VIA MEDICA

PRACE ORYGINALNE I KLINICZNE

Anestezjologia Intensywna Terapia
2016, tom 48, numer 4, 265–269
ISSN 0209–1712
www.ait.viamedica.pl

Anaphylaxis and cardiac surgery for hypertrophic obstructive cardiomyopathy: a case report and review of anaesthetic management

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Abstract

Background: The aim of this paper is to describe clinical management in a situation where patient has experienced anaphylaxis while undergoing surgical septal myectomy for hypertrophic obstructive cardiomyopathy (HOCM).
Case report: A 40-yr-old female was scheduled to undergo surgical septal myectomy for the treatment of HOCM. After induction, the patient developed refractory hypotension that did not respond to escalating doses of vasopressors and volume therapy. Although a clinical examination led to the diagnosis of anaphylaxis, epinephrine, which is the usual treatment of choice, failed to improve the patient's haemodynamics. A transesophageal echocardiography revealed a worsening of left ventricular outflow tract obstruction (LVOTO) after epinephrine administration. In the end, the rapid institution of a cardiopulmonary bypass was required as a rescue therapy instead of to save a patient.
Conclusion: The anaesthetic goals in a patient in HOCM are to maintain preload and afterload and to avoid stimulation of inotropy and chronotropy to leading to left ventricular outflow obstruction. In a patient with anaphylaxis, maintaining these haemodynamic goals becomes much more difficult since the pathophysiology and usual treatment of choice will worsen LVOTO. Special consideration for the need to have extracorporeal life support to treat refractory hypotension in surgical patients with HOCM may be warranted.

Key words: cardiomyopathy, hypertrophic; anaphylaxis; anesthesia

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Hypertrophic obstructive cardiomyopathy (HOCM) is a genetic disorder resulting in the production of abnormal cardiac sarcomere proteins and has a 0.2% prevalence in the general population [1]. The disease is characterized by excessive hypertrophy of the left ventricle with the intraventricular septum being affected to the greatest extent. This hypertrophy can cause a dynamic left ventricular outflow tract (LVOT) obstruction resulting in symptoms ranging from decreased functional capacity to sudden cardiac death. One of the recognized strategies of treatment aiming to reduce LVOT obstruction (LVOTO) is surgical septal myectomy [1].

Here, we describe the case of a patient diagnosed with HCM and LVOT obstruction presenting for a septal myectomy. After the induction of anaesthesia, the patient developed profound hypotension and symptoms suggestive of anaphylaxis. This situation posed unique challenges as the treatment goals for anaphylaxis were in conflict with the anaesthetic goals for a patient with a dynamic LVOT obstruction. The patient has provided written consent for publication of this case report.

CASE REPORT

A 40-yr-old (height: 170 cm, body mass: 81 kg) female diagnosed with HOCM was scheduled for an elective, surgical septal myectomy. The investigations which confirmed this diagnosis had been completed in 2013 as she was found to have a systolic murmur and had an extensive family history of maternal relatives with HOCM. Since the initial diagnosis, she became more symptomatic, developing

Należy cytować wersję: *Yee KF, Wąsowicz M:* Anaphylaxis and cardiac surgery for hypertrophic obstructive cardiomyopathy: a case report and review of anaesthetic management. Anaesthesiol Intensive Ther 2016; 48: 252–256. 10.5603/AIT.a2016.0042.

