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CASE REPORT

A Rare Case Report of Acquired Coagulation Factor XI Deficiency

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SUMMARY

Background: **Acquired coagulation factor deficiency is an autoimmune hemorrhagic disease caused by the production of antibodies to coagulation factor. The incidence of acquired coagulation factor XI deficiency is low and rarely reported.**
Case presentation: **We report a case of a patient with acquired coagulation factor XI deficiency. The patient was a 24-year-old female who presented with mild yellowing of the skin, general malaise, palpitation, and no obvious bleeding symptoms prior to admission, such as skin and mucous membrane petechiae. She was initially diagnosed with anemia because her hemoglobin was 62 g/L. Laboratory results showed activated partial thromboplastin time (APTT) prolonged with a test value of 83.40 seconds and could not be corrected by corrective experiments; Factor XI activity was less than 0.1%, positive for factor XI antibody, and a plasma coagulation factor XI inhibitor was 35.20 BU/mL. She was eventually diagnosed with acquired coagulation factor XI deficiency, Plasmapheresis were performed to clear antibodies, and patient's condition improved.**
Conclusions: **Plasmapheresis played a positive role in the treatment of acquired factor XI deficiency. Clear early diagnosis and proper treatment can help to improve the cure rate of patients.**
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KEYWORDS

acquired coagulation factor deficiency, coagulation factor XI factor XI inhibitor, bleeding disorder

INTRODUCTION

Acquired coagulation factor deficiency is a group of acquired bleeding disorders caused by decreased activity of coagulation factors in the plasma. Its pathogenesis mainly includes depletion or destruction of coagulation factors and the production of anti-coagulation factor antibodies. Among these, acquired coagulation factor deficiency caused by the production of anti-coagulation factor antibodies in the patient's body is relatively rare [1]. Factor XI is a crucial coagulation factor in the endogenous coagulation pathway. Factor XIa is activated by factor VIIa, which then leads to thrombin formation through a series of enzymatic reactions. Additionally, some studies have indicated that factor XIa can be directly activated by thrombin and can activate factor VII through the exogenous coagulation pathway [2]. Anti-factor XI antibodies include neutralizing antibodies that

affect factor XI activity and nonneutralizing antibodies that accelerate clearance. They are commonly associated with autoimmune diseases (primarily systemic lupus erythematosus), malignancies, pregnancy, and infection [3]. The condition usually does not cause spontaneous bleeding, but it can cause severe bleeding during surgery, trauma, or childbirth [4]. The cause of acquired factor XI deficiency remains unclear and is currently associated with partial coagulation inhibitors, such as antibodies to factor XI (FXI), which have a low prevalence and fewer reported cases. Among the cases of factor XI deficiency, reports of congenital factor XI deficiency are more common. In this report, we describe a rare case of a young female anemic patient with acquired factor XI deficiency.

CASE PRESENTATION

A 24-year-old female patient presented with a three-year history of mild yellow discoloration of the skin, panic attacks with conscious dizziness, weakness, palpitations, head swelling and discomfort, postural syncope with dyspnea and discomfort after exertion, petechiae or other bleeding on the skin or mucous membranes, and no other obvious bleeding symptoms. Laboratory examination revealed that hemoglobin and platelets were low, with a hemoglobin of 62 g/L and a platelet count of 46 x 10^9/L. Additionally, the anti-human globulin test and antinuclear antibody were positive, with the antinclear antibody exhibiting nuclear and cytoplasmic granularity, and the titer was 1:100. Furthermore, the anti-RO-52 antibody and anti-mitochondrial M2 antibody were positive. Complement values were also decreased. The concentration of C3 was 0.58 g/L (ref range 0.79 - 1.52), while that of C4 was 0.05 g/L (ref range 0.16 - 0.38). During the patient's hospitalization, she was treated with glucocorticoids and intravenous human immunoglobulin, in addition to symptomatic and supportive treatments such as blood transfusion, acid suppression, and gastric protection, but there was no significant dissimilarity between pre and post treatment.

Duration of hospital stay, the APTT remained prolonged, with a result of 83.40 seconds (ref range 24 - 40). A mixed APTT correction test was also performed, with a result of 82.00 seconds (ref range 24 - 40), which indicated that the APTT had not been effectively corrected. Furthermore, coagulation factor measurements were conducted, revealing a decrease in factors VIII and IX, and a result below the lower limit of detection for factor XI.

