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CASE REPORT

Two probable anaphylactic events during consecutive cranial surgeries: case report

Dos probables eventos de anafilaxia durante cirugías craneales consecutivas. Reporte de caso

Rafael Ramirez-Gonzales^a, Román Augusto Del-Castillo-Gervasi^a, Carlos Javier Shiraishi-Zapata^b, John Neper Laurencio-Ambrosio^a

^a Department of Anesthesiology and Surgical Center, Hospital María Auxiliadora, Ministry of Health, Lima, Peru

^b Surgical Center and Anesthesiology Service, Hospital EsSalud, Talara, Peru.

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Abstract

Perioperative anaphylaxis represents a complex diagnosis due to the varying intensity of the symptoms which are also shared with other pathologies. This article discusses a case of a patient that sustained 2 probable anaphylactic reactions during consecutive cranial surgeries under general anesthesia; the causal agent could not be confirmed. Investigating these reactions is essential for identifying the causal agents and preventing increasingly severe reactions in future exposures.

Resumen

La anafilaxia perioperatoria representa un diagnóstico problemático porque posee manifestaciones clínicas de distinta intensidad y comunes a otras patologías. Reportamos el caso de un paciente que presentó dos probables eventos de anafilaxia durante cirugías craneales consecutivas bajo anestesia general, cuyo agente causal no pudo ser confirmado. La investigación de estas reacciones es crucial para identificar los agentes causales y evitar reacciones de mayor severidad en futuras exposiciones.

Introduction

Anaphylaxis is a systemic life-threatening hypersensitivity reaction (HR).¹ Perioperative anaphylaxis is among the main causes of anesthetic complications, with an incidence rate of 1/1250 to 1/18,600 procedures and a mortality rate between 4% and 4.7% (pharmacological anaphylaxis).² It is caused by the stimulus of bioactive mediators releasing mast cells and basophils, in 2 or more body systems, resulting in increased capillary permeability, vasodilatation, bronchoconstriction, and hypotension.³

Intraoperative anaphylaxis is a complex diagnosis as several symptoms cannot be evaluated in a sedated or unconscious patient, the cutaneous signs are hidden under the surgical drapes, and several drugs are administered simultaneously.^{3,4} A total of 90% of the cases develop during induction, although there are late reactions as well, and the symptoms exhibit varying intensities, ranging from mild HRs with a preponderance of cutaneous manifestations (grade I) to cardiac and/or respiratory arrest (grade IV).^{3,5,6} In the presence of only 1 symptom, intraoperative anaphylaxis

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Correspondence: Servicio de Centro Quirúrgico y Anestesiología, Hospital EsSalud, Avenida Panamericana s/n Pariñas, Talara, Peru. E-mail: Shiraishi52@hotmail.com

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may be misdiagnosed, in addition to the lack of an evaluation by the allergy clinic, and the risk of a new—potentially lethal—exposure to the agent involved.⁶

The most frequent signs in the presence of adverse reactions are the absence of pulse, difficult ventilation from bronchospasm, desaturation, and even cardiovascular collapse or cardiac arrest as the primary manifestation.^{3,5} The reduction in end-tidal CO₂ (ETCO₂) below 20mm Hg has also been considered a valuable marker.^{6,7}

Patient information

A 44-year-old male patient from a rural area, admitted to the intermediate care unit following his discharge from the intensive care unit (ICU), as a result of supraventricular tachycardia (SVT) over an elective cranial surgery which led to the interruption of the procedure (Table 1). A mild right hemiparesis was identified in the patient on clinical examination. The cardiology evaluation failed to identify any alteration and concluded that the SVT was the result of surgical manipulation or autonomic reflex. An amount of 10mg of propranolol b.i.d. were prescribed, with a Goldman 2 index classification. No allergies (neither food nor drugs) were reported during the anesthetic evaluation and the patient was classified as American Society of Anesthesiologists (ASA) class 2 and was rescheduled.