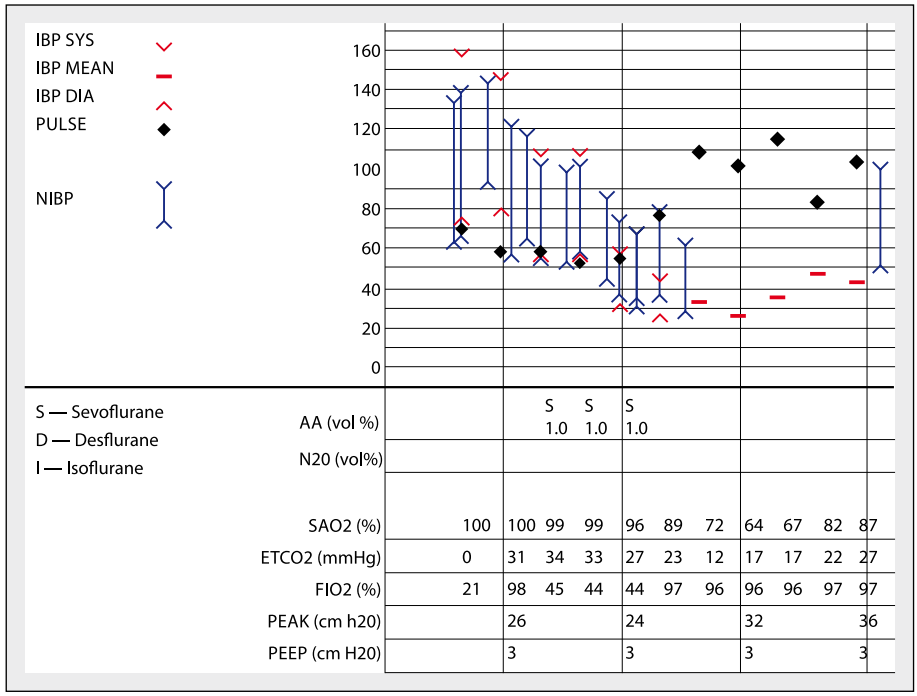

Figure 1. Haemodynamic course, presented on the copy of anesthetic record

presyncopal symptoms with several episodes of non-sustained ventricular tachycardia and decreasing functional capacity. A transthoracic echocardiogram, performed four months prior to surgery, revealed concentric HOCM with septal predominance. A significant LVOT resting gradient of 160 mm Hg was observed, along with moderate systolic anterior motion (SAM), posteriorly directed mitral regurgitation (MR), and biatrial enlargement. No significant increase of the gradient was seen with the Valsalva manoeuvre. Her past medical history was significant regarding a partial nephrectomy performed under general anaesthesia twelve years ago with no perioperative issues. Her only medication was metoprolol 25 mg twice a day. The remainder of her preoperative evaluations were unremarkable.

The patient was prepared for surgery with the placement of a left radial arterial line and a 16 gauge peripheral IV. Sterile technique with chlorhexidine was used to insert the arterial line. After applying standard monitoring, her arterial blood pressure was 140 70 mm Hg^{-1} with a heart rate of 70 per min. An infusion of phenylephrine running at 0.5 µg kg^{-1} min^{-1} was started and once the patient's mean arterial blood pressure (MAP) had risen by 10 mm Hg, general anaesthesia was induced intravenously with 4 mg of midazolam, 500 µg of fentanyl, 50 mg of propofol, and 80 mg of rocuronium. The ultrasound-guided placement of an 8.5 French right internal jugular sheath introducer was performed. However, by the end of placement, approximately 10 minutes post-induction, the patient abruptly developed hypotension of 60/30 mm Hg without tachycardia that was unresponsive to an infusion of 1000 mL of crystalloid and 800 µg of phenylephrine administered in successive boluses (haemodynamic course is presented in Fig. 1).

A second anaesthesiologist and the surgeon were called into the room at this time to assist with patient's haemodynamic management. Successive boluses of vasopressin and norepinephrine totalling 42 units and 64 µg, respectively, were administered over the following 15 minutes, along with an additional two litres of crystalloid and 500 mL of 5% albumin. A norepinephrine infusion at 0.3 µg kg^{-1} min^{-1} was also started. A focused thoracic ultrasound of the chest revealed no signs of pneumothorax. A transesophageal echocardiogram (TEE) probe was then inserted which revealed both ventricles to be small and hyperdynamic with a prominent LVOT obstruction (Fig. 2).