Subsequently, the plasma of the patient was mixed and diluted with normal human plasma in a proportionate manner to determine the factor activity (Table 1). The plasma was subsequently analyzed to quantify the three types of factor antibodies and factor inhibitors. The findings revealed the absence of factor VIII and IX antibodies, with the presence of factor XI antibodies. In addition, the plasma coagulation factor XI inhibitor was 35.20 BU/mL. These results indicated that the patient suffers from acquired factor XI deficiency. The clinician supplemented the treatment with blood transfusion on the basis of rituximab therapy and hormone therapy, and then used frozen plasma to perform plasma exchange on the patient. Following several plasma exchanges, the original experimental result indicating a factor XI coagulation level below the lower limit of detection (< 0.1%) was successfully measured, accompanied with several plasma exchanges. Thereafter, the value gradually increased to 0.3% and 1.1% (Figure 1), resulting in partial symptom relief and relative stabilization of the patient's condition.

The results indicate that this patient exhibited a rare acquired factor XI deficiency and that plasmapheresis had a favorable impact on the interventional treatment of this patient.

DISCUSSION

Acquired FXI deficiency can be differentiated from hereditary FXI deficiency using the APTT mixing assay that cannot be corrected [5]. In the event that clinical laboratory tests indicate an abnormally prolonged APTT, which may be attributed to either an endogenous coagulation factor deficiency or the presence of coagulation factor inhibitors, a mixing test can be employed to differentiate the underlying cause. The mixing test entails the mixing of the patient's plasma with normal plasma in order to evaluate the APTT before and after the mixing process. If a clotting factor inhibitor is present, APTT will remain prolonged. If the prolonged APTT is due to a lack of clotting factors, it will be corrected. It is important to note that incubation at 37℃ for 2 hours is essential when applying the mixing test, as in some cases it may take time to demonstrate an uncorrected APTT due to slow-acting inhibitors [6]. If the APTT is persistently prolonged and cannot be corrected with multiple measurements, it is at this point that it can be considered that it may be prolonged or affected by the presence of certain inhibitors or lupus anticoagulants [7].

In this case, we conducted a comprehensive analysis of the patient's coagulation factors. Our findings revealed a decline in factors VIII and IX, accompanied by an obvious deficiency in factor XI. Following the dilution of the sample, which may have excluded certain interfering substances, the level of factor XI exhibited a notable increase. The measurement of the three factor inhibitors revealed the presence of an inhibitor related to factor XI coagulation factor. This led to the conclusion that the patient had acquired factor XI deficiency, so we speculated that this inhibitor might be related to the autoimmune disease she suffered from. Furthermore, in conjunction with the patient's coagulation factor measurements, it is possible that the inhibitor could have an effect on other coagulation factors through certain pathways. For instance, a decrease in factor VIII and factor

Table 1. Measurement of plasma diluted factor VIII, IX, and XI activity in patient.

Factor activity dilutions	Factor VIII activity	Factor IX activity	Factor XI activity
Normal control plasma	98.50%	110.90%	94.00%
Patient plasma	56.40%	17.70%	< 0.10%
One half control incubation for 2 hours	41.90%	54.20%	46.20%
Patient plasma diluted two-fold	76.70%	55.00%	< 0.10%
The patient's plasma was diluted four-fold	68.60%	59.90%	< 0.10%
The patient's plasma was diluted eight-fold	56.40%	57.40%	0.30%
The patient's plasma was diluted 16 times	48.40%	53.30%	5.90%
The patient's plasma was diluted 32 times	46.90%	56.20%	21.40%
The patient's plasma was diluted 64 times	44.10%	54.50%	31.20%
The patient's plasma was diluted 128 times	41.20%	56.20%	38.10%
The patient's plasma was diluted 256 times	41.90%	55.60%	39.80%
The patient's plasma was diluted 512 times	40.90%	56.20%	44.90%
The patient's plasma was diluted 1,024 times	42.50%	56.80%	44.10%

