

# A case report of congenital factor X deficiency in an adult patient

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## Abstract

Factor X deficiency is one of the rarest coagulation disorders representing 10% of all rare bleeding diseases with a frequency of 1:1,000,000. A 39-year-old male patient with no previous medical conditions was admitted to the hospital with a left carpal ganglion for surgical excision. Routine preoperative laboratory examination revealed a high international normalized ratio of 5.4 IU (0.8–1.1) and a prothrombin time of 72.2 s (10.9–13.6), with an isolated factor X level of less than 5%. Genetic testing for congenital factor X deficiency identified a homozygous mutation c.271 > A (p.Glu91). Vitamin K supplementation did not improve his international normalized ratio or increase factor X levels; hence, surgery was delayed. The patient was re-hospitalized to remove a wisdom tooth, during which fresh frozen plasma was administered. An allergic reaction complicated this procedure in the form of a rash on the body. As a result, the tooth was removed without active bleeding. This report presents a unique factor X deficiency case with limited treatment options to improve factor X levels after failed vitamin K administration and an allergic reaction to fresh frozen plasma. A physician's observation and ongoing follow-up were the only reasonable approaches in treating the patient with mild to moderate factor X deficiency due to lack of prothrombin complex concentrates or factor X replacement at the center at the time.

## Keywords

Hereditary factor X deficiency, blood coagulation disorders, bleeding disorder, therapy, allergic reaction

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## Introduction

Factor X (FX) is a vitamin K-dependent factor essential to the coagulation cascade of the common pathway, which plays a critical role in fibrin formation. FX circulates in the bloodstream, attaches to intravenously injected HAdV-C5 vectors, and connects them to heparan sulfate proteoglycans (HSPG) via a  $\gamma$ -carboxyl-glutamic acid-rich (GLA) domain.<sup>1,2</sup> Patients with low FX levels are more likely to experience mucocutaneous bleeding, and less than 5% may present with hemophilia A and B.<sup>1–3</sup> Clinical assessment of FX includes coagulation screening tests such as activated partial thromboplastin time (aPTT) and prothrombin time (PT).<sup>3–5</sup> Individuals with FX deficiency have prolonged aPTT and PT, a high international normalized ratio (INR).<sup>3–5</sup>

A number of factors lead to FX deficiency, with most cases being associated with liver disease and vitamin K deficiency, acute myeloid leukemia, infection, primary amyloidosis, malignancies, and connective tissue diseases.<sup>6–8</sup> Hereditary FX deficiency affects only 1 in 1,000,000 people. Nevertheless, because it is inherited through an autosomal

recessive pattern, more than a hundred genes can be affected in the hereditary type of FX deficiency.<sup>1,2</sup> Several registries have proposed classifying FX deficiency into three categories: mild, moderate, and severe, based on the factor activity level.<sup>4,9</sup> The disease can also be divided into two types based on the level and activity of the FX antigen in the plasma: (1) low activity and antigen level and (2) low factor activity but normal antigen level.<sup>10,11</sup>

A mild form of the disease occurs at levels in the range of 6%–10%, and in some cases, at this level, there may be some

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nosebleeds or heavy menstruation. Mild FX deficiency may be diagnosed during routine screening or based on positive family history.<sup>4,10,11</sup> The moderate disease occurs when the level is 1%–5%. Moderately affected patients can only be recognized after a hemostatic test, such as surgery, trauma, or menstruation. Severe disease occurs when the activity level is <1%. Severe FX deficiency may be found in the neonatal period during circumcision, bleeding from the umbilical stump, intracranial hemorrhage (ICH), or gastrointestinal bleeding. The risk of bleeding is higher in moderate to severe diseases with hemarthrosis or intraorgan bleeding resembling severe hemophilia A and B.<sup>4,9</sup>

This report presents the case of an asymptomatic 39-year-old male hospitalized with a left carpal ganglion for surgical removal. During the preoperative examination, the patient was incidentally found to have isolated FX deficiency. This clinical case report is intended to contribute to the rare occurrences of FX described in the literature, its therapy, and its side effects.

## Case report

A 39-year-old male patient with no previous medical illness was admitted to King Fahd Military Medical Complex, Dhahran (KFMMC), with a left wrist ganglion for surgical excision. Routine preoperative laboratory examination revealed a high INR of 5.4 IU (0.8–1.1) and a PT of 72.2 s (10.9–13.6). No history of ecchymosis or symptoms related to other systems was identified. There were no reports of consanguinity and of bleeding disorders in family members including siblings. The patient did not have bleeding tendency. In addition, he was unaware of the presence of prolonged PT or PTT. Physical examination of the patient's condition was vitally stable. Skin rash, ecchymosis, lymphadenopathy, and petechial hemorrhages were not detected. In addition, the abdomen was soft, without hepatosplenomegaly.

