phone: +91-8812047778. E-mail: rajesh.kumar.amc1985@gmail.com

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ABSTRACT

Severe coagulation factor XII (FXII) deficiency is a very rare, mysterious, and not well-known inherited condition. Unlike other coagulation factor deficiencies, it is usually asymptomatic in most of the cases. Congenital FXII deficiency is the most common cause of an isolated prolongation of the activated partial thromboplastin time in a non-bleeding child or adult; consequently, most patients are detected during a routine pre-operative coagulation study. Surprisingly, it does not lead to abnormal bleeding, but some cases of severe FXII deficiency experiences thrombotic events in their lifetime. There are only a few reports of FXII deficiency in literature. We are reporting a case of congenital FXII deficiency in a 7-month-old child.

Key words: Factor XII deficiency, Prolonged activated partial thromboplastin time, Recurrent pregnancy losses

CASE REPORT

A 7-month-old 2nd born male child was born to a non-consanguineously married Indian couple at term by normal vaginal delivery with birth weight of 2.6 kg. At the age of 4 months, he developed multiple ecchymotic patches all over the body. These ecchymotic patches were self-resolving in nature and reappeared in every 10-15 days. History of prolong bleeding after minor trauma was present. There was no history of any bleeding disorder in any other family member. The child was exclusively breastfed till the age of 3 months, and thereafter, weaning started with buffalo milk and biscuits.

On physical examination, multiple ecchymotic patches were present over the trunk, back, arms, and legs, largest measuring 3 cm × 2.5 cm (Fig. 1a and b). Except undernutrition: Weight 6.8 kg (~2SD to ~3SD), growth, and development were within normal limits (occipitofrontal circumference 44 cm [between −1SD and +1SD], length 65.5 cm [between −2SD and −1SD]). Systemic examination was normal.

On blood investigation, complete blood count revealed microcytic hypochromic anemia (hemoglobin 9.7 g/dL). Platelet count was 547,000/mm³. Renal and liver function tests were within normal limits. During the hospital stay, the patient was given vitamin K and supportive treatment. Documented evidence of persistent elevation of aPTT at our center is listed in Table 1. To find out the cause of excessively raised level of aPTT, investigation to measure the concentration of clotting factor was...
We found the low level of FXII in this case, which is a rare disorder; so we are reporting this case. Since the child showed no evidence of gross bleeding during his hospital stay, so vitamin K was stopped and discharged on iron-folic acid, calcium, and vitamin D drops. The patient has been advised for regular follow-up at our center (at least every 3 months). The possibility of occurrence of thromboembolic complications has been explained to the parents.

DISCUSSION

Deficiency of coagulation FXII is either acquired or congenital. Acquired FXII deficiency is found in patients who has nephrotic syndrome. The pathological basis of this deficiency has not been recognized since the urinary loss of FXII is not only the cause for the reduced plasma activity. Other causes of acquired FXII deficiency are liver transplantation, autoimmune diseases, in association with von Willebrand disease, FVIII or FIX deficiency, high molecular weight kininogen deficiency, heparin contamination, liver diseases, prekallikrein deficiency, and lupus anticoagulants [10].

Another kind of coagulation deficiency is congenital coagulation FXII deficiency which is a rare autosomal recessive hereditary disease. Its manifestations are low factor concentration without significant bleeding. As a result, deficiency of coagulation FXII is often diagnosed by regular coagulation tests conducted before surgeries. Since no severe bleeding occurs, there is not any requirement of specific treatment [11].

There have been lots of reports of association of Hageman factor deficiency of myocardial infarction (MI), and recurrent pregnancy losses. Therefore, on detection of Hageman factor deficiency, clinician must think about these associated risks in female patients rather than internal or visible bleeding. The patient of low Hageman factor can die due to acute MI and pulmonary embolism. So, better risk management is must for the better prognosis of individuals affected with FXII deficiency.

There should not be any unnecessary delay in surgical interventions and investigations that are not needed in patients of isolated FXII deficiency. In recent years, it is found that fibrinolytic effect of FXII is more important than its role in intrinsic coagulation pathway.Currently, researchers are more concerned on thrombotic complications (cardiovascular and cerebrovascular) in FXII deficiency patients [10]. As most of the patients detected with FXII deficiency are asymptomatic, so no treatment may be needed.

CONCLUSION

FXII deficiency is associated with isolated prolonged aPTT without the risk of bleeding, so it is important to recognize deficiency of FXII in all cases of isolated prolonged aPTT to prevent unnecessary fresh frozen plasma transfusions. The delay in surgical interventions due to fear of bleeding and unnecessary investigations are not needed in patients of isolated FXII deficiency. Furthermore, these patients should be at followed up regularly due to the increased risk of thromboembolic episodes.

REFERENCES


Figure 1: (a and b) Ecchymotic patches over back of arm and flexor aspect of forearm

Table 1: aPTT and clotting time during patient’s stay

<table>
<thead>
<tr>
<th>Date of investigation</th>
<th>aPTT</th>
<th>Clotting time</th>
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<tbody>
<tr>
<td>02-04-2016</td>
<td>89.5 s</td>
<td>&gt;15 min</td>
</tr>
<tr>
<td>12-04-2016</td>
<td>68.5 s</td>
<td>&gt;15 min</td>
</tr>
</tbody>
</table>

aPTT: Activated partial thromboplastin time

Table 2: Measurement of clotting factor in percentage

<table>
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<tr>
<th>Clotting factor</th>
<th>Percentage detected</th>
<th>Normal limits (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VIII</td>
<td>86.0</td>
<td>56-191</td>
</tr>
<tr>
<td>IX</td>
<td>95.0</td>
<td>36-136</td>
</tr>
<tr>
<td>XII</td>
<td>40.4</td>
<td>70-120</td>
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