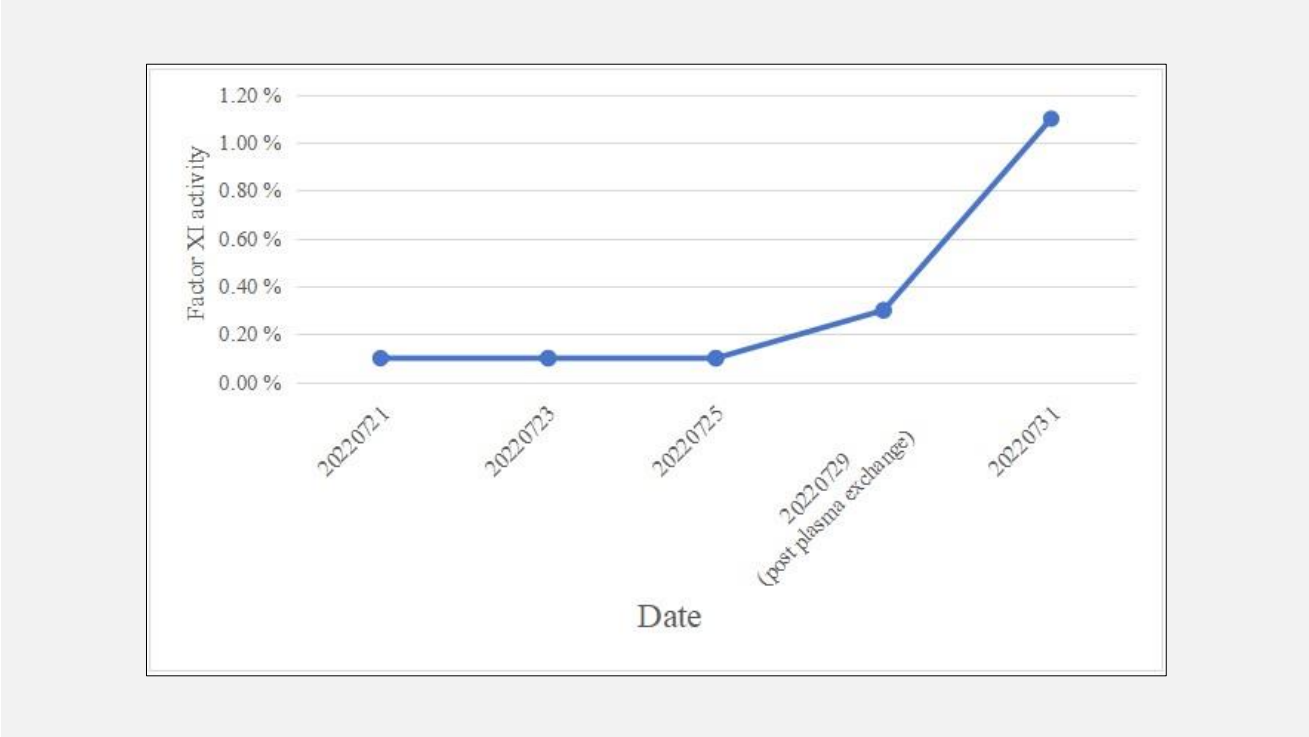

Figure 1. The variations in plasma XI activity observed with TPE.

IX has been observed in this case.

For patients with coagulation factor deficiency, it is recommended that clinicians attempt to perform plasma replacement on several occasions [8]. Once the patient's situation has been effectively improved, plasma replacement may be considered a viable treatment option. In clinical practice, for patients with acquired XI coagulation factor deficiency, the effect of plasma replacement is remarkable. For patients with anemia associated with autoimmune diseases, it is recommended that the relevant coagulation factors be considered in the experimental examination. If the decrease in hemoglobin and

APTT cannot be corrected, it is advisable to consider a factor inhibitor or lupus anticoagulant. This approach is more conducive to the prognosis of subsequent treatment and improves the likelihood of achieving a correct diagnosis.

Furthermore, there is information about the specific composition of the inhibitor and other relevant data that will require further investigation. Furthermore, a genetic screening for coagulation disorders was not performed during the examination to determine whether the patient might also have a factor XI-related inherited mutation [9,10].

The objective of this case study is to provide insight into the laboratory testing and treatment of acquired XI coagulation factor deficiency.

Declaration of Interest:

The authors declare no competing interests.

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