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CASE REPORT

Persistent surgical wound bleeding: A rare condition related to acquired hemophilia A

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Summary Acquired hemophilia A (AHA) is a rare condition that predisposes affected patients to a bleeding tendency, even after a trivial physical insult. We present our experience with a 45-year-old male patient who was referred to our institute because of persistent bleeding from a left forearm surgical wound after fasciotomy. He was diagnosed as having AHA. Surgical treatment in combination with recombinant activated factor VII (rFVIIa) led to a satisfactory result. Clinical awareness and multidisciplinary professional connections are necessary in the treatment of AHA. Acquired hemophilia should be considered in the differential diagnosis of patients with uncontrolled bleeding episodes.

1. Introduction

Acquired hemophilia A (AHA) is a condition in which inhibitor autoantibodies are produced against coagulation factor VIII.[1] It is a rare condition, but the associated morbidity and mortality rates are significant.[2] Furthermore, although autoantibodies for other coagulation factors may also develop, inhibitors of factor VIII are the

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most common.[2] The incidence of AHA is estimated between 1.34 and 1.48 cases per million individuals each year, and most (>85%) individuals with AHA are older than 60 years.[2] Some predisposing factors that have been reported for AHA are postpartum status, underlying autoimmune disease, and hematologic or solid cancer.[3] Approximately one-half of AHA patients have no obvious predisposing factors.[4] The most common predisposing conditions for AHA that have been reported are interestingly autoimmune disease and malignancy, which have prevalence rates of approximately 10% and 12%, respectively.[5] In this report we present a relatively young patient who had only a mild physical insult and a dramatic consequence.

2. Case report

A 45-year-old male patient had a medical history of underlying gouty arthritis and cervical spine stenosis that were surgically treated 5 years previously. He had a 2-month history of repeated episodes of ecchymosis around both forearms after minor contusions; however, these symptomatic episodes usually subsided spontaneously. Nothing of significance was noted after the evaluation of his clinical history, except that he had taken an unknown herbal medication for approximately 3 months prior to hospitalization. His current problem followed an insult to his left forearm, which was hit when playing with his son. Progressive swelling, pain, and ecchymosis developed the next day and did not subside. He was admitted to a local hospital for treatment.

Progressive numbness, increasing swelling, and persistent sharp pain occurred after hospitalization. In addition, weak radial arterial pulsation was also noted (this was documented in the referring summary, which was maintained among the medical records of our institute). Because of suspected compartment syndrome, he underwent emergency fasciotomy on day 2 of hospitalization. His preoperative international normalized ratio (INR) was 0.98, and his activated partial thromboplastin time (APTT) was more than 120 seconds (because of the emergency situation, the result of the prothrombin/APTT [PT/APTT] test had apparently been reported after he had been sent to the operating room). However, persistent postoperative bleeding was encountered at the surgical site. Additional attempts to achieve hemostasis produced no obvious benefit, and the patient's clinical condition deteriorated. On postoperative day (POD) 1, he had hypovolemic shock, changes in consciousness, and a hemoglobin level of 4.9 g/dL. Emergency resuscitation such as transfusion and fluid challenge were persistently maintained. On POD 2, the patient was transferred to our institute for further management.

At our emergency department (ED), his initial vital signs, including his level of consciousness, were documented as follows: body temperature of 36°C, pulse rate of 138 beats per minute, respiratory rate of 26 breaths per minute, systolic/diastolic blood pressure of 110/81 mmHg, and alert. As Fig. 1 shows, the left forearm has a large wound with diffuse oozing. Computed tomography was performed at our ED. Active arterial bleeding was noted at the elbow area (Fig. 2). The on-duty plastic surgeon was consulted immediately. However, no definite bleeding site could be identified for suture and ligation. Epinephrine gauze, elastic bandages, and a tourniquet system were all applied for hemostasis. The patient was immediately admitted to the intensive care unit (ICU) for close observation and correction of coagulopathy.