At this time, the peak airway pressures began to rise from 24 cm H_2O to 40 cm H_2O, and the SpO_2 dropped to 71%, along with a decrease of end-tidal CO_2 from 33 mm Hg to 17 mm Hg. An arterial blood gas analysis revealed a pH of 7.31, pCO_2 of 42 mm Hg, pO_2 of 34 mm Hg, and a bicarbonate concentration of 20.4 mEq L^{-1}. The most likely diagnosis at this time was anaphylaxis. A physical exam of the patient revealed very quiet air entry bilaterally with no wheezing. An urgent bronchoscopy found the endotracheal tube to be patent and in the proper position. However, the main bronchi appeared oedematous and swollen. Further support for the diagnosis of anaphylaxis included the development of marked facial swelling and a papular rash on the patient's lower abdomen and extremities.

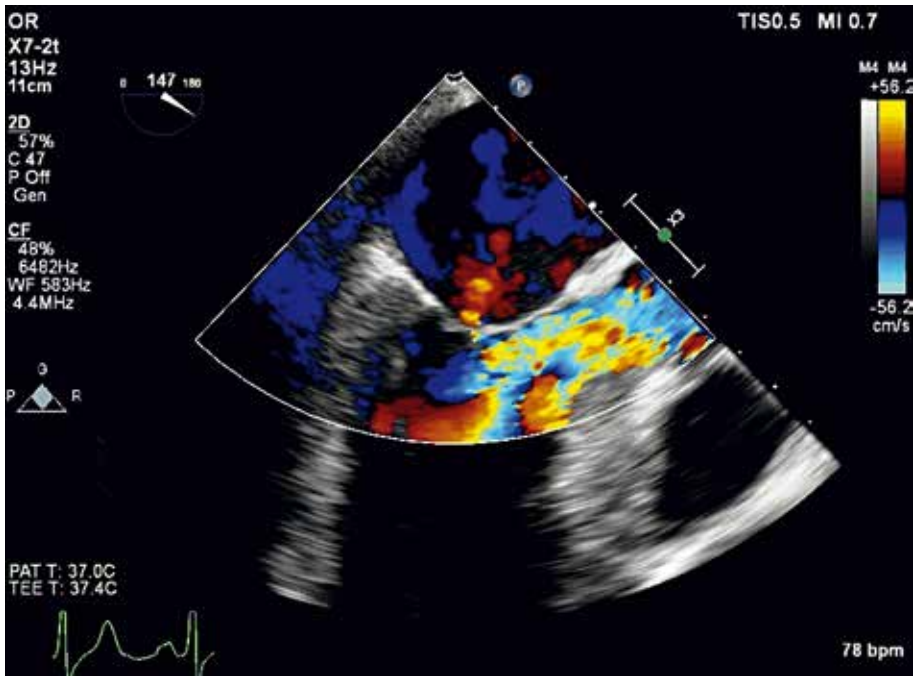

Figure 2. Picture obtained from transesophageal echocardiographic examination demonstrating LVOT after haemodynamic collapse

