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CLINICAL REPORT

Perioperative management of factor XI deficiency in a patient undergoing hip arthroplasty

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Abstract Factor XI deficiency, or hemophilia C, is a rare autosomal recessive bleeding disorder often diagnosed by inappropriate bleeding associated with trauma or a surgical procedure, and reports of anesthetic management of this disorder are rare. We experienced an 85-year-old man with femoral neck fracture who was diagnosed preoperatively with factor XI deficiency based on abnormally long activated partial thromboplastin time (APTT). He was scheduled for bipolar hip arthroplasty and was prepared for surgery by transfusion of fresh frozen plasma (FFP), instead of factor XI concentrates, which are not commercially available in Japan. Five units of FFP were transfused 6 days before surgery, and 10 units of FFP with 2 units of red concentrated cells (RCC) were used on the day of surgery. Transfusion of FFP shortened the APTT to a level sufficient to allow hemostasis, although not to within the normal range. Although the patient required transfusion of 2 units of RCC postoperatively, no bleeding complications occurred. For bipolar hip arthroplasty, transfusion of FFP produced sufficient hemostasis without the use of tranexamic acid, factor VII preparations, or desmopressin.

Keywords Factor XI deficiency · APTT · Hemophilia

Introduction

Factor XI deficiency, also known as hemophilia C, is an autosomal recessive bleeding disorder. It is often recognized by inappropriate bleeding associated with trauma or with a surgical procedure, and it is usually silent [1]. The estimated incidence of factor XI deficiency is 1 per 1,000,000 persons; it is common in Ashkenazi Jews [1]. We describe here a patient with hip fracture who was diagnosed preoperatively with factor XI deficiency by coagulation tests and was successfully managed by transfusion of fresh frozen plasma (FFP).

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Case report

Written informed consent was obtained from the patient and his family for this case presentation.

A 85-year-old man who presented with femoral neck and right radius fractures was scheduled for bipolar hip arthroplasty. He had hypertension, asthma, and Alzheimer's disease but had never undergone surgery. Family history was negative for bleeding tendencies, purpura, and hemophilia. Blood tests showed renal dysfunction (blood urea nitrogen, 34 mg/dl; creatinine, 2.0 mg/dl) and hyperkalemia (5.69 mEq/ml). Other tests were normal, including normal liver function. Blood coagulation tests showed normal prothrombin time (PT, 13.8 s; PT-INR, 1.10) and very long activated partial thromboplastin time (APTT, >240 s). Platelet count was normal. When APTT was reexamined, 2 days after admission, the result was almost the same (174.9 s). He was suspected of hemophilia A or B, but plasma activities of coagulation factors VIII and IX were normal (factor VIII, 138 %; factor IX, 133 %). Therefore, factor XI was examined. As factor XI activity was below the detection limit of 3 %, he was diagnosed with factor XI deficiency or hemophilia C.

Factor XI preparations are not available in Japan, and accordingly the first-choice treatment for factor XI deficiency was administration of fresh frozen plasma (FFP).

After establishing the diagnosis, five units of FFP were transfused to ensure hemostasis following bone fractures, which led to shortening of the APTT to 58.4 s as measured 1 day after the transfusion. Bipolar hip arthroplasty was performed 6 days after the diagnosis. As factor XI activity could not be measured again after the diagnosis for reasons of cost, APTT was measured as a marker of coagulability.

On the morning of the day of surgery, APTT was 75.0 s. General anesthesia was selected, considering the risk of epidural hematoma. Electrocardiogram, noninvasive blood pressure, percutaneous oxygen saturation, and rectal temperature were monitored. Anesthesia was induced with fentanyl 50 μg and propofol 170 mg (total). Rocuronium was administered at 35 mg for tracheal intubation. Anesthesia was maintained with sevoflurane (1.0–1.5 %), remifentanil (0.10–0.15 μg/kg/min), and oxygen-in-air gas mixture. Operation time was 100 min and anesthesia time was 182 min. Total intraoperative blood loss was 590 g; total urine volume was 100 ml. Intraoperative hypotension was corrected by a bolus injection of phenylephrine (0.1 mg). Five units of FFP were transfused immediately after the induction of anesthesia. At the end of surgery, hemoglobin (Hb) was 8.4 g/dl and hematocrit (Ht) was 23.3 %. Another five units of FFP and two units of red concentrated cells (RCC) were transfused after the operation to prevent possible postoperative bleeding. On postoperative day (POD) 1, APTT was 52.4 s and Hb was 9.8 g/dl. On POD4, APTT was 79.6 s but Hb was 7.8 g/dl. Accordingly, another two units of RCC were transfused. There was no apparent bleeding from the wound during the postoperative period, and the patient was discharged on POD14 with no bleeding complications. At discharge, APTT was 102.9 s and Hb was 9.2 g/dl.

