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Case Report

Acquired Coagulopathy Type Hemophilia A and Loco-Regional Anesthesia: Case Report

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Abstract

Acquired hemophilia A is the most common acquired disease of hemostasis. It is often responsible for minor bleeding. However, it can becomplicated by serious bleeding that can be life-threatening, especially during surgery. The objective of anesthetic management is to correct haemostasis in order to control the per- and postoperative haemorrhagic risk. We describe, through the observation of a patient We describe, through the observation of a patient who underwent two emergency surgeries for a leg hematoma revealing an acquired coagulopathy, the perioperative management strategy for this condition.

Keywords: Acquired hemophilia; Anesthesiology; Surgery; Factor VIII; Recombinant factor VIIIA

Introduction

Acquired Hemophilia A (AHA) is a true orphan disease, a rare condition linked to the development of an autoantibody directed against factor VIII (FVIII). It's frequency of occurrence possibly underestimated, appears to be very low, with approximately one to four cases per million inhabitants and increases with age, switching from less than two per million before the age of 65 to over 15 per million after the age of 85 in the English registry over a two-year period [1] The rarity of the disease poses challenges in delivering a precise description, capturing its evolving profile, and conducting therapeutic studies. As a result, current recommendations are based solely on expert opinions, and the primary objective of perioperative management in patients with this deficiency is to prevent hemorrhage [2,3]. Through the observation of a patient afflicted with this condition, scheduled for a cutaneous skin flap at the site of the ulcer, we describe the perioperative management strategy.

Patient and Observation

Clear and written consent from the patient was obtained before the publication of this case report. The patient in question was Mrs. C.F., a 59-year-old multiparous woman, with a history of psoriasis since childhood treated with corticosteroid-based therapy, and a bullous dermatosis in 2018. She was admitted to the emergency department for the management of an acute swollen right leg. The remainder of the clinical examination was unremarkable. Soft tissue ultrasound was performed, ruling out deep vein thrombosis and suggesting the presence of a calf collection. Surgical intervention was indicated for drainage and irrigation of the collection.

During the pre-anesthetic consultation, her medical history included: psoriasis treated with corticosteroids and the bullous dermatosis. Also the patient had no known allergies, no prior surgeries, and no history of alcohol or tobacco use.

The clinical examination revealed a weight of 60kg, a height of 1.68m, a body mass index of 21.3kg/m, a good tolerance to exercise with a functional capacity greater than 4 METs, and no angina triggered by physical exertion. Blood pressure was 120/60mmHg, and the SpO2 was at 98% in ambient air.

The general examination revealed the swollen acute leg. The remaining cardiovascular and pleuro-pulmonary exams were

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normal. Assessment of the upper airway revealed intact native dentition, a thyromental distance greater than 6.5cm, a Mallampati score of II, and a buccal opening greater than 35mm with a flexible neck.

Based on this evaluation, the patient was classified as ASA II, Mallampati II, and was scheduled for low-risk hemorrhagic and cardiovascular surgery, specifically, drainage and irrigation of the collection with bacteriological testing of the aspirated fluid.

The anesthesia protocol included loco-regional anesthesia after informing and obtaining consent from the patient.

The procedure took place on the same day, a few hours later. After verifying pre-operative fasting, the patient was admitted to the operating room. Positioned in a supine position position, monitoring included Non-Invasive Blood Pressure (NIBP), arterial oxygen saturation (SpO2), and Heart Rate (HR) was initiated. A peripheral venous access (18G) was established on the left hand, and an infusion of 250ml of isotonic saline 0.9% was initiated. The Antibiotic prophylaxis was administered with cefazoline (2g).

A median spinal anesthesia using a 25G needle, with the administration of hyperbaric Bupivacaine (7.5mg) combined with Fentanyl 50µg and Morphine 100µg, was subsequently performed without notable incidents.

The surgical procedure proceeded without complications or major bleeding. The immediate post-operative course was uneventful in the Post-Anesthesia Care Unit (PACU), with a return of motor function to level H5 and sensory function to level H6, along with an observation of diuresis. The patient was transferred to the trauma service.

After 48 hours, the patient experienced a recurrence of the acute leg swelling on the same side. Ultrasound revealed a collection in the leg, and a follow-up leg CT scan confirmed the presence of a hematoma in the gastrocnemius muscle. The surgical intervention was indicated for the purposes of conducting surgical exploration, hematoma drainage, and irrigation.

