



Case Report

A rare combination of undiagnosed hypertrophic cardiomyopathy revealed by intraoperative anaphylaxis resulting in acute left ventricular outflow obstruction and cardiac arrest



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Received 28 November 2015; revised 2 February 2016; accepted 12 February 2016

Keywords:

Hypertrophic
cardiomyopathy;
Left ventricular outflow
obstruction;
Anaphylaxis;
Vancomycin anaphylaxis;
Pulseless electrical activity

Abstract A 75-year-old female presented for left total hip reimplantation and suffered pulseless electrical activity arrest upon lateral positioning and administering vancomycin. Resuscitation was achieved according to Advanced Cardiac Life Support protocol. Post-event echocardiography showed hypertrophic cardiomyopathy with asymmetrical septal thickening, an under-filled left ventricle, dynamic left ventricular outflow obstruction, and severe mitral regurgitation related to systolic anterior motion of the mitral valve. Laboratory analysis showed a tryptase level of 209 ng/mL. After multispecialty evaluation, it was concluded that the patient's arrest was due to vancomycin anaphylaxis in the setting of previously undiagnosed hypertrophic cardiomyopathy leading to acute left ventricular outflow tract obstruction. After medical optimization of the patient's cardiomyopathy and an evaluation of potential intraoperative allergic triggers, the patient underwent a successful hip reimplantation without incident. This case presents a novel combination of events leading to intraoperative cardiac arrest. Rapid identification and an understanding of the cause(s) of cardiac arrest in this setting are critical for effective perioperative care.

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A 75-year-old woman with controlled hypertension, nicotine dependence, and degenerative joint disease presented to Rochester Methodist Hospital, Mayo Clinic, Rochester, MN, for left total hip reimplantation. She had undergone uneventful resection of an infected left total hip arthroplasty with

vancomycin spacer placement four months prior. Preoperative evaluation revealed an electrocardiogram (ECG) with non-specific ST changes in the anteroseptal territory but no evidence of active cardiac disease was elicited on history or physical examination. Functional status was reported as >4 metabolic equivalents. The patient had a history of both penicillin and cephalosporin allergies.

A preoperative lumbar plexus block was placed by nerve stimulator localization and 30 mL of 0.5% bupivacaine was administered. An arterial line was placed in conjunction with

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standard American Society of Anesthesiology monitors prior to uneventful induction of general anesthesia with fentanyl, lidocaine, propofol and succinylcholine. An infusion of vancomycin 750 mg was started at 12.5 mg/min. Approximately 15 minutes later, upon lateral positioning the patient became acutely hypotensive with a blood pressure of 60/40 mmHg, followed shortly thereafter with a flattened arterial line tracing and loss of palpable pulses. The patient was immediately placed in the supine position and resuscitation was performed according to Advanced Cardiac Life Support protocol including high-quality chest compressions. Epinephrine 0.5 mg IV was given, with a repeat dose of 0.5 mg IV one minute later. Return of spontaneous circulation was achieved after 90 seconds. The patient developed a second episode of pulseless electrical activity (PEA) arrest approximately 5 minutes later and return of spontaneous circulation was achieved after a brief period of chest compressions and epinephrine 0.5 mg IV in 2 divided doses. Due to the temporal relation between these events and vancomycin administration, the infusion was discontinued immediately upon loss of pulses and diphenhydramine 50 mg IV was given. The surgical procedure was aborted and the patient was transferred to the intensive care unit.

Prompt post-event evaluation revealed an ECG that was unchanged from baseline. Workup for pulmonary embolism was negative. Transthoracic echocardiography (TTE) showed an under-filled left ventricle, hypertrophic cardiomyopathy (HCM) with asymmetrical septal thickening (basal septal thickness of 15 mm), dynamic left ventricular outflow obstruction with a peak gradient of 100 mmHg and severe mitral regurgitation related to systolic anterior motion of the mitral valve. Tryptase level drawn at the time of initial resuscitation was markedly elevated at 209 ng/mL (normal ≤ 11.5 ng/mL) making the diagnosis of anaphylaxis likely.

An elevated troponin T of 0.11 ng/mL and 0.13 ng/mL at 3 and 6 hours post-event (from a baseline of 0.04 ng/mL) in addition to hypokinesis and akinesis in the anterior/septal regions on postoperative TTE prompted cardiac catheterization which showed no significant coronary obstruction. Subsequently, a diagnosis of a non-ST-elevation myocardial infarction was made. A repeat TTE revealed a left ventricular outflow tract (LVOT) gradient of 16 mmHg at rest that increased to 124 mmHg with amyl nitrite. The patient was diagnosed with both intraoperative anaphylaxis and HCM, which was previously undiagnosed. It was felt that the patient's anaphylactic event created an acute decrease in preload, producing dynamic left ventricular outflow obstruction and subsequently PEA arrest.

Due to an ongoing need for definitive hip replacement, the patient underwent multispecialty evaluation following her initial event. Given the patient's lack of outflow obstruction at baseline and advanced age, cardiology consultation recommend medical optimization by increasing the metoprolol dose for further negative inotropic treatment along with initiating diltiazem instead of amlodipine and hydrochlorothiazide for management of hypertension.