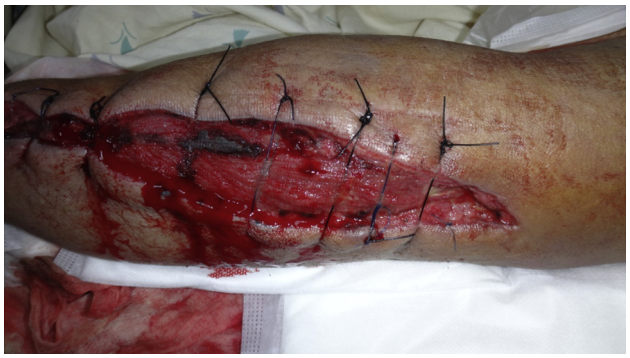

Figure 1 The left forearm on the third day after admission to our hospital. There were no obvious bleeders, but diffuse wound oozing is present.

During the ICU admission, repeated episodes of massive bleeding were noted, requiring multiple blood transfusions. In addition, bedside suture ligation was performed several times to control bleeding. Because of persistent bleeding with coagulopathy, we consulted a hematologist for further evaluation. The hematologist recommended several surveys to assess the coagulopathy, including surveys that evaluated mixing APTT, factor VIII, markers for autoimmune conditions, and possible malignancy.

On account of a prolonged mixing APTT (60.8 seconds) and a low factor VIII level (1.5%), the hematologist recommended a supplemental factor VIII prescription and measurement of factor VIII inhibitor titers. However, even after supplementation of factor VIII, diffuse oozing persisted. The factor VIII inhibitor titer was later reported to be 23.52 Bethesda units (BU). A diagnosis of AHA was established because of the high titer of factor VIII inhibitor and low concentration of factor VIII. On POD 8, recombinant activated factor VII (rFVIIa; NovoSeven RT; Novo Nordisk Inc., West, Princeton, NJ, USA) was prescribed (using 1-mg vials) to activate the extrinsic hemostasis pathway, and prednisolone and cyclophosphamide were administered to suppress factor VIII inhibitors.

Recombinant activated factor VII was administered by intravenous infusion with seven vials every 2 hours for three doses and was then changed to three vials every 6 hours for 2 days. After completing the first treatment cycle, mild oozing of the wound persisted. We then initiated another cycle of rFVIIa treatment, which was completed on POD 16. The patient's later hospital course was uneven (he had an episode of recurrent bleeding), however, he was fully recovered on POD 31 and was discharged with oral immunosuppressant agents. Fig. 3 summarizes the serial hematological data and his coagulation profile during the hospital stay.

This patient was then followed-up at the outpatient departments of the trauma surgery and hematology departments. Three months after the hospital discharge, the factor VIII level had recovered up to 48% (the reference is above 50%) and the immunosuppressant therapy was discontinued.