The second procedure took place on the same day. After confirming pre-operative fasting, the patient was readmitted to the operating room. The anesthesia protocol included loco-regional anesthesia with prior informed consent from the patient. The intervention proceeded without complications.

The Immediate post-operative recovery in the Post-Anesthesia Care Unit (PACU) was uneventful, with a return of motor function to level H5 and sensory function to level H6, as well as the observation of diuresis. The patient was then readmitted to the trauma service, where she remained for 72 hours. Due to significant improvement and the absence of both immediate and delayed complications, as well as sterile bacteriological samples, the patient was discharged.

Two months later, the patient presented to the emergency department with a hemorrhagic syndrome characterized by purpura ecchymosis, gingivorrhagia, and clotting hematuria. General examination revealed an ulceration on the right leg, with the rest of the examination being unremarkable.

The initial hemostasis assessment showed a hemoglobin level of 11.9g/dl, a Quick time by normal chronometric method at 14.8/13.5 (INR 1.11), and an extended activated partial thromboplastic time (aPTT) at 116/36 (a ratio of 3.2).

Further hemostasis evaluation revealed the presence of inhibitors against coagulation factors VIII, IX, XI, and XII, with predominant activity against FVIII, showing an activity level of 1% and an inhibition level of 99%. The anti-FVIII dosage yielded a measurement of 748UB/ml. The diagnosis of acquired hemophilia A was established, and other investigations ruled out infection, autoimmune disease, and neoplasia. During the pre-anesthetic consultation, the patient was classified as ASA II, Mallampati II, and scheduled for low-risk hemorrhagic and cardiovascular surgery: a cutaneous skin flap at the site of the ulcer.

The anesthesia protocol included general anesthesia following informed consent from the patient.

The procedure took place three days later. After confirming pre-operative fasting, the patient was admitted to the operating room and placed in a supine position. Monitoring was initiated, including Non-Invasive Blood Pressure (NIBP), arterial oxygen saturation (SpO2), and Heart Rate (HR). A peripheral venous access (18G) was established on the left hand, and an infusion of 250ml of isotonic saline 0.9% was initiated.

The recombinant FVIIa treatment was initiated 30 minutes before the procedure at a dose of 4.5KIU/kg of body weight, equivalent to 5.4mg administered over 5 minutes. The antibiotic prophylaxis was administered with cefazoline (2g). Preoxygenation was performed with a high-concentration mask at 8L/min.

The Anesthetic induction was achieved with 250µg of fentanyl, 120mg of propofol, and 40mg of rocuronium bromide. Orotracheal intubation was performed without difficulty (Cormack and Lehane grade I, vocal cords in abduction) using a size 7.0-mm endotracheal tube, and the patient was connected to the ventilator after confirmation of tube placement and symmetrical lung auscultation. Ventilation was maintained in volume-controlled mode.

The surgical procedure, lasting 45 minutes, involved a skin flap at the ulcer site. Blood loss was negligible, with a total fluid input of 1.5L of isotonic saline 0.9%. Throughout the procedure, the patient maintained stable blood pressure between 100-110/55-60mmHg and a heart rate between 70 and 80 beats/min. SpO2 remained at 100%, and end-tidal CO2 was maintained at 35mmHg. In the Post-Anesthesia Care Unit (PACU), after warming and full awakening, the patient was extubated twenty minutes after the end of the procedure and then transferred to the ward. At the end of the intervention, a reinjection of recombinant FVII at the same dose administered.

Discussion

The Acquired Hemophilia A (AHA) results from the development of autoantibodies directed against Factor VIII (FVIII), leading to the inhibition of the coagulation cascade, which can cause sometimes severe hemorrhages. Typically, the diagnosis is suspected when a sudden and often pronounced hemorrhagic syndrome occurs, with no personal or family history of hemorrhagic disorders.

The clinical presentation differs from that observed in congenital hemophilia (excluding mild forms), where hemorrhages predominantly affects joints and muscles. In fact, the hemarthrosis are less common in acquired hemophilia, and patients often develop hemorrhagic complications, which can be life-threatening or not. These complications can encompass the

diffuse spontaneous ecchymosis, as well as muscular, gastrointestinal, intracerebral hemorrhages, hematuria, and epistaxis. (>90% of cases). The laboratory diagnosis of AHA is straightforward and defined by the combination of isolated prolonged activated partial thromboplastic time (aPTT), a low FVIII level (<30% or 50%), and the presence of a detectable anti-FVIII antibody dose ≥ 0.4 IU/ml as determined by the "Bethesda" method [3-5].

