Large hemorrhage due to venipuncture in the elbow of a patient with severe hemophilia: A case report and literature review

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Abstract. Hemophilia A, which is the most common form of hemophilia, is caused by a deficiency of clotting factor VIII. The incidence of hemophilia A is 1:10,000 people worldwide. The most common complication associated with hemophilia A is bleeding into joints, predominantly the knees, ankles, and elbows, which may lead to destruction or osteoarthritis of the specific joint. Various degrees of disability may follow these initial or recurrent hemorrhages. Subsequent to improvements in medical management, patients with hemophilia A currently have a life expectancy similar to that of the normal population. However, the management of patients with hemophilia A remains a clinical challenge for various reasons, including the lack of reliable and cost-effective treatment, and the high risk of intra- or post-operative hemorrhages. Large hemorrhages due to the phlebotomizing of young patients are very rare. To the best of our knowledge, the present case is the first report regarding the occurrence of a large hemorrhage due to venipuncture in the elbow of a patient with hemophilia A.

Case report

A 22-year-old boy was diagnosed with hemophilia A 20 years prior to the present report, despite no relevant family history of hemophilia. Written informed consent was obtained from the patient. One month prior to admission in February 2013, a blood sample was taken from a vein in the right elbow of the patient. The venipuncture was followed by pain in the right arm, which is associated with the development of a hemorrhage. An ulcerative hemorrhage with local cutaneous necrosis was detected 10 days following the venipuncture, and the patient was admitted to the Department of Internal Medicine of West China Hospital (Chengdu, China) for further treatment. Coagulation function tests were conducted at 37˚C. Firstly, kaolin was used to activate the XII, in order to replace the platelet factor 3 with cephalin. Then, Ca²⁺ was added to the solution to initiate clotting and observe the coagulation time. The time required for plasma coagulation was the activated clotting time. The activated partial thromboplastin time (APTT) of the patient was 104.6 sec (normal, 20-40 sec), and factor VIII activity was 1.0% (normal, 60-150%). An X-Ray of the elbow exhibited bone erosion and cyst formation. Hemorrhage of the elbow with hemophilic arthropathy and clotting factor VIII inhibitor formation was initially diagnosed. The hemorrhage of the hemophilic arthropathy was caused by the formation of clotting factor VIII. Paraffin fixing and staining with hematoxylin and eosin, the hemorrhagic, with synovium and hemosiderin were distinguished by different color and morphology.

Evacuation of the hematoma in the elbow was initially performed (Figs. 1-5). Intraoperatively, the lesion appeared initially tough with various stages of liquid and solid dark blue hemorrhage. The lesion, which adhered closely to the brachial artery, was completely removed. In addition, part of the musculus biceps brachii and biceps tendon were removed. Considering
the large size of the skin wound (~3x6 cm), the surgeon could not suture the incision; instead, the incision was covered with petrolatum gauze. Coagulation function tests demonstrated that, prior to the surgery, the APTT was 102.3 sec and remained unchanged following surgery. A total of 2,800 units of clotting factor VIII were prescribed every 12 h for the following 4 days, and the APTT was measured to be 102.3 sec following the continuous infusion of factor VIII.

A second operation was performed 10 days after the initial operation. The lesion appeared to be covered with granulation tissue, with necrotic tissue detected in the basal area of the lesion. In the second operation, the skin wound...
Recombinant activated FVII or activated PCC should be used, the dosage intervals may be increased to 3, 4 or 6 h, according at least during the initial 24 h period of treatment; subsequently, bleeding patients, or those undergoing surgery, at 2 h intervals, concentration of activated and non‑activated prothrombin complex concentrates (PCC) and, more frequently, the use of rFVIIa treatment is the primary choice (7). Surgical treatment in patients with hemophilia remains challenging due to the high risk of rebreeding can be avoided, the aggressive treatment is the conservative treatment with both conservative and aggressive therapeutic strategies is necessary. The factor VIII injection is used as the conservative treatment, surgical hematoma clearance is used as the aggressive treatment. The conservative treatment involves control of bleeding and may avoid operational risks, for example, the hemorrhage formation again, and can control bleeding by systemic administration. By contrast, the aggressive treatment may completely resolve the hematoma surgically. If rebreeding can be avoided, the aggressive treatment is the better choice. For the treatment of bleeding in patients with hemophilia, conservative treatment with factor VIII replacement is the primary choice (7). Surgical treatment in patients with hemophilia remains challenging due to the high risk of intra- or post‑operative hemorrhage. In addition, fatal bleeding must be controlled during the perioperative period.

Conservative management in bleeding patients with severe hemophilia and factor VIII inhibitors includes the administration of activated and non‑activated prothrombin complex concentrate (PCC) and, more frequently, the use of rFVIIa concentrate (8). It is recommended that rFVII be administered to bleeding patients, or those undergoing surgery, at 2 h intervals, at least during the initial 24 h period of treatment; subsequently, the dosage intervals may be increased to 3, 4 or 6 h, according to the type and extent of the surgical procedure or bleeding (9). Recombinant activated FVII or activated PCC should be used to control the symptoms (10,12), and recombinant products are increasingly regarded as the preferred choice, due to a low risk of viral infection (5). Rituximab monotherapy may also be considered in the case of surgery‑associated acquired hemophilia; however the effects of immunosuppressive therapies on postoperative wound healing remain unclear (13).

In the present case, the time between the use of conservative (the transfusion of factor VIII) and aggressive treatments (the surgery for evacuation of hematoma) was crucial, as an informed decision can avoid complex or frequent operations. For large hemorrhages, aggressive factor VIII replacement and emergency surgical treatment is still considered at the primary stage. The surgeon and hematologist must work together closely in order to obtain a successful outcome. Data from a previous prospective randomized controlled trial demonstrated that the co‑treatment of a patient by a hematologist and surgeon reduces the incidence of joint hemorrhages and protects against the development of joint damage (5). Blood counts and coagulation function should be routinely monitored following surgery. In addition, it is recommended that factor VIII be infused regularly; the level should be raised to 80‑100% for 7 days, and to 50% for a further 14 days (14).

The present case is the first, to the best of our knowledge, to report a case of a large hemorrhage caused by venipuncture in the elbow of a patient with hemophilia. The results indicate that a systematic analysis of patients to determine the appropriateness of transfusion with factor VIII should be considered for patients with hemophilia A prior to surgery.

In the future, it seems likely that modified molecules, which possess enhanced properties such as reduced immunogenicity and increased half-life, will become available. Numerous clinical trials targeting hemophilia A and B are currently underway (15,16). In addition, developments in gene therapy may provide an attractive model for the treatment of hemophilia, eliminating the need for regular injections of clotting factor VIII.

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References