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Case Report

Anesthesia Management of Severe Hypofibrinogenemia: A Case Report and Literature Review

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Abstract

Hereditary fibrinogen disorders are a group of rare coagulation diseases subdivided according to the quantity or quality of circulating fibrinogen. Hypofibrinogenemia's prevalence is unknown, but it is considered more frequent than afibrinogenemia, which has an estimated prevalence of around 1 in 1,000,000. So, it is not commonly seen in clinical practice. Yet, it may present a relevant challenge for the anesthesiologist, as patients with hypofibrinogenemia are more prone to complications related to bleeding following the slightest trauma or surgery.

We report the case of a 5-year-old boy who was diagnosed with severe hypofibrinogenemia following mucosal bleeding in the neonatal period and who was scheduled for a circumcision. He was admitted initially to the hematological department for preoperative preparation. Due to the unavailability of plasma-derived fibrinogen concentrate, he received a single dose of 20cc/kg fresh frozen plasma before surgery and then was admitted to the operating theatre. The surgical procedure was uneventful, with minimal intraoperative bleeding.

Our case emphasizes the role of prevention in the perioperative management of patients with hereditary fibrinogen disorders. To improve patient outcomes, proper assessment, rigorous preparation before surgery, and optimal intraoperative management are required. Prophylactic treatment remains the gold standard for these patients, but more work needs to be done, especially regarding the correct way to achieve more effective treatment.

Keywords: Hereditary fibrinogen disorders; Coagulation diseases; Anesthesia; Surgery

Introduction

Hypofibrinogenemia is a rare inherited abnormality of agulation. It is a quantitative fibrinogen disorder characterized by a low ibrinogen level [1]. Its prevalence is unknown but considered more frequent than afibrinogenemia which has an estimated prevalence of around 1 in 1,000,000. Nevertheless, this rate tends to rise in countries with a high prevalence of consanguinity, making it more frequently observed in clinical practice. Yet, it may present a relevant challenge for the anesthesiologist, as patients with hypofibrinogenemia are more likely to experience severe bleeding complications even from minor injuries or surgeries. Their perioperative management remains crucial to prevent this outcome that could be life-threatening.

Case Presentation

We report the case of a 5-year-old boy weighing 18 kg, born to consanguineous parents, who was scheduled for a circumcision. His family history includes two deceased brothers, one of whom died due to severe bleeding caused by the fall of the umbilical cord. The boy was diagnosed with severe hypofibrinogenemia during the neonatal phase following a spontaneous mucocutaneous hemorrhage. Following the pre-anesthetic visit, and considering his medical history, blood tests were done. The results revealed a plasma fibrinogen concentration of less than 0.2 g/l, a low prothrombin ratio (PR) of 29%, a prolonged patient/control activated partial thromboplastin time (aPTT) ratio of 1.37, anemia with hemoglobin at 10 g/dl, and a normal platelet count at 150000/mm^3. Physical examination revealed stable vital signs without hemorrhagic manifestation. Subsequently, he was admitted to the hematological department for preoperative care. According to our local protocol, given the unavailability of plasma-derived fibrinogen concentrate, he received a single dose of 20 ml/kg fresh frozen plasma before surgery. The patient was then admitted to the operating theatre with a 24-gauge venous line, while being constantly monitored by the electrocardiogram, pulse oximeter, and non-invasive blood pressure. Anesthetic sedation was achieved using increased concentration of sevoflurane in oxygen. A dorsal penile nerve block was then performed by the surgeon using Lidocaine 1%. The surgical procedure was uneventful, with minimal intraoperative bleeding estimated. The fibrinogen level remained stable at approximately 1 g/L during the postoperative period, with no hemorrhagic manifestations. Thereby, the patient was then discharged on day 3.

Discussion

Hypofibrinogenemia is a rare autosomal recessive bleeding disorder characterized by a low fibrinogen level. According to the European Network of Rare Bleeding Disorders (EN-RBD) with the support of the International Society of Thrombosis and Hemostasis, quantitative fibrinogen disorders are classified into mild hypofibrinogenemia (lower limit of normal level—1.0 g/L), moderate hypofibrinogenemia (0.9–0.5 g/L), severe hypofibrinogenemia (0.5–0.1 g/L), and afibrinogenemia (unmeasurable fibrinogen level < 0.1g/L) [2,3].