Clinical findings

The patient was admitted to the OR with normal vital signs and 95kg of body weight. Balanced anesthesia was administered for induction (Tables 1 and 2) and endotracheal intubation was performed with a No. 8.5 endotracheal intubation tube (ETT). The surgical procedure began with a 99% oxygen saturation (SpO₂) and 30mm Hg of ETCO₂. Vital signs were normal during maintenance. One hour after induction, suddenly and with no previous blood pressure (hypotension) or heart rate (bradycardia) alterations, sustained and progressive declines in ETCO₂ and SpO₂ (down to 24mm Hg and 92%, respectively) were recorded.

Diagnostic evaluation

Due to the alterations in ETCO₂ and SpO₂, malfunction of the ETT device was ruled out initially. Immediately after, the absence of palpable pulse and SVT was identified in the multiparameter monitor, with signs of pulseless electrical activity (PEA). Furthermore, when removing the surgical drapes, generalized edema was evidenced and consequently the patient was diagnosed with probable grade IV anaphylaxis.

Table 1. Timeline.

Date	Surgical and medical therapy events	Adverse reaction	Management
02/19/2007	Emergency surgery: DC to remove the acute subdural hematoma secondary to severe TBI. Position: ventral decubitus. Balanced general anesthesia. Monitoring: noninvasive blood pressure, electrocardiography (3 bipolar electrodes), capnography and pulse oximetry	None	ICU monitoring
11/7/2007	1st elective surgery: CP with autologous cranial bone flap. Position: dorsal decubitus. Balanced general anesthesia. The same monitoring	SVT	Surgery was interrupted. The patient was cardioverted in the OR and admitted to the ICU
11/8/2007–11/12/2007	IMCU admission	None	Cardiology and anesthesia evaluation. Surgery rescheduled
11/22/2007	2nd elective programming: DC with autologous cranial bone flap. Position: dorsal decubitus. Balanced general anesthesia. The same monitoring	PEA due to probable anaphylaxis	Advanced CPR. PACU management during the immediate postoperative period

CP=cranioplasty, CPR=cardiopulmonary resuscitation, DC=decompressive craniotomy, ICU=intensive care unit, IMCU=intermediate care unit, PACU=postanesthesia care unit, PEA=pulseless electrical activity, SVT=supraventricular tachycardia, TBI=traumatic brain injury.
Source: Authors.

Table 2. Detailed list of drugs used in the 3 surgical procedures.

Date	Surgical procedure	Preinduction medication	Induction	Maintenance
02/19/2007	Emergency DC	5 mg of Midazolam and 8 mg of Dexamethasone	Fentanyl 200 µg and Vecuronium 8mg	Sevoflurane 100% 2.5% to 2% in 2L of O ₂ at 100%. Two additional doses of 100 µg of fentanyl
11/07/2007	1st elective CP (interrupted because of SVT)	8 mg of Dexamethasone, 10 mg of Metoclopramide, 5 mg of Midazolam	160 mg of propofol, 250 µg of fentanyl, 70 mg of rocuronium	Sevoflurane 100% 2.5% in 2 l of O ₂ at 100%
11/22/2007	2nd elective CP (PEA event)	80 mg of Lidocaine	Fentanyl 250 µg, 400 mg of sodium thiopental and 8 mg of Vecuronium	Sevoflurane 100% 2.5% in 2L of O ₂ at 100%. Additional doses: 50 µg of fentanyl and 2 mg of Vecuronium

Operative asepsis: iodine povidone in the 3 surgeries

CP=cranioplasty, DC=decompressive craniotomy, PEA=pulseless electrical activity, SVT=supraventricular tachycardia.

Source: Authors.

Therapeutic intervention

Advanced cardiopulmonary resuscitation (CPR) was initiated with continuous chest compressions, IV administration of 1 mg of adrenalin and manual ventilation. Two minutes later, return of spontaneous circulation (ROSC) developed and the compressions were discontinued. However, they had to be reinitiated 1 minute later because of ventricular fibrillation (VF) requiring a 200 joules biphasic shock. A second dose of adrenaline was administered. The VF relapsed on 3 occasions and the same treatment was repeated. After 2 minutes, ROSC was confirmed and a subclavian venous catheter and a radial arterial catheter were placed.

