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Case Report

Rocuronium-Induced Anaphylaxis Causing Systolic Anterior Motion of the Mitral Valve and Hemodynamic Collapse

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ABSTRACT

We present an unexpected case of systolic anterior motion of the mitral valve (SAM) caused by anaphylaxis to rocuronium, in a patient who presented for an elective total knee replacement. We present this case to increase clinical suspicion of both rocuronium anaphylaxis and SAM in the peri-operative patient who presents with shock, to highlight the importance of focussed echocardiography in the diagnosis of SAM, and to educate trainees on the acute management of the condition.

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Systolic anterior motion of the mitral valve (SAM) is an uncommon phenomenon with a broad range of predisposing factors and precipitants. It can have significant hemodynamic consequences and should be ruled out in the presence of undifferentiated shock states. However, the management of certain shock states such as cardiogenic shock, may actually exacerbate SAM and lead to further hemodynamic instability. The incidence of SAM post-mitral valve (MV) surgery is well documented (1). However, the incidence of SAM unrelated to MV surgery is not known. We present a case of SAM caused by rocuronium anaphylaxis and the use of focussed echocardiography in its diagnosis, as well as highlighting the need for SAM to be included in a clinician's differential diagnosis.

Case Presentation

A 67-year-old man presented for an elective total knee replacement. His past medical history included controlled hypertension, mild asthma, obesity with the body mass index (BMI) 37, hypercholesterolemia, benign prostatic hypertrophy, a 30- pack year smoking history and no known drug allergies. His pre- operative work-up included routine bloods and electrocardiogram (ECG) and had 3 previous transurethral resections of prostate (TURP) operations with no surgical or anesthetic complications.

In the anesthetic room pre-operatively, the patient had dual heart sounds with no murmurs on auscultation and observations were within the

normal range. A spinal anesthetic was administered without complication and then proceeded to induction for a general anesthetic. He was given 200 mg propofol, 50 micrograms of fentanyl and 100 mg rocuronium intravenously. Almost immediately, his blood pressure dropped to 43/11 mmHg and he became tachycardic. He was given 100 micrograms of intravenous adrenaline and crystalloid fluid boluses but he suffered a ventricular fibrillation (VF) arrest and cardio-pulmonary resuscitation (CPR) was commenced. He was intubated and the arrest was managed as per advanced cardiac life support (ACLS) guidelines. He was given a total of 5 mg adrenaline in boluses before an infusion was commenced. Additionally, he was also given 500 mg of sugamadex to reverse the effects of rocuronium. Return of spontaneous circulation (ROSC) was achieved after 35 minutes of CPR but he was significantly adrenaline- dependent, requiring an infusion of 80 micrograms/minute to maintain his blood pressure. A focused intra-operative trans-esophageal echocardiogram (TOE) was performed by an available cardiac anesthetist during CPR. The limited study excluded pericardial tamponade, right ventricular failure due to massive pulmonary embolus, severe aortic stenosis and significant regional wall motion abnormality as potential causes of shock. The mitral valve was not interrogated. Following ROSC, all ventricular walls were reported to be contracting. Given the rapid deterioration and arrest so soon after administration of propofol and rocuronium, the working diagnosis was that he suffered an anaphylactic reaction to rocuronium with subsequent VF arrest. He was transported to ICU for ongoing care.

Investigations

On arrival to ICU, the patient was found to have a new harsh systolic murmur at the left sternal edge. An urgent bedside transthoracic echocardiography (TTE) study was performed. On 2D B- Mode imaging, the left ventricular size was small and hyperdynamic with severe concentric LV hypertrophy. On close inspection of the mitral and aortic valves (Figure 1), the anterior leaflet of the mitral valve was seen obstructing the left ventricular outflow tract (LVOT) in the parasternal long axis view (PLAX) in systole. In the apical 5 chamber view (A5C), Doppler interrogation with Continuous Wave (CW) across the aortic valve showed a high velocity flow of 644 cm/s and a peak gradient of 150 mmHg with late systolic peak (Figure 2). There was evidence of mitral regurgitation on color flow and continuous wave Doppler. Following the findings of transthoracic imaging, noradrenaline infusion was commenced, 1.5 L of intravenous 4% albumin was administered and the adrenaline infusion was gradually weaned off.