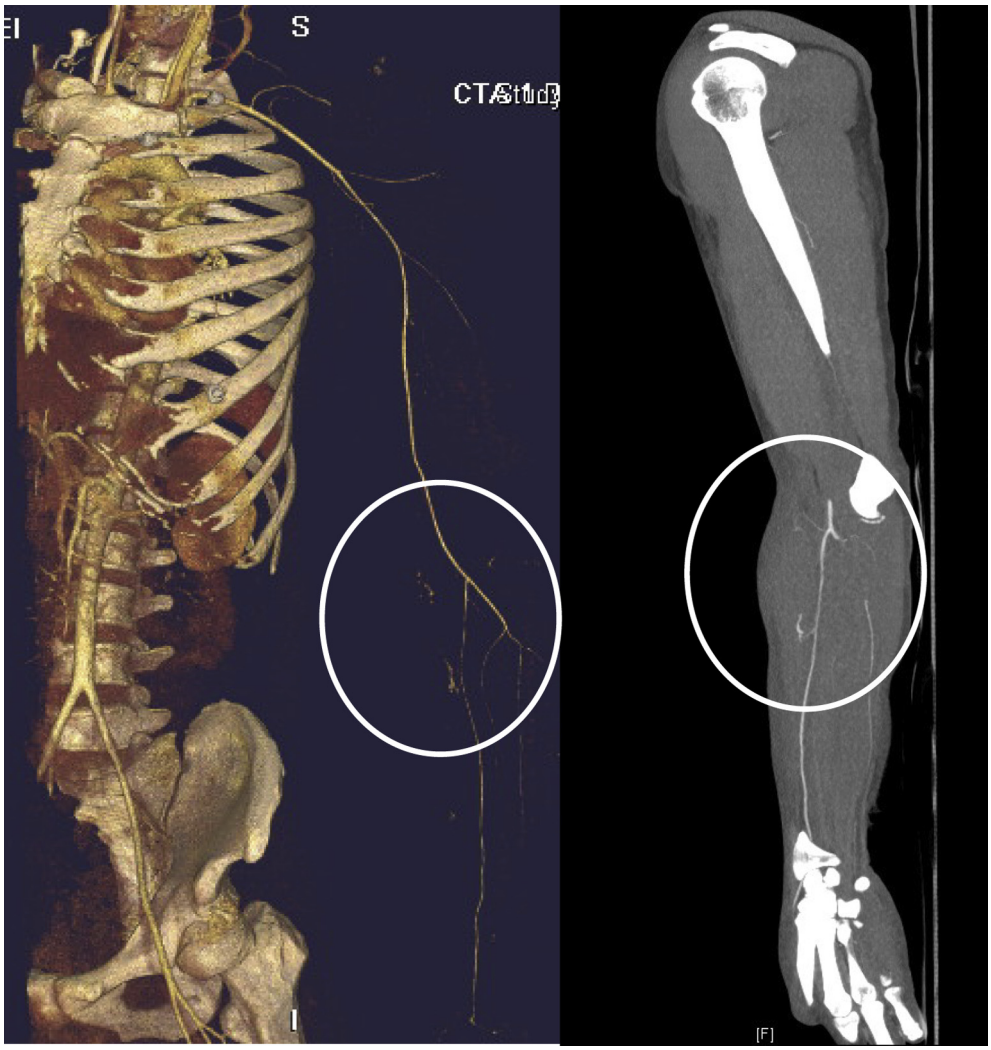

Figure 2 Computed tomography angiography revealed multiple small bleeders in the muscular branch of the left radial artery.

3. Discussion

The most common manifestation of AHA is acute bleeding without an obvious family or personal history of a bleeding disorder.[2] The bleeding episodes are usually induced by minor, easily ignored injuries or by certain invasive procedures. The most common bleeding sites include the skin, subcutaneous tissue, muscle, and occasionally the retroperitoneum.[6] Hemarthrosis, which is commonly noted in congenital hemophilia, interestingly is rarely observed in its acquired counterpart. Well-organized, large series of data are lacking because of the rarity of this disease. The results of the European Acquired Hemophilia (EACH2) Registry were recently released with more than 500 enrolled patients.[5] This relatively large series included patients from more than 100 treatment centers in 13 European countries. It provided valuable demographic data and some clinical information; however, heterogeneity of the included case studies could not be avoided because of the rarity of this condition. According to the EACH2 study, the 5-year survival rate in patients who underwent inhibitor clean-up was 54%, and a poorer result was noted in patients without inhibitor clean-up.[5]

The compartment syndrome of the extremities is a surgical emergency and emergency fasciotomy for pressure release and limb preservation is always the first priority in treatment. A combination of AHA and upper extremity compartment syndrome has been reported, although very rarely.[7] Both surgical intervention and the cutting-edge biopharmaceutical agent recombinant activated coagulation factor VII[8] have been reported with some limited experience.[9] The patient in our report could be a case of successful treatment, if we could confirm the diagnosis of compartment syndrome. Because the patient was transferred from another hospital to our care, we did not have his complete primary clinical documentation or preoperative image. In this report, we therefore cannot insist that a relationship exists between compartment syndrome and AHA.