Follow-up and results

The patient was admitted to the postanesthesia care unit with 70/50 mm Hg of invasive arterial pressure, 130 bpm, 90% SpO₂, central venous pressure of 10 cmH₂O, under volume controlled mechanical ventilation and dopamine at adjustable dose. 250 mg of hydrocortisone t.i.d. were administered 10 hours after PEA, and the patient was extubated without any complications with a Glasgow score of 14 points, 15 hours later. The patient was then transferred to the intermediate care unit where dopamine was then withdrawn after 3 days and 6 days later was transferred to the general hospitalization floor from where he was finally discharged.

Discussion

The intermediate care unit evaluation focused on the SVT that led to the interruption of surgery because of an initial

suspicion of cardiac pathology. However, the medical record indicated that the patient was admitted to the ICU following distributive shock resulting from anaphylaxis secondary to an adverse drug reaction (ADR), with hypotension and generalized erythema. Consequently, this first event was probably consistent with grade III anaphylaxis.

The primary cause of perioperative HRs is neuromuscular relaxants (NMRs) (50% to 70%), followed by latex (12% to 16.7%), and antibiotics (15%).^{2,6} Reviewing the role of the various drugs administered over surgery in the case of immediate HRs (Table 2), sodium thiopental is often involved (incidence 1:30,000), although propofol may also be the culprit. Midazolam (administered in 2 surgeries) and fentanyl (administered in all of them) rarely trigger these reactions.⁸

Two steroid monoquaternary compounds were used (Rocuronium and Vecuronium), with replaced ammonia ions. These ions represent allergenic sites involved in the specific immunoglobulin E (IgE) recognition which could explain the crossed reactivity (CR) in skin tests of 60% to 70% of patients allergic to NMRs. CR to all relaxants is more frequent when a steroid compound triggered the initial reaction. There were also HRs in NMRs-naïve patients because there is CR with cosmetics, foods, and disinfectants.⁹

Other late intraoperative anaphylaxis-causing agents are iodine povidone and chlorhexidine.¹⁰ In a previous report¹¹ Naranjo's algorithm was used to assess the causality of an ADR. This algorithm enabled the analysis of a second HR, with a score of 5 for the relaxant and povidone, which makes them potential ADR agents.¹² Considering that few cases were reported in response to topical povidone, the NMR would then be the causal agent.¹³

Investigating the cause of anaphylaxis may be complex, since there may be several agents involved.⁸ 3 necessary evidences have been described: medical record, biological

evaluation, and skin tests.¹⁴ The biological evaluation identifies the presence of an allergic mechanism in the reaction through early laboratory tests (total tryptase blood test and plasma histamine) and late laboratory tests (prick test, basophil activation, challenge tests, and specific IgE immunoassays).^{1,3,5,8,14} In this 2 potential anaphylactic events, only clinical evidence was available. Moreover, the availability of the other tests required in our setting at the time of presentation is unclear.

The critical situation was neglecting the first HR since the patient should have been evaluated by the allergy clinic and the procedure rescheduled, once the agent involved was identified. Failure to do so led to a new exposure to the agent, resulting in a more severe preventable reaction.^{6,15} Actually, every perioperative reaction must be investigated to ensure safe anesthetic procedures in the future, because even a mild reaction may be due to hypersensitivity and hence be neglected or attributed to unspecific reactions.^{8,16,17}

Table 3. Differential diagnosis and management of perioperative anaphylaxis in the adult.

