

Incidental diagnosis of moderate congenital factor XI deficiency in a child during preoperative screening : a case report

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Case Report

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Abstract

Background

Congenital factor XI (FXI) deficiency, also known as hemophilia C or Rosenthal disease, is a rare inherited bleeding disorder characterized by a quantitative or qualitative defect of factor XI. Unlike hemophilia A and B, its clinical expression is highly variable, and bleeding risk cannot be accurately predicted solely by plasma factor XI activity. Diagnosis is often made incidentally after the detection of an isolated prolonged activated partial thromboplastin time (aPTT), particularly during preoperative evaluation.

Case presentation

We report the case of a 3-year-old Moroccan boy, born to non-consanguineous parents, with no significant personal or family history of bleeding disorders. The patient was referred for evaluation of an isolated prolonged aPTT discovered during preoperative assessment before planned circumcision. Clinical history revealed recurrent bruising after minor trauma but no history of epistaxis, gingival bleeding, hemarthrosis, or spontaneous bleeding.

Complete blood count was normal, with a hemoglobin level of 12.2 g/dL, leukocyte count of 10,000/mm³, and platelet count of 428,000/mm³. Coagulation testing showed a normal prothrombin time (100%), prolonged aPTT (49.8 seconds; control: 29.6 seconds), and normal fibrinogen level (2.2 g/L). Von Willebrand factor activity was normal (76.5%). A mixing study demonstrated complete correction of the prolonged aPTT, with a Rosner index of 9.44%, suggesting a coagulation factor deficiency rather than the presence of an inhibitor.

Specific coagulation factor assays showed normal factor VIII (110.2%) and factor IX (74%) activities, whereas factor XI activity was reduced to 41.2%, confirming a moderate factor XI deficiency. Factor XI activity was measured using a one-stage clotting assay on an automated ACL TOP 750 coagulation analyzer (Instrumentation Laboratory, Bedford, MA, USA).

Conclusion

Congenital factor XI deficiency should be considered in children presenting with an isolated prolonged aPTT, even in the absence of significant bleeding history. Bleeding risk assessment requires an individualized approach based on both laboratory findings and clinical history. Close collaboration between clinicians and laboratory specialists is essential for appropriate management, particularly before invasive procedures.

Introduction

Congenital factor XI (FXI) deficiency, also known as hemophilia C or Rosenthal disease, is a rare inherited coagulation disorder caused by a quantitative or qualitative deficiency of factor XI, a plasma

protein synthesized mainly by the liver and involved in the intrinsic pathway of coagulation. The disorder is usually inherited in an autosomal recessive manner and results from pathogenic variants in the **F11** gene located on chromosome 4q35. However, clinical manifestations are highly variable, and patients with similar factor XI activity levels may exhibit different bleeding phenotypes [1,2].

The prevalence of severe factor XI deficiency is estimated at approximately one case per million individuals in the general population. However, it is significantly higher among certain populations, particularly Ashkenazi Jews, due to founder mutations associated with severe forms of the disease [3,4]. Nevertheless, cases have been reported worldwide, indicating that this disorder is not restricted to specific ethnic groups.

Clinically, most patients remain asymptomatic until exposed to a hemostatic challenge. Bleeding episodes mainly occur after surgical procedures, dental extraction, trauma, or childbirth, particularly in tissues with high fibrinolytic activity, such as the oral cavity, nasopharynx, and genitourinary tract. In contrast to hemophilia A and B, spontaneous deep bleeding, hemarthrosis, and muscle hematomas are uncommon [2,5].

Laboratory diagnosis is usually suspected when an isolated prolonged activated partial thromboplastin time (aPTT) is observed with a normal prothrombin time. Diagnosis requires a mixing study to differentiate a coagulation factor deficiency from a circulating inhibitor, followed by specific factor XI activity measurement. The diagnosis is frequently incidental during preoperative investigations in patients without significant bleeding history. Importantly, bleeding risk assessment relies more strongly on personal bleeding history than on factor XI activity alone [1,2,6].

We report the case of a child with moderate congenital factor XI deficiency diagnosed incidentally during preoperative screening before circumcision. This case highlights the diagnostic challenges associated with this rare coagulation disorder and emphasizes the importance of individualized bleeding risk assessment before invasive procedures.

Case presentation

A 3-year-old Moroccan boy was referred to the Central Hematology Laboratory of Ibn Sina University Hospital, Rabat, Morocco, for evaluation of an isolated prolonged activated partial thromboplastin time (aPTT) detected during preoperative assessment before planned circumcision.

