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Case Report

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First case report of perioperative management in a novel entity of macrothrombocytopenia: the autosomal dominant macrothrombocytopenia with platelet dysfunction associated with reduction of surface αIIbβ3

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Abstract

Autosomal dominant macrothrombocytopenia with platelet dysfunction associated with reduction of surface αIIbβ3 (ADM) is an autosomal dominant form of Glanzmann's thrombasthenia reported in few families in the literature. This case presents the first report of perioperative approach of a patient with ADM successfully submitted to a surgical procedure. The multidisciplinary approach including immunohaemotherapy consultation was considered the best clinical approach to avoid bleeding. The use of desmopressin and tranexamic acid in the preoperative period followed by desmopressin plus aminocaproic acid in the postoperative period showed to be safe and effective in the perioperative approach of the patient with ADM.

Keywords: Glanzmann's Thrombasthenia, Thrombocytopenia, Haemorrhage, Risk Management

Introduction

Glanzmann's thrombasthenia (GT) is the most frequent inherited autosomal recessive platelet bleeding disorder characterized by the platelets failure to aggregate due to physiological agonists stimulation, albeit a normal platelet count and size. GT is caused by mutations of the *ITGA2B* or *ITGB3* genes producing defects of integrin αIIbβ3 also known as glycoprotein IIb-IIIa, the most abundant platelet surface receptor [1]. Although large heterogeneity has been described for GT in the literature, there are only few reports of unrelated families described as having an autosomal dominant form of this disease [2-5]. This new entity was described as an autosomal dominant macrothrombocytopenia with platelet dysfunction associated with previously undescribed *ITGA2B* and *ITGB3* mutations and has been included in the list of hereditary platelet disorders [6]. The characteristics of this autosomal dominant macrothrombocytopenia are moderate to severe mucocutaneous bleeding, mild macrothrombocytopenia associated with platelet dysfunction with a moderate reduction of surface αIIbβ3, reduced fibrinogen binding and expression of activated αIIbβ3 upon stimulation, impaired platelet aggregation to physiological agonists but not to ristocetin, normal clot retraction, normal platelet adhesion to immobilized fibrinogen but reduced platelet spreading and tyrosine phosphorylation, indicating defective αIIbβ3-mediated outside-in signalling [3, 7-9].

While there are multiple reports of patients with Glanzmann's thrombasthenia undergoing surgery, to the best of our knowledge there has been no report of a patient with autosomal dominant macrothrombocytopenia with platelet dysfunction associated with reduction of surface αIIbβ3 (ADM) submitted to surgery. The authors report the first and successful perioperative management of a 22-year-old female suffering from ADM submitted to elective pilonidal cyst surgical removal under monitored anaesthesia care (MAC) with preoperative administration of intravenous (IV) desmopressin plus tranexamic acid and postoperative desmopressin nasal plus oral aminocaproic acid.

We consider critical the publication of this case report in order to standardize the perioperative care of patients with ADM.

Case Report

A 22-year-old female with ADM was scheduled for surgical removal of a pilonidal cyst. A positive past history of frequent episodes of epistaxis, abundant menorrhagia with blood clots, prolonged bleeding time with direct trauma and easy bruising. There was no record of other medical history and never had surgery before. No other alterations in the physical examination were found. Her height was 170 cm and her weight 68 kilograms. The patient was classified as American Society of Anesthesiologists (ASA) physical status 2. The results of preoperative laboratory testing revealed isolated thrombocytopenia with 92,000 platelets/μL and a mean platelet volume of 12.3 fL. Preoperative clotting

screen (PT, APTT, INR) was within normal range. After multidisciplinary discussion, the immunohaemotherapy prescription included 24 µg of desmopressin in a slow intravenous infusion, lasting 30 minutes, and 1 g of intravenous tranexamic acid all administered one hour preoperatively. Surgery was performed under MAC with ASA standard monitoring, using 150 µg of fentanyl and 2 mg of midazolam IV plus local infiltration with lidocaine (250 mg). Intraoperative period was uneventful. The surgical incision was left open with *Inadine*® dressings. Postoperative analgesia was achieved with paracetamol IV avoiding nonsteroidal anti-inflammatory drugs. Desmopressin nasal (300 µg) at 24 and 48 hours and oral aminocaproic acid (6 g) 3 times a day for 7 days after surgery were prescribed. The lowest platelet count was seen on the first postoperative day (83,000 platelets/microL) without clinical signs of bleeding. The patient recovered without any episode of bleeding and was hospital discharged in 48 hours. During the 1-month follow up no complications were identified.

Discussion

Thrombocytopenia is the most prevalent haemostasis disorder in clinical practice, however congenital forms are rare [10]. Congenital macrothrombocytopenias comprise a heterogeneous group of rare disorders often not diagnosed and characterized by abnormal giant platelets, thrombocytopenia and bleeding tendency with variable severity.

Autosomal dominant macrothrombocytopenia with platelet dysfunction associated with reduction of surface αIIbβ3 caused by specific mutations in one or both of the two integrins of the GPIIb–IIIa complex is a new entity reported in few families in the literature [2-5]. This entity features include a quantitative platelet disorder and a degree of platelet impaired function as the expression of the platelet glycoprotein IIb-IIIa membrane receptor is reduced and it has been shown to be the pivotal mediator of platelet aggregation [11]. Bleeding risk of this syndrome has not been yet quantified and may be highly variable during surgery. The perioperative use of desmopressin in the described case was supported by the available data. The efficacy of desmopressin is demonstrated in macrothrombocytopenia disorders and, more generally, in congenital platelet dysfunctions. The mechanism of action of desmopressin is related to an increase in the plasma concentration of von Willebrand factor with consequent promotion of platelet adhesion and aggregation, which was consensual as a viable approach for the described syndrome after some debate among the concerned clinicians [12]. On the other hand, tranexamic and aminocaproic acid, antifibrinolytic agents, are also widely used to prevent and treat haemorrhage [13, 14]. To the extent of our knowledge no other cases have been reported of patients with ADM submitted to surgery. Therefore, the anaesthetic management of the potential bleeding risk in patients with this syndrome is not well known and may be challenging. Since this entity is underdiagnosed, in the case of intraoperative haemorrhage in a patient with low platelet count, we should suspect of ADM and consider performing treatment as described by the authors in this case, making a postoperative investigation of the clinical situation. Further studies are required to know more about the frequency of the mutations in the ITGA2B and ITGB3 genes as a cause of macrothrombocytopenia and to establish the bleeding risk of these patients and whether other therapies are necessary to control potentially life-threatening haemorrhage. It would be also important to understand if it would be useful to screen for these mutations in the wide range of patients associating lifelong thrombocytopenia and platelet anisocytosis but where the molecular cause remains unknown as, for example, patients with immune thrombocytopenic purpura without detectable antibody production for eventual optimized bleeding treatment [15].

Conclusion

Anti-fibrinolytics and desmopressin have been used in the perioperative management of a patient with autosomal dominant macrothrombocytopenia with platelet dysfunction associated with reduction of surface αIIbβ3 submitted to minor surgery. This strategy for the anaesthetic management of the bleeding risk has proven successful, although other occurrences of the described syndrome haven't been found in the literature and further data is essential to validate this approach.

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