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Case Report

Perioperative Anaesthetic Management of Hereditary Angioedema in the Context of Adrenalectomy for Pheochromocytoma Surgery: About a Case

Rubén Rey-Escudero[1], Daniel Salgado-García[2], José L. González-Rodríguez[3] and Agustín Díaz-Álvarez[3,4*]

[1]Training in Anesthesiology and Critical Care, Complejo Asistencial Universitario de Salamanca, Gerencia Regional de Salud de Castilla y León (SACYL), Paseo San Vicente, Salamanca, Spain

[2]Anesthesiology and Critical Care, Hospital Virgen de la Concha, Gerencia Regional de Salud de Castilla y León (SACYL), Zamora, Spain

[3]Anesthesiology and Critical Care, Complejo Asistencial Universitario de Salamanca, Gerencia Regional de Salud de Castilla y León (SACYL), Paseo San Vicente, Salamanca, Spain

[4]Department of Surgery, Faculty of Medicine, Salamanca University, Alfonso X El Sabio, Salamanca, Spain

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ABSTRACT

Hereditary angioedema (HAE) is a rare genetic disease which consists of the appearance of sudden bursts of edema of the skin and mucous membranes. Stress is the main trigger for this crisis, which are usually self-limited but at the same time have a poor response to corticosteroids and antihistamines. Pheochromocytoma is an uncommon neuroendocrine tumor, affecting the chromaffin cells of the adrenal medulla and which typically course with a hyperproduction of catecholamines. Moreover, between 5-11% of them can be associated with Takotsubo (TKS) syndrome, a transient cardiomyopathy which is caused by the hipercatecholaminergic state associated to these tumors. We present the case of a patient with type II HAE scheduled for a laparoscopic adrenalectomy to remove a pheochromocytoma, which was diagnosed during the etiological screening for a second episode of TKS triggered by a corticoid infiltration. The necessity for an especially accurate perioperative management of this patient resides in the difficult hemodynamic management related to pheochromocytoma surgeries (which normally require the administration of hypotensors like short-acting vasodilators and beta blockers); in combination with the underlying TKS cardiomyopathy and with the hazard of the associated HAE, a potentially serious pathology that requires being prepared to treat a perioperative crisis.

Introduction

Hereditary angioedema (HAE) is a rare genetic disease characterized by a quantitative or qualitative deficiency of C1 inhibitory protein (C1-Inh-Prot). It mostly has autosomal dominant inheritance, but sometimes it can be recessive. There are two classes: Type 1 with quantitative deficit of C1-Inh-Prot (more frequent) and Type 2 with qualitative deficit of C1-Inh-Prot. The result of this deficiency is the activation of the complement, kinins kallikrein, coagulation, and fibrinolysis systems altogether [1]. Consequently, they appear recurrent and self-limited crises of non-pruritic edema that do not respond to corticosteroids or antihistamines. In addition, they can pose a vital risk by compromising the airway [2].

Pheochromocytoma is an adrenal tumor of the chromaffin cells, which frequently carry a hyperproduction of catecholamines. This situation causes the typical symptoms consisting of headache, tachycardia, hypertension and profuse sweating [3]. Moreover, in 4.8% of cases it is associated with Takotsubo syndrome, a transient cardiomyopathy which consists of a reversible apical dyskinesia, secondary to the elevated levels of circulating catecholamines [4].

Correspondence to: Agustín Díaz-Álvarez, M.D., Ph.D., Anesthesiology and Critical Care, Complejo Asistencial Universitario de Salamanca, Gerencia Regional de Salud de Castilla y León (SACYL), Paseo San Vicente 58-182; Department of Surgery, Faculty of Medicine, Salamanca University, Alfonso X El Sabio, 37007, Salamanca, Spain; ORCID: 0000-0002-6229-8311; E-mail: agustin.diaz@usal.es

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Surgery is the treatment of choice for pheochromocytoma. Hemodynamic control represents an important anaesthetic challenge per se, and in this case it is necessary to handle two complimentary, delicate concomitant pathologies, as they are the underlying cardiomyopathy related to TKS, and the possibility of appearance of a HEA crisis [5]. Although HEA crises rarely affect the upper airway, perioperative stress and orotracheal intubation are high-risk situations to trigger them, which are inherent to any surgical procedure under general anaesthesia [1]. Therefore, it is of great importance to know the prophylactic and therapeutic measures to prevent and treat these crises as soon as they appear.

