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A Potentially Fatal Reaction to Dipyrone: Should we Continue Using it?

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Introduction

Perioperative anaphylaxis is a severe systemic allergic reaction that can endanger the lives of patients undergoing surgical procedures. It is characterized by an exaggerated immune response to a substance previously recognized by the immune system, leading to the release of vasoactive mediators and other inflammatory compounds. Although its incidence is relatively low, perioperative anaphylaxis is an event that demands immediate diagnosis and treatment to prevent potentially fatal complications [1-4].

We present the case of an elderly patient scheduled for a modified radical mastectomy, who experienced perioperative anaphylaxis after the administration of dipyrone as part of multimodal analgesia. Understanding this case is crucial for comprehending the complexity and importance of recognizing and properly treating perioperative anaphylaxis, ensuring successful outcomes for patients undergoing surgical procedures. Likewise, it is important to correctly identify the indications and scenarios for the use of dipyrone, as it is a medication that has fallen out of use in recent years.

Case Description

An 84-year-old female with a history of arterial hypertension, coronary artery disease with percutaneous revascularization, and chronic kidney disease, as well as a diagnosis of infiltrating ductal carcinoma of the left breast. She was admitted to the institution for a scheduled left modified radical mastectomy.

Anesthetic induction was performed with 1 mg/kg of lidocaine, 1.5 mg/kg of propofol, and 3 mg/kg of fentanyl. The procedure was carried out with balanced anesthesia using 1 MAC of sevoflurane and intermittent fentanyl boluses. Antiemetic prophylaxis was administered with dexamethasone and ondansetron, and 2 grams of dipyrone were chosen for analgesia.

Following the administration of 2 grams of dipyrone diluted in saline solution at an infusion rate of 200 ml/h, the patient experienced severe hypotension. Initial management with etilefrine was ineffective, leading to the initiation of noradrenaline infusion with a partial response. Anaphylactic shock was considered as a potential diagnosis, considering that upon removal of the surgical drapes after surgery, facial edema, erythema, and increased airway pressures were evident.

Management began with approximately five to ten bolus doses of 50-100 mcg of adrenaline, followed by 200 mg of hydrocortisone and 2 mg of clementine, resulting in an improvement of hemodynamic parameters. An endotracheal tube was inserted to secure the airway, and a Trans esophageal echocardiogram was performed. This revealed a short-axis view of the left ventricle, known as the "kissing" sign, without segmental contractility disorders. The left ventricle appeared hyperdynamic with good biventricular contraction. Additionally, the inferior vena cava showed a collapsibility of more than 50%, supporting a suspected diagnosis of relative hypovolemia related to distributive shock and ruling out a cardiogenic etiology.

Arterial blood gas analysis was performed, showing mixed academia with evidence of bicarbonate at 12.5, base excess at -17.9, and lactate at 9 mmol/L. Therefore, administration of 20 mL of hypertonic solution (3% NS), 20 mEq bicarbonate, and fluid resuscitation was decided. Repeat arterial blood gas analysis showed persistent mixed acidemia with deterioration.

Arterial Blood Gasses									
	PH	pCO2	pO2	HCO3	BE	PAFI	Lactato	Hb	Hto
1º hour post shock	6,89	55,2	123,3	11	-22,3	123,3	10,1	14,3	42%
24 hours post shock	7,33	34	81	18	-8,1	253	5,73	10	31%

The patient was transferred to the ICU due to the requirement of ventilator support and triple high-dose vasopressor support. Noradrenaline was administered at a rate of 0.08 mcg/kg/min, vasopressin at 2 IU/h, and adrenaline at 0.1 mcg/kg/min, with a progressive decrease in vasopressor support requirements.

During her ICU stay, for the first 24 hours, the patient was under mechanical ventilation in A/C mode by volume, with adequate ventilator synchrony. Sedation was managed with dexmedetomidine, achieving a RASS-5 level of sedation. Chest X-ray showed no consolidations, atelectasis, or other abnormalities. Extubation was successfully performed after more than 24 hours of intubation. The patient completed 48 hours of intrahospital monitoring and was discharged with recommendations and follow-up by the surgical team.

Discussion

Perioperative anaphylaxis is a serious systemic allergic reaction that can be potentially life-threatening. It is marked by an overactive immune response to a previously encountered substance. This response leads to the release of vasoactive mediators and various inflammatory compounds [1,3,4]. This clinical case illustrates an example of perioperative anaphylaxis.