Discussion

Factor XI deficiency is often diagnosed by abnormal bleeding occurring during parturition, surgery, and dental extraction [1]. Plasma levels of factor XI do not always correlate with bleeding tendency, although the reason for this observation remains unclear [2]. Severe factor XI deficiency is represented by blood factor XI levels below 15 %.

Factor XI deficiency is treated by supplementation of factor XI. Such treatment is reported to be effective for hip arthroplasty [3]. However, factor XI concentrates are not commercially available in Japan; instead, the first choice of treatment in this country is replacement therapy using FFP transfusion, especially when plasma factor XI levels are lower than 15 % [4]. Activated factor XI reduces fibrinolysis by promoting activation of thrombin-activatable fibrinolytic inhibitor (TAFI) [2, 5].

Antifibrinolytic drugs, such as tranexamic acid, were reported to be effective in patients with factor XI deficiency [1, 2]. Desmopressin, a synthetic analogue of the natural antidiuretic hormone, is also reported to be effective by increasing factor XI activity [6]. Factor VII preparations (recombinant activated factor VIIa, rFVIIa) were also reported to be effective for patients with factor XI deficiency, probably because of the direct activation of factor X [7]. Administration of tranexamic acid could reduce total blood loss, but this intervention is only recommended during surgery in cases with enhanced fibrinolysis, such as tonsillectomy and dental extraction [1, 2]. Furthermore, administration of factor VII concentrates could lead to thrombosis; in fact, a clot was observed in the surgical field in our patient. Thus, it was considered that these agents were unnecessary in this patient.

FFP was transfused 6 days before surgery (5 units) and on the date of operation (10 units). FFP was administered 6 days before surgery to enhance hemostasis following bone fractures. FFP administered on the date of surgery secured intraoperative hemostasis, and no other drugs such as tranexamic acid or factor VII preparations were necessary to establish hemostasis. The required plasma activity of factor XI for hemostasis is 15–30 %, and the plasma half-life of factor XI is 3–4 days [8]. Because 90–100 % of factor XI is absorbed, the required transfusion of FFP is about 10 units. Transfusion of 10 units of FFP only shortened APTT to 52 s in our patient. A much greater transfusion of FFP was probably needed to normalize APTT, but this was considered inappropriate in this elderly patient based on risk of volume overload and consequent dilution anemia, which would cause tissue hypoxia or transfusion of a much greater amount of RCC. In addition, accurate monitoring of the circulating volume during FFP transfusion would be very difficult under our standard monitoring. Direct arterial pressure or cardiac output monitoring might be helpful for appropriate circulating volume monitoring during FFP transfusion. Therefore, although APTT did not decrease to normal values in this patient, transfusion of 10 units of FFP was clinically effective to allow surgery for bipolar hip arthroplasty.

Measurement of plasma factor XI activity was not performed after the diagnosis of factor XI deficiency. It is desirable to measure its activity, although the activity level does not correlate with bleeding tendency in this disorder [9]. Instead of plasma factor XI activity, we used APTT as a marker for coagulation activity in this study. Although APTT did not fall to normal levels, clinical coagulability was adequate in this patient. Previous reports indicated that APTT of 40–50 s is associated with hemostasis in this disorder [10].

In summary, we have reported a patient with factor XI deficiency for whom transfusion of FFP provided adequate

hemostasis to perform bipolar hip arthroplasty. APTT was a valuable marker of hemostasis in this patient. No other drugs such as rFVIIa, tranexamic acid, or desmopressin were necessary for hemostasis in this patient.

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