The patient was born to non-consanguineous parents and had no significant medical or surgical history. There was no known family history of bleeding disorders. Clinical questioning revealed recurrent bruising following minor trauma, but no episodes of epistaxis, gingival bleeding, hemarthrosis, or spontaneous hemorrhage.

Complete blood count was normal, with a leukocyte count of 10,000/mm³, hemoglobin level of 12.2 g/dL, and platelet count of 428,000/mm³. Coagulation tests revealed a normal prothrombin time (100%),

prolonged aPTT (49.8 seconds ; control : 29.6 seconds), and normal fibrinogen concentration (2.2 g/L).

Von Willebrand factor activity was normal (76.5%), excluding a significant von Willebrand factor deficiency.

To distinguish between a coagulation factor deficiency and the presence of a circulating inhibitor, a plasma mixing study (patient plasma mixed with normal pooled plasma) was performed. Complete correction of the aPTT was observed. The Rosner index was 9.44%, supporting the diagnosis of a coagulation factor deficiency rather than an inhibitor.

Specific intrinsic pathway factor assays showed normal factor VIII and factor IX activities (110.2% and 74%, respectively). Factor XI activity was reduced to 41.2%, consistent with a moderate congenital factor XI deficiency.

Factor XI activity was measured using a one-stage clotting assay performed on an automated **ACL TOP 750 coagulation analyzer** (Instrumentation Laboratory, Bedford, MA, USA), according to the manufacturer's recommendations. Results were expressed as percentage activity compared with a calibration curve obtained using normal reference plasma. No other coagulation factor deficiency was identified. (**Table I**)

Table I : Hematological and coagulation laboratory findings at initial presentation

Parameter	Result	Reference Range
Hemoglobin	12.2 g/dL	11.5–13.5 g/dL
Leukocytes	10 × 10 ⁹ /L	5–15 × 10 ⁹ /L
Platelets	428 × 10 ⁹ /L	150–450 × 10 ⁹ /L
Prothrombin Time (PT)	100%	Normal
Activated Partial Thromboplastin Time (aPTT)	49.8 s	25–35 s
Fibrinogen	2.2 g/L	2–4 g/L
Von Willebrand Factor (VWF) Activity	76.5%	> 50%
Factor VIII (FVIII)	110.2%	50–150%
Factor IX (FIX)	74%	50–150%
Factor XI (FXI)	41.2%	50–150%

A diagnosis of moderate congenital factor XI deficiency (hemophilia C or Rosenthal disease) was established. Given the absence of major bleeding episodes and the moderate severity of the deficiency, a

multidisciplinary approach was adopted, including individualized bleeding risk assessment before any invasive procedure, particularly the planned circumcision.

The planned circumcision was subsequently performed without bleeding complications. No specific factor replacement therapy was administered, and no postoperative hemorrhagic event was reported.

A chronological summary of the patient's clinical evaluation, laboratory investigations, diagnosis, and subsequent management is presented in (**Table II**)

Table II Chronological summary of the patient's clinical evaluation, diagnosis, and management

Time point	Clinical event
Preoperative evaluation	Isolated prolonged aPTT detected before planned circumcision
Initial hematological assessment	CBC, PT, aPTT, fibrinogen and VWF evaluated
Diagnostic evaluation	Mixing study showed complete correction ; Rosner index 9.44%
Specific factor assays	FVIII 110.2%, FIX 74%, FXI 41.2%
Diagnosis	Moderate congenital factor XI deficiency established
Perioperative management	Individualized bleeding-risk assessment; no factor replacement administered
Surgical procedure	Circumcision performed without bleeding complications
Postoperative follow-up	No postoperative hemorrhagic event reported

Discussion

Congenital factor XI (FXI) deficiency, also known as hemophilia C or Rosenthal disease, is a rare inherited coagulation disorder characterized by reduced quantitative or functional factor XI activity. Its clinical phenotype is highly heterogeneous, ranging from asymptomatic forms to significant bleeding episodes occurring mainly after hemostatic challenges [7,8].

First described by Rosenthal et al. in 1953, factor XI deficiency is usually inherited in an autosomal recessive pattern and results from pathogenic variants of the **F11** gene located on chromosome 4q35. Several hundred genetic variants have been identified, including founder mutations observed in specific populations, particularly among Ashkenazi Jewish and Iraqi Jewish individuals. However, recent studies have demonstrated that the relationship between genotype, plasma factor XI activity, and bleeding phenotype is complex and cannot be accurately predicted solely from laboratory parameters [7,9].