The diagnosis of anaphylaxis in this case is based on observed clinical manifestations, such as severe hypotension, tachycardia, bronchospasm, erythema, and facial edema, as well as the hemodynamic deterioration evidenced in arterial blood gasses, with mixed academia, elevated lactate, and decreased base excess. Immediate initiation of treatment was crucial in reversing the condition, with administration of adrenaline, hydrocortisone, and antihistamines leading to improvement of the hemodynamic parameters.

It is assumed that the anaphylactic reaction in this patient occurred due to the administration of dipyrone, also known as metamizole, which is used as an analgesic and antipyretic medication, whose safety has been debated due to its potential risk of serious adverse reactions such as agranulocytosis and anaphylactic reactions. Its main action is mediated through its active metabolite, which has analgesic, antipyretic, and spasmolytic properties. Its mechanism of action involves the inhibition of central and peripheral cyclooxygenase (COX) as well as modulation of endogenous neurotransmitter systems [5-7].

The fact that the patient experienced such a reaction highlights an individual sensitivity to dipyrone and underscores the importance of carefully evaluating risks and benefits prior to administration of this medication, especially in patients with a history of allergies or adverse reactions. Given the patient's history, it is essential to weigh possible benefits in terms of pain and fever relief against potential risks, particularly in patients with a history of allergic reactions or other risk factors. In situations where alternatives are available, opting for other treatment options might be prudent. The patient's medical history and individual conditions should always be taken into account when deciding on the use of dipyrone. It should be noted that this patient did not have a previous history of allergic reactions to dipyrone or other medications.

This patient also had various conditions in which dipyrone may not be a viable analgesic option. It is important to note that the use of dipyrone in patients with coronary artery disease is associated with a higher cumulative incidence of death, myocardial infarction, or stroke, as well as all-cause mortality and ischemic events [8]. Additionally, regarding chronic kidney disease, some studies have suggested a potential association between dipyrone and the risk of analgesic nephropathy, as well as exacerbation of the disease [9].

Given the complexity of the patient's medical situation, it is crucial for the medical team to have discerned the true indication of this medication in the presented case. Generally, the use of dipyrone should be individualized and based on a thorough assessment of risks and benefits [5,10].

Anaphylaxis is a differential diagnosis in patients experiencing cardiovascular collapse or acute respiratory failure preoperatively [11]. However, its recognition can be challenging because its manifestations vary based on severity, reaction phase, and surgical environment characteristics [1,3]. Objective signs and clinical history are crucial for accurate diagnosis. Tachycardia, hypotension, and bronchospasm are frequent findings in anaphylaxis, and in this case, the patient presented these symptoms, along with mixed academia and elevated lactate, indicative of compromised hemodynamic function and tissue perfusion.

Management of perioperative anaphylaxis is based on rapid identification and discontinuation of the offending agent, appropriate cardiovascular and respiratory support, and administration of specific pharmacological treatments [12,13]. Early administration of adrenaline is crucial as its alpha-1-adrenergic effects promote vasoconstriction, countering the vasodilation and fluid extravasation characteristics of anaphylaxis [1-14]. Additionally, adrenaline's beta-adrenergic stimulation improves cardiac and respiratory function, alleviating bronchospasm and hypoxemia [15,16].

The patient's positive evolution in the ICU was facilitated by timely and appropriate treatment, along with hemodynamic stabilization achieved through triple vasopressor support. The choice of dexmedetomidine for sedation allowed effective control of sedation level (RASS-5) with eventual successful extubation and satisfactory recovery.

Conclusions

In conclusion, perioperative anaphylaxis is a potentially fatal complication that requires a high index of suspicion in patients presenting with hypotension, tachycardia, bronchospasm, and other suggestive signs of systemic allergic reaction. Early recognition and immediate initiation of treatment, focusing on adrenaline administration and supportive measures, are essential to avoid serious complications and ensure successful recovery. Adequate individualization of the use of dipyrone in the surgical context is crucial in patients with multiple comorbidities, where

it is vital to weigh the risks and benefits of its administration. A multidisciplinary approach involving the surgical team, anesthesiologists, and intensive care staff is vital for the proper management of such cases.

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