As a result of a persistently evaluated serum tryptase (18.1 ng/mL), a complete evaluation for systemic mastocytosis, including a bone marrow biopsy, was performed. The patient did not meet criteria for systemic mastocytosis and potential intraoperative allergens were evaluated through skin testing as previously described in the Mayo Clinic Division of Allergic Diseases [1]. Common intraoperative allergens including latex and chlorhexidine showed negative skin testing. Vancomycin skin testing was not performed due a high rate of false positivity. Based on the sequence of events and a lack of evidence for other allergic triggers, vancomycin was considered the most likely causative agent for the patient's intraoperative anaphylaxis. Recommendations were made to avoid vancomycin and pre-medicate with montelukast, fexofenadine, and prednisone prior to any future surgical procedures. The patient subsequently underwent an uncomplicated left hip reimplantation two months after her initial event following the above recommendations.

Discussion

Intraoperative cardiac arrest is associated with high mortality [2]. Prompt identification of the etiology is crucial to acute treatment and prevention of such events in the future. This unique case is the first observation of documented anaphylaxis unmasking previously undiagnosed HCM leading to LVOT obstruction and intraoperative PEA arrest.

Hypertrophic cardiomyopathy can present at any age, may remain clinically silent until late in life, and is compatible with a normal life expectancy. Subaortic obstruction is significantly more common in elderly patients, many of which are completely asymptomatic at the time of diagnosis [3]. Abnormal ECG findings are common in patients with HCM, with only 5% to 10% of patients having a completely normal ECG [4]. In our patient, a preoperative ECG showed non-specific ST changes in the anteroseptal territory but there was no history of coronary or structural heart disease and her functional status was reported as >4 metabolic equivalents. A preoperative murmur, especially a late systolic ejection murmur, split second heart sound and a fourth heart sound can be another indication of undiagnosed HCM in elderly patients presenting for surgery [5]. A clinical diagnosis of HCM is defined by echocardiographic findings of unexplained increased left ventricular wall thickness (≥ 15 mm), whereas obstructive HCM implies LVOT obstruction due to systolic anterior motion of the mitral valve [6].

The underlying cardiac and circulatory pathophysiology present in this confluence of conditions presents a clinical challenge both during acute care as well as when considering future management. Proper anesthetic care of patients diagnosed with HCM strives to maintain sinus rhythm, normal left ventricular diastolic volume (preload), and normal systemic vascular resistance (afterload) while

limiting increased myocardial contractility and sympathetic stimulation. Irregular heart rhythms, reduced preload secondary to hypovolemia and/or acute blood loss, reduced afterload, and enhanced myocardial contractility are known to worsen LVOT obstruction [5,7].

Typical manifestations of anaphylaxis include multisystem organ involvement with urticaria, bronchospasm, and cardiovascular collapse often within minutes of contact with the offending agent. A diagnosis of anaphylaxis can be made with only one organ system involved if there is known allergen exposure [8]. Tryptase, an enzyme released from secretory granules of mast cells is reliable marker of acute anaphylaxis. Measurable amounts of tryptase are detected 30 to 60 minutes following allergen exposure and decline according to first-order kinetics with a half-life of approximately 2 hours [9]. In our case, serum tryptase was critical in identifying the presence of anaphylaxis given the lack of multiple organ involvement.

Vancomycin is a known direct mast cell activator and can cause flushing and hypotension secondary to histamine release. Slow infusion, over 30 to 60 minutes is known to prevent these effects [10]. In our case, the patient had a non-articulating vancomycin-impregnated cement spacer implanted into the left hip joint four months prior. The spacer delivers antibiotic directly to the infected joint, limits systemic uptake, and is completely absorbed over a period of weeks [11]. Intraoperative vancomycin anaphylaxis has been described following repeated and prolonged previous exposure to vancomycin [12]. It is possible our patient became sensitized following prior vancomycin exposure and upon receiving intravenous vancomycin during the procedure, experienced significant mast cell degranulation.

During anaphylaxis, multimeric antigen cross-linking of 2 IgE receptors on mast cells and basophils sensitize individuals resulting in a signal-transduction cascade that leads to release of vasoactive mediators (histamine, prostaglandins, and leukotrienes) [13]. Although difficult to assess in the complex situation, the quick and robust response to resuscitation along with an absence of classic signs of severe allergic reaction make it likely that the actual allergic reaction was mild-to-moderate in severity. The main contributing factor to the cardiac arrest was likely her HCM physiology, which was unmasked by an acute decrease in preload and vasodilation from anaphylaxis and also exacerbated by preoperative fasting, general anesthesia, and lateral positioning. This combination of factors precipitated LVOT obstruction and PEA arrest.

In conclusion, this case illustrates the important physiological consequences of intraoperative anaphylaxis, the utility in obtaining a tryptase level when encountering

significant hemodynamic changes without obvious cause, and the consequences of HCM-related LVOT obstruction. Although anaphylaxis and undiagnosed HCM are distinct entities that by themselves can be managed uneventfully, the unexpected combination of the two led to a “perfect storm” in this patient.

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