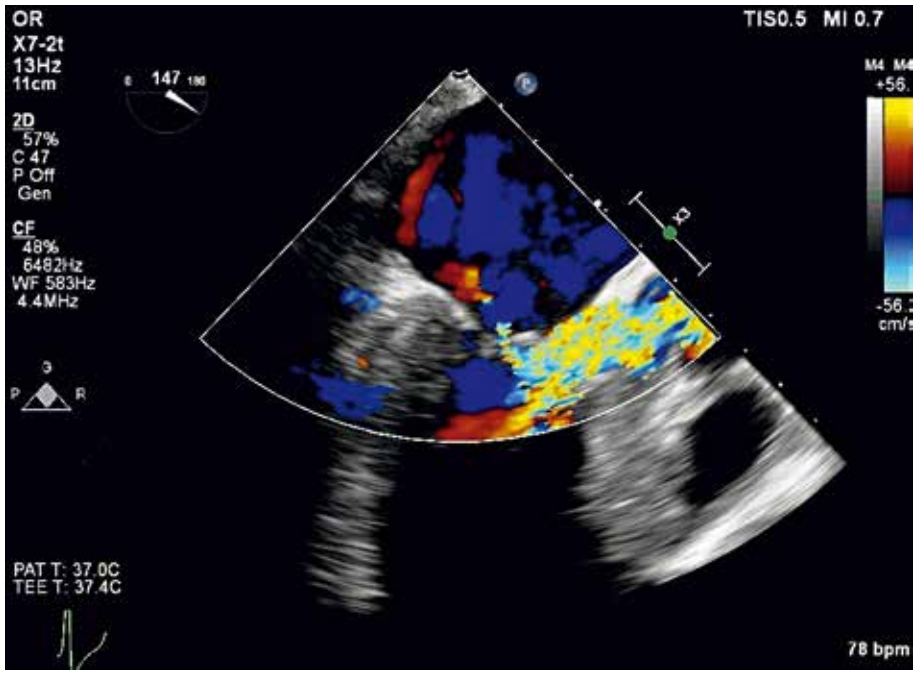

Figure 3. Picture obtained from transesophageal echocardiographic examination after bolus of epinephrine demonstrating worsening of LVOT obstruction with significant turbulence

Subsequently, 200 µg of IV epinephrine was given in 50 µg boluses but failed to demonstrate any improvement in blood pressure or ventilation. The adjunctive anaphylaxis medications including 100 mg hydrocortisone, 40 mg of famotidine, and 50 mg of diphenhydramine were administered. Salbutamol was delivered through the ventilator circuit with no improvement in airway pressures or oxygenation. With a real-time TEE, it could be seen on a colour-flow Doppler that the epinephrine boluses had caused a worsening of the LVOT gradient and obstruction (Fig. 3). The

patient's heart rate had increased to between 110–120 beats per min while the MAP fell to as low as 30 mm Hg. Because her hypotensive shock was refractory to medical treatment, the decision was made to put the patient urgently onto cardiopulmonary bypass (CPB), which was initiated 25 minutes after the initial onset of hypotension.

Once CPB was started, the patient was kept anaesthetized with propofol and her blood pressure was supported with a norepinephrine infusion. A blood probe for serum tryptase activity was drawn immediately after CPB had commenced, and was found to be elevated at 16.6 mg mL^{-1}. Cefazolin administration was delayed until this moment. After one hour of CPB, the patient's norepinephrine requirements were 0.04 μg kg^{-1} min^{-1}. Two hours after the initiation of CPB and after separation from CPB, protamine was administered by the surgeon directly into the aorta to decrease the possibility of new episodes of severe hypotension. The patient was brought to the ICU requiring only 0.125 μg kg^{-1} min^{-1} of phenylephrine. At the end, her total fluid balance was net positive 8 litres. An excellent surgical result was seen with the LVOT obstruction completely resolved on the TEE. Her myocardial function was preserved with no wall motion abnormalities observed.

Due to airway swelling and facial oedema, extubation was delayed until the second postoperative day (24 h post surgery). The patient initially complained of mild word-finding difficulties, which were resolved by discharge. No other neurologic symptoms were detected. A computed tomography scan of the head performed on postoperative day 5 did not reveal any abnormalities. An allergy specialist referral was made and the patient was discharged home one week after her surgery. Although she had a negative skin test to rocuronium, she was confirmed to have an allergy to chlorhexidine.

DISCUSSION

The pathophysiology of HOCM is caused by the abnormal hypertrophy of the left ventricle with the ventricular septum disproportionately affected, leading to LVOT obstruction. As increased contractility and hypovolaemia promote this obstruction, the haemodynamic goals for such a patient is focused on maintaining a slow sinus heart rate and a good preload [1, 2]. An optimal anaesthetic would include augmenting LV preload and afterload and decreasing both contractility and heart rate. In the presented case report, the patient experienced concomitant anaphylaxis and these goals became very difficult to achieve. Ultimately, after all standard resuscitation measures had failed we had to institute CPB, which most likely became life-saving treatment.

