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Case Report

Anesthetic Management of a Patient with ARC Syndrome - Arthrogryposis, Renal Dysfunction, and Cholestasis: A Case Report

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Abstract: ARC Syndrome, characterized by arthrogryposis, renal dysfunction, and cholestasis, is a rare genetic disorder often resulting in early mortality due to complications such as bleeding. This report details the anesthetic management of a 14-year-old male with type 1 ARC Syndrome, scheduled for gastrostomy and incisional hernioplasty due to severe malnutrition. The patient was presented with minor but relevant oral bleeding during surgery and, after receiving desmopressin, platelets transfusion and tranexamic acid, was able to be safely extubated. This case underscores the importance of thorough pre-anesthetic evaluation and tailored management strategies to address unique challenges presented by ARC Syndrome, particularly concerning coagulopathy and airway management. While existing literature on anesthetic approaches for ARC patients is limited, strategies such as desmopressin and tranexamic acid may offer benefits in managing bleeding tendencies, warranting further investigation into their effectiveness in this context.

Keywords: ARC Syndrome; Platelets; Tranexamic Acid; Desmopressin.

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1. Introduction

ARC Syndrome — arthrogryposis, renal dysfunction, and cholestasis — is a rare autosomal recessive genetic disorder caused by mutations in the *VPS33B* or *VIPAR* genes, with relatively recent documentation, the first report published in 1973 [1]. The broad spectrum of phenotypes generated by different mutations remains incompletely characterized, particularly in cases with milder symptoms where diagnosis may be more challenging and delayed [2, 3]. Furthermore, it is known that most patients with this diagnosis succumb within the first year of life due to bleeding, recurrent infections, or acidosis [2]. Managing surgical cases in patients with this syndrome can be challenging due to the lack of information regarding management and the complexity of the clinical presentation.

Considering these challenges, we present a case that highlights a successful surgical management and outcome in a patient with ARC Syndrome who was scheduled for gastrostomy and incisional hernioplasty and subsequently encountered intraoperative bleeding, which required careful intervention.

2. Case Report

The patient was a 14-year-old male, weighing 24 kg, diagnosed with type 1 ARC Syndrome, who was, at the time, being fed via nasoenteric tube (NET) and presented with severe malnutrition. He also exhibited hypersplenism, hepatic steatosis, sensorineural

hearing loss, and significant developmental delay. His preoperative labs revealed pancytopenia (hemoglobin 11 g/dL; platelets 37,000/μL; leukocytes 1,550/μL), compromised renal function, and conventional coagulation tests within normal limits.

He was scheduled for a gastrostomy and incisional hernioplasty. Airway assessment showed good cervical mobility, an oral opening greater than 3 cm, and Mallampati classification class 2. ASA standard monitors were employed, and anesthesia was induced with fentanyl, propofol, and rocuronium. Ventilation and orotracheal intubation proceeded without complications. Throughout the case, anesthesia was maintained with sevoflurane. Desmopressin 0.3 mcg/kg was initiated and infused over 30 minutes.

Since the incisional hernioplasty carried significant pain potential and neuraxial blocks were contraindicated due to thrombocytopenia, multimodal venous anesthesia was chosen (methadone, ketamine, and magnesium sulfate were administered). The choice of methadone was primarily driven by its NMDA receptor antagonism and the safer profile in a patient with chronic kidney disease. There was no reported complication intraoperatively. The estimated blood loss was minimal. Neuromuscular reversal was achieved with sugammadex 4 mg/kg, guided by neuromuscular block monitoring.

After removal of the NET, near the end of the surgical procedure, sanguineous secretions were noted during aspiration of the upper airway, which were recurrent. It was decided to keep the patient intubated to protect the airway until the bleeding resolved. Postoperative labs revealed a hemoglobin of 9,8 g/dL and platelets of 36,000/μL. A pool of platelets was transfused, and 10 mg/kg of tranexamic acid was administered. The patient was extubated the next morning after complete resolution of oral cavity bleeding, with no recurrence and adequate pain control.