A blood test was performed for the complete blood count with hemoglobin 15 g/dL, MCV 81.9 fl, MCH 26.5 pg, white blood cell counts  $7.25 \times 10^3/\mu\text{L}$ , platelet count  $197 \times 10^3/\mu\text{L}$  (140–450); aPTT 3.7 s (27–38), bleeding time 4 min, thrombin time 20.4 s (16.7–22.1). The renal function of liver enzymes was normal. The peripheral blood smear was unremarkable.

A plasma mixing analysis corrected both PT and APTT to normal levels, indicating the percentage of FX deficiency. A differential diagnosis of types of hemophilia was proposed, and plasma analysis for factors II, V, VII, VIII, X, XI, and XII was sent. The operation was postponed, and the patient was discharged home with subsequent hematological follow-up pending the expected level of necessary factors. The result confirmed the FX deficiency (Table 1). Anticardiolipin antibodies IgG and IgM, lupus anticoagulant, serum immunoglobulin, and immune fixation by serum protein electrophoresis were within normal limits. Genetic testing for congenital FX deficiency identified a homozygous mutation c.271 > A (p.Glu91).

**Table 1.** The result of coagulation factors showed isolated low FX.

Test name*	Result (%)	Reference range
F II	93.4%	77–129
F IX	170.8%	73–131
F V	96.5%	74–129
F VII	68.9%	65–125
F VIII	120.6%	66–130
F X	<5%	71–133
F XI	68%	60–130
F XII	95%	73–121

\*F=Factor. II=2, V=5, VII=7, VIII=8, IX=9, X 10, XI=11, XII=12.

In preparation for the procedure, the patient was started on trial supplementation of vitamin K for 7 days, with no improvement in FX or INR. The patient was then hospitalized for fresh frozen plasma (FFP) administration before a wisdom tooth extraction surgery. It was decided to start FFP with four units. However, the patient's allergic reaction began 10 min after the infusion, a rash accompanied by severe itching. As a result, the FFP package was not fully spent. This amount of FFP was not enough to treat or increase his FX levels. The patient claimed to have previously had a tooth filling with no prior therapy and bleeding during the procedure. Hence, under his own responsibility with informed consent, the tooth was removed after 3 h from the moment the FFP was stopped. The patient was treated for an allergic reaction and was under regular outpatient follow-up without any episodes of bleeding or treatment.

## Discussion

Congenital FX deficiency is an autosomal recessive disorder in which two copies of the mutation are inherited.<sup>12,13</sup> Congenital FX deficiency can be heterozygous or homozygous.<sup>12</sup> Symptomatic homozygous patients with severe hemorrhagic symptoms present early in life, while symptomatic heterozygotes may bleed only after major hemostatic cases such as trauma or major surgery.<sup>5,9</sup> The findings of this case report confirmed a FX activity of less than 5% on multiple occasions which is considered mild to moderate disease; however, never had experienced any prior bleeding symptoms.

For mild bleeding symptoms, specific therapy and antifibrinolytic agents are confirmed to be sufficient.<sup>12–14</sup> FX replacement therapy can be performed for more severe bleeding episodes using FFP or plasma-derived prothrombin complex concentrates (PCC) containing a significant amount of activated vitamin K-dependent factors. Essentially, this can lead to side effects or no effect.<sup>5,9,14</sup> Thus, in this case, vitamin K supplementation for 7 days showed no increase in FX or INR. Moreover, FFP therapy resulted in an allergic reaction. The patient's allergic reaction to FFP was consistent with the evidence in research reporting that FFP was

associated with allergic reactions and transfusion-related acute lung injury.<sup>4,5,9,14</sup> Therefore, further therapeutic procedures (tooth extraction) were carried out without preventive measures and bleeding episodes were not registered.

In addition to FFP, FX deficiency can also be managed with Coagadex, a factor concentrate, manufactured by Bio Products Laboratory Limited and approved by the Food and Drug Administration (FDA).<sup>12,13</sup> Indications for the use of factor concentrate should be on-demand for the control of bleeding episodes, perioperative management of bleeding in patients with mild to moderate hereditary FX deficiency.<sup>12,13</sup>

This case report found that mild or moderate FX deficiency may not require any correction in the absence of active bleeding.<sup>13–16</sup> Observation and ongoing follow-up by a physician may be one of the reasonable approaches for patients with mild to moderate FX deficiency who are scheduled for minor procedures such as tooth extraction. Still, this study should be viewed as a stand-alone case report and is not meant to guide or recommend all cases relating to FX deficiency. This case was a unique experience in Saudi Arabia worth reporting to enrich the international scientific evidence on FX deficiency.

## Conclusion

This case report highlighted the unique presentation of FX deficiency with limited treatment options to improve FX levels after a failed vitamin K trial, an allergic reaction to FFP, and the lack of PCC at the center. This case study should be viewed as a stand-alone case report where a physician's observation and ongoing follow-up were the only reasonable approaches.

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## Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

## Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

## Patient's consent

Written informed consent was obtained from the patient for publication of this case report.

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