Case Presentation

We present the case of a 73-year-old woman, weighted 51kg and heighted 150cm, with a history of type II Hereditary Angioedema (two previous crises 20 years ago, one during a vaginal hysterectomy as well as another one without a known etiologic association); insulin dependent Diabetes Mellitus type 2, high blood pressure, and an acute myocardial infarction five years ago which required percutaneous transluminal coronary angioplasty with the finding of a one vessel disease, which was stented; and an episode of TKS diagnosed in the context of a lactic acidosis by metformin secondary to an acute gastroenteritis 2 years ago. The patient arrived at the Emergency department of our institution with the following symptoms: epigastric pain, dyspnea and accompanying vegetative courtship in the context of a recent articular infiltration with corticosteroids due to arthrosis of the knees. It was diagnosed as a second episode of inverted TKS, suspected by transthoracic echocardiogram with apical hypercontractility and dyskinesia of basal segments and confirmed by catheterization and magnetic resonance imaging, which showed the absence of coronary lesions. She was admitted to the Cardiology ward and, as a part of the etiological diagnosis of KTS, catecholamine levels in plasma and urine were requested, which results came out in very high numbers (both noradrenaline and adrenaline).

During her stay, she presented a newly diagnosed atrial fibrillation which required to start anticoagulation with edoxaban, as well as an episode of monomorphic non-sustained ventricular tachycardia with complete right branch block morphology. A mass in the right adrenal gland measuring 2.2 × 2.6 × 3 cm (T×AP×CC) suspected of pheochromocytoma was evidenced by MRI. Once ventricular function was recovered after 6 days (LVEF 72%), she was evaluated by the General Surgeons and began medical preparation prior to surgical removal of the pheochromocytoma, which consisted of alpha-blockade with increasing doses of prazosin until meeting the clinical criteria of Roizen (6 mg / 24h); not being necessary in this case a beta-blockade of the patient.

In the anaesthetic preoperative study, no apparent difficulties in airway management were observed. The anticoagulant was discontinued according to the institutional protocol, and the patient's clinical alpha-blockade was confirmed. The routine analysis (blood count, biochemistry and coagulation) showed no significant alterations.

Through the Hospital Pharmacy Service, plasma purified C1INH concentrate (Berinert -CSL Behring) was prepared at doses of 20U/kg, to have it ready for administration in the case of a HAE crisis would appear.

Prior to entering the operating room, the patient's airway was re-evaluated. The monitoring was carried out according to the SEDAR (Spanish Society of Anesthesiology and Resuscitation) recommendations and the left radial artery was cannulated with local anaesthesia. Minimally invasive, arterial wave form analysis hemodynamic monitoring was attached (Vigileo - Edwards Lifesciences). The bispectral index - Aspect BIS VISTA - was also used to ensure correct hypnosis throughout the procedure. A right internal jugular vein was cannulated to allow the administration of vasoactive drugs. The objective was to maintain a hemodynamic profile of +/-20% of baseline BP, HR, CO, CI, SV and SVV. Infusion pumps of remifentanil, insulin, magnesium sulfate, noradrenaline, esmolol and clevidipine were prepared.

After preoxygenation, 1.5 mg/kg of intravenous (iv) lidocaine was administered, followed by 2 mcg/kg fentanyl and 3 mg/kg etomidate. After BIS dropped from 60, rocuronium bromide was administered at 0.9 mg/kg. Likewise, several pulses of lidocaine spray were applied to the pharynx in order to minimize the hemodynamic response to laryngoscopy. Orotracheal intubation was performed with direct laryngoscopy using a Macintosh shovel number 3, obtaining a grade II Cormack-Lehane view of the glottis. A standard no. 7, ¡5 endotracheal tube with cuff was used. General anaesthesia was maintained with Sevoflurane (% guided by BIS values between 40-60) and remifentanil between 0.05-0.2 mc/kg/min. Volume controlled ventilation was performed with FiO2 40%, tidal volume 6ml/kg, PEEP 5cmH2O. EtCO2 was recorded.

During the peritoneal gas insufflation for laparoscopy, it was necessary to start the infusion of clevidipine ranging from 4 to 8 ml/h in a timely manner. After the tumor venous ligation and the removal of the piece, it was precise to start the infusion of noradrenaline 0.08-0.15 mc/kg/min. Considering the low bleeding, the hemodynamic stability, and the possibility of triggering a crisis by the stimulation of the endotracheal tube itself, it was decided to awaken and extubate the patient in the operating room. To provide postoperative analgesia, we performed a transversus abdominis plane block with 30 cc of levobupivacaine 0.375% and IV acetaminophen 1g plus IV metamizol 2g were administered.