3. Discussion

Given that this syndrome affects multiple systems, a thorough pre-anesthetic evaluation is essential. Depending on the patient's age and degree of cooperation, airway assessment can be challenging. Our patient was 14 years old, possibly the oldest reported child with this syndrome, and despite neurodevelopmental delays, he demonstrated good cooperation. Generally, despite joint involvement in the syndrome, difficulties in ventilation and/or intubation do not appear to be the norm. A brief literature review found no reports of difficult airway management in this patient population.

Regarding laboratory examinations, requesting a complete blood count, coagulation profile (especially in the presence of a history of bleeding), and renal function tests is mandatory. Although fibrinogen alterations are not usually described, requesting such a test is relevant in the context of bleeding, and this is one of the criticisms regarding the management of the current case.

For this particular case, prophylactic administration of desmopressin was performed. This drug, primarily used for the treatment of von Willebrand disease, is a vasopressin analogue that stimulates the release of von Willebrand factor and factor VIII, optimizing platelet adhesion. It is known that patients with ARC Syndrome, even with normal platelet counts, can present with coagulopathy due to various alterations in platelet morphology and function, similar to Gray Platelet Syndrome, where alpha-granules are lost. In this syndrome, the use of desmopressin is well documented in the literature [4;5]. Ideally, qualitative platelet studies should be conducted prior to surgical procedures.

Although in the case presented the patient, despite having chronic kidney disease, was not uremic, it is important to note that the use of desmopressin as a hemostatic agent in acute or chronic uremia to control acute bleeding appears to be beneficial [6]. Additionally, the use of desmopressin is considered safe, but it is important to emphasize that it is associated with some adverse effects, such as facial flushing, antidiuresis, hypotension, compensatory tachycardia, hyponatremia, and, rarely, seizures [6;7].

Weyand et al. describe a successful case of recurrent prophylactic platelet transfusions associated with antifibrinolytic administration in a patient with frequent severe

bleeding episodes secondary to ARC Syndrome [4]. In our case, the transfusion was therapeutic. This more restrictive approach aims to prevent the development of antibodies and the occurrence of various potential adverse effects. HLA alloimmunization is the main cause of refractoriness to platelet transfusions [8], and therefore, alternative strategies to transfusion should always be considered when possible.

The use of lysine analogues, such as tranexamic acid, reduces bleeding and is associated with a decrease in bleeding time in patients with platelet disorders [9]. This class of drugs inhibits fibrinolysis by reversibly binding to plasminogen, preventing its binding to tissue plasminogen activator. Consequently, plasminogen is not activated to plasmin, reducing fibrin cleavage. Its effect in platelet disorders is due, in part, to stabilizing the clot and potentially decreasing the degradation of von Willebrand factor itself. However, although there is no robust evidence for its use in thrombocytopenia, especially in ARC Syndrome, its use is encouraged due to its potential benefits with minimal adverse effects and low cost [7].

Considering that the clot is primarily formed by the platelet plug and the fibrin network, another potential strategy to prevent and treat bleeding in patients with platelet disorders would be increasing the concentration of fibrinogen. The use of fibrinogen concentrates and/or cryoprecipitate, however, lacks studies showing evidence of benefit in thrombocytopenic patients in general and, especially, in patients with ARC syndrome [7]. Finally, it is essential to emphasize that basic care for maintaining normothermia, adequate plasma calcium levels, treatment of acidosis, and anemia remain priorities in this patient population.

4. Conclusion

As a rare disease with high mortality within the first year of life, most approaches to anesthetic management, particularly concerning bleeding, are based on a few reports and extrapolation from current knowledge about other disorders. It is still not possible to guarantee the effectiveness of drugs like desmopressin and tranexamic acid in the pathophysiology of coagulation disorders in these patients but considering the recurrence of life-threatening bleeding and the need for repeated transfusions, every effort should be made to reduce the number of transfusions, thereby minimizing the occurrence of alloimmunization and other adverse effects (including sepsis). Therefore, further research should be conducted to validate the use of such strategies in patients with ARC syndrome, especially since these are medications with an excellent safety profile and low cost.

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