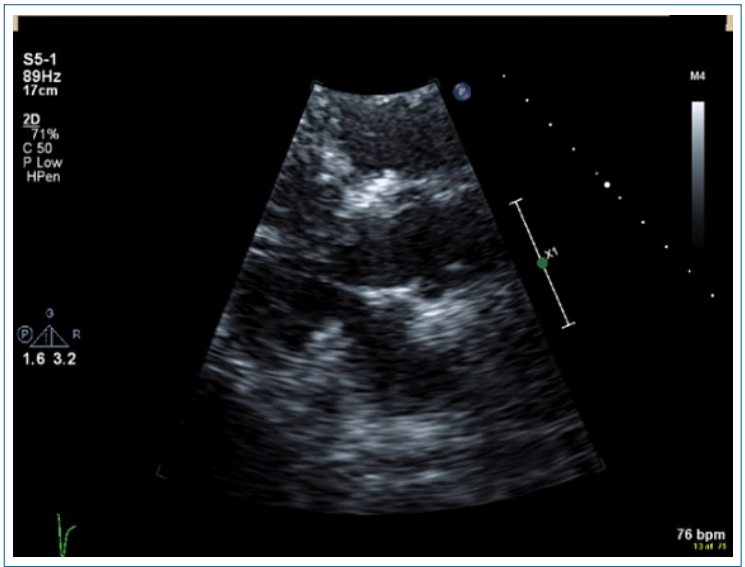

Figure 1. Parasternal Long Axis View of Anterior Leaflet of Mitral Valve Across the LVOT in Systole (arrow). Note that the aortic valve is opened in systole.

Serial TTE studies over the following days demonstrated the LVOT obstruction and SAM resolving with normalization of the left ventricular systolic function (Figure 2). The murmur also resolved. The patient remained intubated and ventilated for seven days before being extubated and weaned off vasopressor support. Mast cell tryptases taken at the time of the arrest came back strongly positive (214 µg/L). He was sent to an allergy and immunology specialist on discharge who agreed with the diagnosis of rocuronium anaphylaxis. Other investigations included a coronary angiogram which showed only mild to moderate left anterior descending

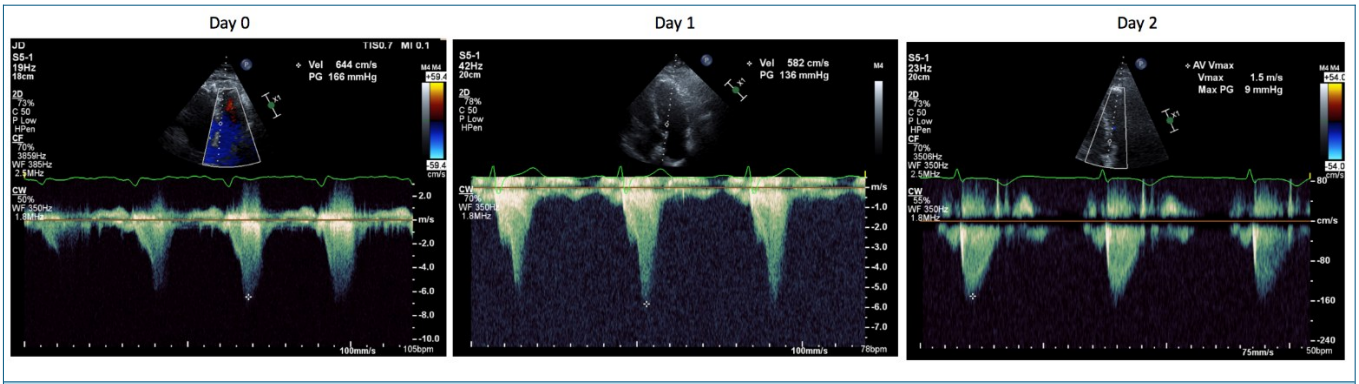

Figure 2. Serial TTE Images Using Continuous Wave Doppler Ultrasound to Assess the Aortic Valve Peak Gradient Which Showed Reducing LVOT Obstruction from Day 0 to Day 2.
Day 0 = 166 mmHg, day 1 = 136mmHg, and day 2 = 9 mmHg.