Then, she was moved to the Post-Anaesthesia Care Unit (PCU) where she remained for four more days due to a progressive anemia secondary to a hematoma of the abdominal wall and a consumption thrombocytopenia, which motivated the transfusion of 2 red blood cell concentrates and a platelet pool. Vasoactive drugs were progressively decreased and were ceased in the first 24 hours. There was no crisis related to HAE neither at the PCU nor later at the hospitalization ward. Five days after the surgery, she was finally discharged to her home, with an anatomopathological study which confirmed the pheochromocytoma diagnosis, and normal catecholamine levels. At the follow-up visit at 3 months, the patient was asymptomatic, with normal analytical and echocardiographic values and pending a genetic study.

Discussion

The possibility of a HAE crisis due to orotracheal intubation and surgical stress, in addition to the hemodynamic instability during pheochromocytoma manipulation and the history of stress

cardiomyopathy, all of them present in our patient, required meticulous anaesthetic planning.

On the one hand, HAE type II represents only 15% of HAE cases and is a consequence of mutations that generate the production of non-functional C1-INH protein [2]. Recurrent crises of edema without pruritus, without erythema and without urticaria are the characteristic signs of HAE. Although only 1% of HAE crisis affect the larynx, more than half of HAE patients experience laryngeal edema at some point during their disease and can be fatal if left untreated [1]. These are more frequent in women, especially in adolescents and young adults. Intubation is considered a high-risk procedure as a potential trigger for laryngeal crisis, and the administration of a pre-procedure prophylaxis with C1INH nanofiltered Cinryze (Viro Pharma) may be considered [1]. As the patient was of advanced age, in addition to the fact that she did not report having suffered recurrent crisis; and since crisis can occur despite having received prophylaxis, the Berinert -CSL Behring pasteurized C1INH concentrate, derived from plasma subjected to viral inactivation-, included in the hospital guide and accepted for the early treatment of a HAE crisis, was requested if necessary.

Laparoscopic adrenalectomy requires general anaesthesia with orotracheal intubation. The recommendations for the management of pheochromocytoma are invasive blood pressure monitoring prior to anaesthetic induction, central vascular access for the administration of vasoactive agents and a large-caliber route [5]. Regarding the pharmacological arsenal necessary to face the predictable hemodynamic changes during the surgery, we decided to have all of the following drugs available: i) clevidipine as a calcium antagonist, which is an ultrafast acting agent with a short half-life that allowed rapid control of possible hypertensive peaks during tumor manipulation without causing residual hypotension when stopping the infusion after tumor exeresis; ii) esmolol as an ultra-short acting beta-blocker (for the same reason than previously exposed); and iii) norepinephrine as the vasoconstrictor of first choice [5-7]. In the same way an insulin pump was prepared, as well as another one with magnesium sulfate which has shown effectiveness in cases of TKS secondary to pheochromocytoma [5, 6, 8, 9].

As for the anaesthetic agents, we used etomidate due to its more favourable hemodynamic profile for induction; along with fentanyl to blunt sympathomimetic response to orotracheal intubation, and rocuronium bromide (since we intended to avoid fasciculations because it is a potential source of catecholamine release). Sevoflurane was our anaesthetic choice for the maintenance of general anaesthesia, due to its less irritating action on the airways compared to other halogenates and its absence of arrhythmogenic potential; as well as Remifentanil, because due to its properties it can be very helpful for hemodynamic control during laparoscopy, as it allows quick concentration changes and acts in a complementary way to the vasoactive agents [5, 6]. Reinforced postoperative analgesia and careful extubation were as well practiced ensuring a secure anaesthetic eduction and transfer to the Post-Anaesthesia Care Unit (PACU).

In high complexity scenarios such as the one exposed, there are multiple options available. Although the focus of attention is usually the striking pathology, we must not forget the concomitant pathology of the patients since all of them can raise the perioperative risk. Even more, it is mandatory to prepare and to have available all the necessary tools to deal with possible unforeseen events arising from them.

Conflicts of Interest

None.

Data Availability

All data supporting the conclusions are available. Some of them are open access while the others are paid articles.

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