Differential diagnosis	Management of severe anaphylaxis
Always keep in mind	
Bronchial asthma Cardiac arrhythmia Myocardial infarction Pericardial tamponade Pulmonary edema Pulmonary embolism Tension pneumothorax Venous embolism Sepsis Hereditary angioedema Mastocytosis Drug overdose Malignant hyperthermia (secondary to succinylcholine) Myotonia and masseter spasm (secondary to succinylcholine) Hyperpotassemia (secondary to succinylcholine)	Airway (A), breathing (B), circulation (C), disability (D), and exposure (E) Ask for help Position the patient on a flat surface Raise the patient's legs Evaluate any life-threatening issues for the patient: airway (laryngeal edema, hoarseness, stridor), breathing (dyspnea, tachypnea, wheezing, fatigue, cyanosis, SpO ₂ <92%), circulation (paleness, cold and humid skin, hypotension, lipothymia) Assess mental health disorders: confusion, somnolence, comma Pre-cardiac arrest management Discontinue or remove the causal agent (relaxants, antibiotics, blood products, contrast media or latex). Stop the surgical procedure if possible. In the presence of respiratory distress, intubate immediately; use FIO ₂ 100%. If severe bronchospasm develops, monitor auto-PEEP Repeated doses of adrenaline (100–300 µg) every 5 minutes and increase the dose if no improvement is identified (in the absence of an IV line, 300–500 µg IM) ± 2 UI of IV Vasopressin Start the adrenalin infusion (0.05–0.3 µg/kg/minute IV) for maintaining a SBP ≥ 90 mm Hg under constant monitoring (check for myocardial ischemia) Vasopressin or norepinephrine infusion in cases of hypotension refractory to a dose of >2 mg of adrenalin IV fluid challenge, IV access using a large catheter: 500–1000 mL (20 mL/kg) of crystalloid. Discontinue the colloid infusion when this could be the causal agent H1 blockers: 50 mg of diphenhydramine, 10 mg of chlorphenamine H2 blockers: 20 mg of famotidine IV Corticosteroid: 50–200 mg of hydrocortisone or 1–2 mg/kg of methylprednisolone
Cardiac arrest management	
	Start CPR in the absence of carotid pulse in 10 seconds Adrenalin 100–1000 µg IV; you may repeat the dose administration every 3–5 minutes, or replace for a dose of 40 U of IV vasopressin Briefly disconnect the ventilator if auto-PEEP is suspected Administer H1 and H2 blockers and steroids at the above-mentioned doses Consider extracorporeal support in patients with good CPR without ROSC

CPR=cardiopulmonary resuscitation, FIO₂=fraction of inspired oxygen, PEEP=positive end-expiratory pressure, ROSC=return of spontaneous circulation. Adapted from Chapman and Lalkhen,¹ Mertes et al,⁶ and McEvoy et al.¹⁹
 Source: Authors.

Some therapeutic approaches to these potential HRs may be optimized; for instance, administering IV fluid challenges, Chlorphenamine and Amiodarone (to avoid the relapse of atrial fibrillation)^{1,18} (Table 3). The value of the acronym dislodgement, obstruction, suspected pneumothorax and equipment or operator problem (DOPE) has been recognized to address the deterioration of the patient in mechanical ventilation.²⁰

Following a HR, the anesthesiologist shall request laboratory tests that contribute to a clinical diagnosis, in addition to interconsulting with the allergy clinic to investigate the causal agent. Furthermore, all the Peruvian anesthesiology services nowadays have a mandatory record of adverse events. Finally, the early identification of the disruption in ET_{CO}₂ y SaO₂ enabled the introduction of timely CPR measures to avoid a fatal outcome.

Patient's opinion

There were no follow-up anesthesia visits to give the patient a detailed written pharmacological report, and the result of the patient's allergy evaluation is unknown.

Informed consent

The Hospital Ethics Committee approved the publication of this case report because the patient is not a resident of the hospital jurisdiction to be able to obtain a written consent.

Ethical responsibilities

Protection of persons and animals: The authors declare that the procedures followed were consistent with the ethical standards of the responsible human experimentation committee and pursuant to World Medical Association and the Declaration of Helsinki.

Confidentiality of the information: The authors state that they have followed the institutional protocols regarding the publication of patient information.

Right to privacy and informed consent: The authors have obtained the informed consents of the patients and/or individuals mentioned herein. The custodian of this document is the corresponding author.

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Conflicts of interest

The authors have no conflict of interest to disclose.

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