(LAD) disease that did not require stenting.

Discussion

SAM was first described nearly 40 years ago, initially as a complication of MV repair (2) and has been well studied and documented since then, with Hwang et al. describing the factors that influence SAM as the geometrical arrangement of the mitral sub-valvular apparatus and a small left ventricle (LV) (3). The majority of cases are related to hypertrophic cardiomyopathy (HCM) or post-mitral valve repair surgery, although a number of medical causes have been identified including diabetes mellitus, myocardial infarction, hypertension and general anesthetic.

Inhaled and intravenous anesthetic agents can cause a reduction in cardiac output by means of reduction in systemic vascular resistance (SVR). This change in loading conditions results in a compensatory increase in LV contractility and alterations in flow across the LV outflow tract (LVOT), contributing to hemodynamic collapse. As a result of drag forces and the Venturi effect, blood flow velocity increases and the movement of the anterior mitral valve leaflet into the LVOT during systole results in obstruction to forward flow in late systole. In this case, the increased gradient across the LVOT was possibly exacerbated using spinal anesthetic technique prior to induction of general anesthesia. The hemodynamic balance was already compromised and then the circulation was challenged further by an anaphylactic reaction to rocuronium, resulting in cardiac arrest.

Neuromuscular blocking agents (NMBA) are the most common precipitants of anaphylaxis in the peri-operative setting (4), with rocuronium and suxamethonium having higher incidences when compared to vecuronium or atracurium (5, 6). In addition to the standard approach to treating anaphylaxis with adrenaline, several case reports have suggested that high dose sugammadex (12-14 mg/kg) has a role in accelerating the recovery from rocuronium-induced anaphylaxis (7, 8). However, in the setting of SAM and LVOT obstruction, the increase in inotropy from adrenaline therapy can exacerbate the obstruction and has been shown to induce SAM in both the structurally normal heart and those with HCM (9, 10).

The initial treatment of SAM with hemodynamic comprise is often delayed due to a lack of prompt recognition and delay to diagnosis using TTE. Once diagnosed, medical therapy is often successful in achieving hemodynamic stability (11). This is managed by increasing intravascular volume with fluids, vasopressor therapy, beta blockade and cessation of inotropes. Adrenaline was changed to noradrenaline as part of our hemodynamic management but beta blockade was not employed in our patient due to relative bradycardia. Surgical treatment options also exist once the patient is stable, although these depend

Take home messages.
• Systolic anterior motion of the mitral valve (SAM) needs to be included in the differential diagnosis of shock, especially if the patient is not responding to conventional shock therapy.
• The management of SAM involves increasing the intravascular volume, vasopressor therapy, weaning of inotropic agents and beta blockade.
• Bedside echocardiography is not only essential in the diagnosis of SAM, it is an achievable skill for clinicians looking after the critically ill.
• A thorough preoperative assessment can highlight higher risk patients and properly inform treatment decisions throughout the peri-operative period.

on the exact cause of SAM and the anatomy of the heart.

This was a rare and unexpected constellation of circumstances that had led to hemodynamic collapse in our patient. To our knowledge, this is only the second documented case of rocuronium-induced anaphylaxis causing LVOT obstruction secondary to SAM with the first case reported last year (12). Given the patient's impaired exercise tolerance, hypertension and high body mass index, dobutamine stress echocardiography may have been useful to elicit inducible LVOT obstruction on provocation. This could potentially influence the peri- operative management of the patient's volume status and the use of beta blockers.

Focused echocardiography is now a recognised part of critical care training. The majority of training guidelines, including the College of Intensive Care Medicine of Australia and New Zealand, mandates that trainees should be able to carry out a focussed cardiac ultrasound (FCU) assessment which focusses on ventricular function, recognition of pericardial effusions and volume assessments (13, 14). However, recognition of SAM is not part of the FCU algorithm to ruling it out as a cause of obstructive shock. This case highlights that an understanding of the pathophysiology of SAM, as well as Doppler ultrasound physics, will enable a bedside physician to rapidly diagnose and manage this important cause of shock.

The authors declare no conflicts of interest.

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