In the context of scheduled surgery, the treatment aims to correct the coagulation in order to prevent and control the hemorrhages. Consequently, perioperative management necessitates a multidisciplinary approach, requiring close collaboration among the anesthesiologist, hematologist, medical biologist, and surgeon.

The perioperative management begins with a thorough patient history, which includes details regarding the circumstances of the diagnosis and any prior hemorrhagic episodes, including how they were managed. Hemostasis assessment, initially included Prothrombin Time (PT), Activated Partial Thromboplastic Time (aPTT), and platelet count, in addition it was supplemented by the measurement of factor VIII levels, allowing for the quantification of the severity of the disease.

Thus the disease is classified into three severity grades: high if the factor activity is <1%, intermediate if it is between 1% to 5%, and low risk if it's >5%. The level of autoantibodies also needs to be specified to determine the therapeutic protocol. These clinical-biological data serve to evaluate the hemorrhagic risk associated with surgery hence it guides us towards the appropriate therapeutic strategy aimed at correcting coagulation [6,7].

In the case of our patient, the diagnosis of intermediate-severity Acquired Hemophilia A (AHA) was established due to recurrent cutaneous-mucosal hemorrhages, low factor VIII (FVIII) activity levels, and the presence of anti-FVIII autoantibodies. The surgery for which she was scheduled is considered low-risk for hemorrhages. There are two perioperative preparation strategies: "Bypass Hemostatic Therapy" and "Replacement Therapy Preparation," the choice of which depends on the level of autoantibodies [7].

The first strategy, "Bypass Hemostatic Therapy," is the first-line treatment. It aims to bypass the FVIII inhibitor by using either activated prothrombin complex concentrate (FEIBA®) or recombinant FVII (NovoSeven®) [8]. For FEIBA, it is administered at doses of 50-100U/kg two or three times a day, with a maximum of 200U/kg/day until bleeding is controlled. Its efficacy is approximately 86% [8,9].

As for recombinant FVII (NovoSeven®), it is initiated with doses of 90mcg/kg every 2 hours, followed by lower doses to prevent recurrence [10, 11]. The efficacy of FVIIa is 100% when used as first-line therapy and approximately 75% in cases used in the advanced stage of the disease, despite its thrombotic tendencies, which remain around 7% [12,13].

Regarding the second preparation strategy, it is only recommended when the level of autoantibodies is very low (<5IU/ml) [14]. Its goal is to neutralize these autoantibodies, and hemostasis can be achieved with high doses of FVIII [15]. However, the response to this treatment is unpredictable, and its use should not delay the use of agents more likely to control bleeding. Nevertheless, FVIII is more effective when used as part of a multimodal therapeutic regimen that includes immunosuppressant capable of eliminating the inhibitor temporarily [16].

For our patient, the first strategy was recommended by administering recombinant FVIIa (NovoSeven®) at a dose of 90mcg/kg 30 minutes preoperatively, given the low hemorrhagic risk associated with the surgical procedure. In the absence of post-operative bleeding, we opted for reinjections every 2 to 4 hours for 48 hours, with a favorable outcome.

The choice between General Anesthesia (GA) or Loco-Regional Anesthesia (LRA) depends primarily on pre-operative preparation, although guidelines do not recommend LRA for patients with hemophilia. A recent systematic review of 507 loco-regional anesthesia techniques (spinal anesthesia, combined spinal-epidural, epidural analgesia, and paravertebral block) for patients with hemophilia and Von Wille brand disease reported only one complication in which the bleeding diathesis was not diagnosed before needle insertion. This case involved a spinal hematoma following lumbar puncture in a hemophiliac, leading to permanent paraplegia [17].

Post-operative analgesia includes analgesics from various classes. Nonsteroidal anti-inflammatory drugs should be avoided as they increase the risk of hemorrhages. Thromboprophylaxis should be implemented in accordance with guidelines, along with supplementation with recombinant FVIIa. In our case, analgesia was provided with acetaminophen, and the thromboprophylaxis was insured by mechanical means.

Conclusion

Acquired Hemophilia A (AHA) is the most common acquired disorder affecting the hemostatic system. It often leads to minor bleeding episodes but can also result in severe hemorrhages that may be life-threatening, especially during surgical procedures. To reduce this operative risk, it is imperative for every anesthesiologist to have a better understanding of the pathophysiology of the disease and the principles of perioperative management.

Author Statements

Conflicts of Interest

The authors declare no conflicts of interest.

Authors' Contributions

All authors have read and approved the final version of the manuscript.

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