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Fibrinogen is a hexamer composed of two identical parts of three homologous polypeptide chains (Aα, Bβ, and γ), interconnected by a complicated series of disulfide bonds [4,5]. The disorder is caused by variations in the FGA, FGB, and FGG genes, located on chromosome [4,5]. Afibrinogenemia is associated with homozygous or compound heterozygous mutations, and hypofibrinogenemia is usually secondary to heterozygous mutations [6].

Clinical presentations of quantitative fibrinogen disorders are very variable. For afibrinogenemia, bleeding incidents are the major symptoms, whereas hypofibrinogenemia presentations depend on the fibrinogen levels [4]. There are two clinical phenotypes. Firstly, the classic bleeding phenotype is mainly presented by umbilical cord bleeding in neonates manifesting in more than 85% of cases [4], or intracranial bleeding in childhood which could lead to death. Secondly, patients could paradoxically present the thromboembolic phenotype. Both arterial and venous locations have been reported [4]. Theoretically, fibrinogen deficiency does not compensate for a hypercoagulability state. Moreover, the thrombin half-life in circulation is prolonged in cases with low fibrinogen levels as the antithrombin function of fibrin is absent, and its generation is also increased [7]. However, the rationale behind the increased thrombotic risk has yet to be entirely understood. Some risk factors were identified [4] such as genetic thrombophilia, use of fibrinogen replacement therapy, immobilization, pregnancy, or trauma. Therapeutic management remains unclarified for these clinical situations. Low molecular weight heparin was validated in certain cases, but no data is available on the safety of direct oral anticoagulants [7].

The key goal in managing fibrinogen disorders is to prevent and treat severe bleeding and any thrombotic complications. Systematic prophylaxis is usually unnecessary. Nonetheless, patients with afibrinogenemia or severe hypofibrinogenemia can be treated prophylactically in the perioperative period. Depending on the nature of the surgery and the bleeding risk, a residual circulating level of at least 1 g/L or 1.5 g/L until cicatrization is necessary [8]. Despite the absence of recommendations, it is not acceptable to aim for higher fibrinogen levels due to the associated thrombotic risk. Fibrinogen concentrate is the therapy of choice. Compared with fresh frozen plasma (FFP), plasma-derived factor concentrate allows better dosage adaptation and reduces the risk of transfusion complications. In case of unavailability, cryoprecipitate or FFP could be administrated. FFP has several drawbacks: such as a decreased amount of fibrinogen, so the volume transfused is important with a fluid overload risk; in addition, there are transfusion-related risks e.g. transfusion-related acute lung injury and transmission of virus infections [9]. On the other hand, cryoprecipitate needs compatibility testing, and thawing, making its usage complicated [9].

Antifibrinolytic treatment (tranexamic acid) may also be proposed to prevent bleeding during the perioperative period. The usual posology for children is 15 mg/kg. On the other hand, antifibrinolytics are contraindicated in patients at risk of thrombotic events [2]. Some precautions must be taken in the operating theatre. Nasal intubation must be avoided unless necessary to prevent submucosal hemorrhages. Additionally, pressure points must be protected during patient positioning to avoid intramuscular hematomas or hemarthrosis. Hemodynamic stability is a major requirement since tachycardia and hypertension can worsen bleeding and complicate surgical hemostasis. We must not overlook the surgeon's responsibility to ensure meticulous hemostasis. This latter can be controlled during surgery using thromboelastometry or routine coagulation tests.

Conclusion

Congenital fibrinogen disorders represent an unusual and challenging case for the anesthesiologist. It requires proper assessment, rigorous preparation before surgery, and optimal intraoperative management to improve patient outcomes. Unfortunately, data on the perioperative management of quantitative fibrinogen disorders patients is scarce and primarily consists of case reports or small patient series. Thus, further research is essential in this field, especially regarding the correct way to achieve more effective treatment.

Authors' Contributions

Safae Dehbi, Fatima Zahera Filahi, Aziza Bentalha: patient management,

Safae Dehbi, Larbi Dafali, Alae Elkoraichi, Aziza Bentalha: data collection,

Safae Dehbi and Aziza Bentalha: manuscript drafting,

Aziza Bentalha and Salma ECH Cherif El Kettani: manuscript revision.

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

Consent

The author obtained written informed consent from the patient's family for submission of this manuscript for publication.

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