Anaphylaxis is defined as "a serious allergic reaction that is rapid in onset and may cause death" [3]. Its incidence is estimated at 1 in 3,500 to 1 in 20,000 surgeries with a mortality rate from 3% to 9% [4]. The clinical symptoms of anaphylaxis are thought to result from a sudden massive release of mast cell and basophil-related mediators into the systemic circulation causing multiple organ systems to be affected. The effects on the cardiovascular system include hypotension, cardiovascular collapse, and increased vascular permeability [5]. Effects on the respiratory system manifest as bronchospasm and airway oedema while typical cutaneous signs include urticaria and flushing. After discontinuing any potential offending agents, the most important pharmacologic treatment is epinephrine [6–8]. Other adjunctive medications include fluid administration, corticosteroids, and antihistamines [9].

Various agents including latex, antibiotics, antiseptics, and neuromuscular blockers have been linked to anaphylaxis occurring in the operating room [10]. Neuromuscular blockers are implicated in approximately 63% of perioperative anaphylaxis episodes, making them the most likely culprit in our patient [11]. More specifically, the incidence of rocuronium anaphylaxis is 1 in 2,499 [12]. Chlorhexidine is an increasingly recognized cause of anaphylaxis. Although the actual incidence of anaphylaxis regarding this agent is unknown, a study of patients that had had perioperative anaphylaxis revealed that 9.6% of them had a positive skin test to chlorhexidine [13, 14].

To our knowledge, no other case reports have discussed the perioperative management of anaphylaxis in combination with HOCM. We were fortunate to have CPB capability available immediately because, despite the typical medical management of anaphylaxis, the patient failed to improve and most likely would have died. In a non-cardiac operating room, veno-arterial extracorporeal life support has been used to resuscitate a patient with anaphylaxis in concomitant cardiogenic shock and would have been an alternative option if CPB had not been available [15]. In patients with refractory anaphylaxis, vasopressin has been used successfully [16–18]. Another alternative would be vasopressin, which is thought to cause vasoconstriction through multiple mechanisms different from epinephrine without any increase in myocardial contractility and which may be desirable in HOCM; this agent also failed to improve our management. In this context, the authors of this case report would suggest that patients with HOCM scheduled for non-cardiac surgery should be referred to tertiary care centres which are able to offer the aforementioned treatment modalities, not only in cases of severe anaphylaxis but also in the occurrence of haemodynamic instability.

We should also mention that other strategies were used to avoid exacerbating the patient's condition in the operating room. The first was to administer cefazolin only once CPB had been established in order to avoid aggravating the patient's condition by another drug commonly implicated in anaphylaxis. The second was to administer protamine by

the intra-aortic route, which has been shown to decrease the incidence of hypotensive events [19–21].

CONCLUSIONS

In summary, the presented patient had two conditions that, when combined, were virtually incompatible with life. Despite high doses of vasopressors, volume therapy and antihistamine treatment, the patient's blood pressure never improved until she was put onto CPB. Epinephrine failed to improve haemodynamics due to the enhancement of the LVOT obstruction from the resulting tachycardia and increased contractility. The initiation of CPB allowed the anaesthesia team to stabilize the patient's haemodynamic situation and allowed her anaphylaxis pharmacotherapy to take effect; after the discontinuation of CPB, the patient was haemodynamically stable. Unlike the typical anaphylactic patient, her underlying HOCM pathophysiology made resuscitation much more difficult and she likely would not have survived in a non-cardiac centre. Thus, clinicians should recognize this possibility and consider having patients with HOCM undergo non-cardiac surgery at a tertiary care centre that is equipped with extracorporeal lung support to provide rescue therapy for this type of patient.

ACKNOWLEDGEMENTS

1. Source of funding: none.
2. Conflict of interest: none.

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Otrzymano: 12.06.2016 r.
Zaakceptowano: 23.09.2016 r.