The prevalence of severe factor XI deficiency is low in the general population, with an estimated frequency of approximately one case per million individuals. However, it is considerably higher in certain populations because of a founder effect. Moderate or partial forms are probably underdiagnosed, as they may remain clinically silent for many years and are often discovered incidentally during routine laboratory investigations performed before surgery [9].

The severity of factor XI deficiency is generally classified according to residual factor XI activity. Severe deficiency is usually defined by factor XI activity below 20%, whereas partial deficiency is characterized by activity levels ranging from 20% to 70%. However, unlike factor VIII and factor IX deficiencies, plasma factor XI activity alone does not reliably predict bleeding risk. The clinical phenotype is influenced by several factors, including the patient's personal bleeding history, the type of surgical procedure, and the anatomical site involved. Consequently, some patients with very low factor XI activity may remain asymptomatic, whereas others with moderate deficiency may experience significant bleeding complications during surgical interventions. This lack of a direct correlation between factor XI activity and bleeding risk has recently been emphasized by Barg et al., who advocate an individualized approach to bleeding risk assessment based primarily on the patient's clinical history [8,9].

From a laboratory perspective, factor XI deficiency is usually suspected in patients with an isolated prolonged aPTT and normal prothrombin time. The mixing study is an essential diagnostic step, allowing differentiation between a coagulation factor deficiency and the presence of a circulating inhibitor. In our patient, complete correction of the aPTT and a Rosner index of 9.44% supported the diagnosis of a coagulation factor deficiency. Specific factor assays confirmed normal factor VIII and factor IX activities and demonstrated a reduced factor XI activity of 41.2%, consistent with a moderate deficiency.

In our case, the diagnosis was made incidentally during preoperative evaluation in a child with only minor bleeding manifestations consisting of bruising after trauma. The absence of significant bleeding history and the moderate factor XI deficiency led to a personalized management strategy rather than systematic factor replacement. This case emphasizes the importance of investigating isolated prolonged aPTT in children and highlights that management decisions should be based on the patient's overall clinical profile rather than factor XI activity alone.

Management of factor XI deficiency requires an individualized assessment based on factor XI activity, previous bleeding history, family history, and the type and location of the planned invasive procedure. Available therapeutic options include antifibrinolytic agents, particularly tranexamic acid, fresh frozen plasma when replacement therapy is required, and factor XI concentrates in countries where they are available. The use of factor XI concentrates should be carefully considered because of the potential risk of thrombotic complications [9,10].

The main strength of this case is the detailed laboratory evaluation of an isolated prolonged aPTT, including a mixing study, Rosner index, and specific coagulation factor assays, which allowed the diagnosis of moderate factor XI deficiency. This case also highlights the importance of individualized

bleeding risk assessment rather than relying solely on factor XI activity. A limitation of this case is the absence of molecular genetic analysis of the FXI gene.

Conclusion

Congenital factor XI deficiency is a rare coagulation disorder with a highly variable clinical expression that may remain clinically silent for many years. It should be considered in children presenting with an isolated prolonged activated partial thromboplastin time, even in the absence of a significant bleeding history.

Diagnosis requires a structured laboratory approach combining mixing studies and specific factor XI activity measurement. Bleeding risk assessment should not rely solely on factor XI activity but should also incorporate the patient's personal bleeding history and the nature of the planned invasive procedure.

Close collaboration between laboratory specialists and clinicians is essential to ensure appropriate preventive and therapeutic strategies and to reduce the risk of bleeding complications.

Patient perspective

The patient's parents expressed their satisfaction with the care provided. They appreciated the identification of the coagulation abnormality before the planned circumcision and the individualized management approach. They were particularly reassured that the circumcision could be performed safely without bleeding complications. The parents reported that being able to proceed with the circumcision while ensuring appropriate management of the coagulation disorder was a positive and reassuring outcome for the family.

Declarations

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Authors' contributions

☒ **SE** : Conceptualization, literature search, and drafting the manuscript.

☒ **SL** : Case analysis, critical revision

☒ **HM** : Case analysis, critical revision

✉ **AM** : Supervision, validation, and critical review of the final draft.
All authors have read and agreed to the published version of the manuscript.

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All data generated or analyzed during this case report are included in this published article.

Ethics and Consent to Participate declarations : applicable.

Consent for publication

Written informed consent was obtained from the patient's parents for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

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