According to the EACH2 study, the initiation of a hemostatic agent occurred within 1 day in 38.2% of patients, although no significant prognostic difference was noted.[5] In the patient we have described, we initiated rFVIIa on POD 8. Further improvement in the diagnostic process is expected for similar cases. For the orthopedic or trauma surgeon, knowing resuscitation skills is required. The

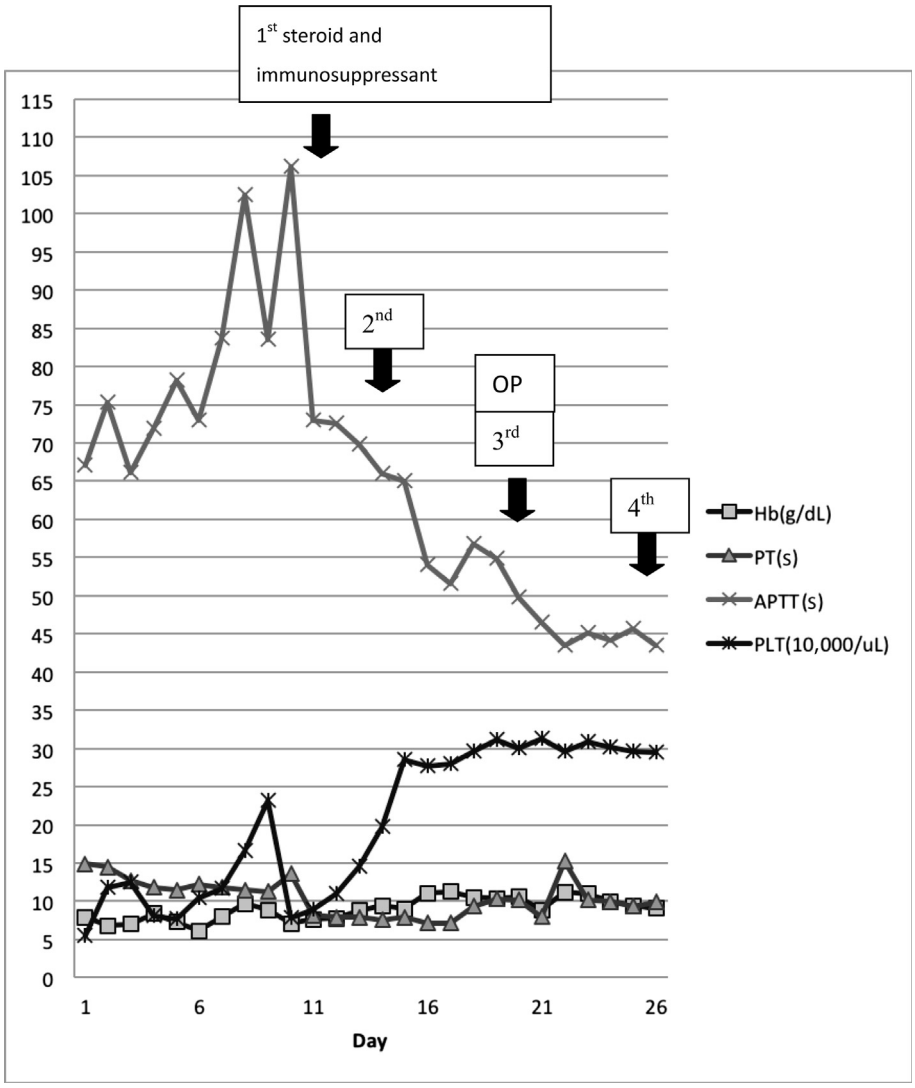

Figure 3 Hematological data during the hospital course. The arrows indicate the start of each cycle of recombinant factor VIIa treatment (4 cycles in total). APTT = activated partial thromboplastin time; Hb = hemoglobin; OP = operation; PLT = platelets; PT = prothrombin time.

surgeon should also know the best practices for the survey of diathesis. For patients with known acquired hemophilia, prophylactic intervention is indicated. However, only a few reports have provided clinical descriptions of the perioperative management of these patients.[10–12] Moreover, the current literature does not provide a consensus for prophylactic intervention, with regard to the administered agent or the strategy. Regular perioperative laboratory check-ups with hematologist consultation and proper medication (for example, rFVIIIa) will be essential in the management of acquired hemophilia in patients for whom surgery is inevitable.

Consent

The patient gave written, informed consent for the publication of this case report and any accompanying images. A copy of the written consent is available for review from the Editor-in-Chief of this journal.

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