



Catecholamine-Refractory Anaphylactic Shock to Vecuronium in a Patient with Tetralogy of Fallot: A Case Report

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Abstract

Serious anaphylactic reactions to anesthetics can be life-threatening events. Vecuronium is promoted as a neuromuscular blocking drug that is least likely to cause anaphylaxis due to its low histamine-releasing potential. Perioperative hypoxemia in patients with tetralogy of Fallot (TOF) due to anaphylactic reactions can be easily misdiagnosed as anoxic spells. We report a patient with TOF who suffered from symmetrical peripheral gangrene after undergoing catecholamine-refractory anaphylactic shock to vecuronium perioperatively. CPB (cardiopulmonary bypass) is the most effective support for severe anaphylactic shock during the perioperative period. Intradermal test screening for anaphylaxis to anesthetics is an effective method for prevention and diagnosis.

Keywords

Anaphylactic Shock, Vecuronium, Tetralogy of Fallot, Cardiopulmonary Bypass, Symmetrical Peripheral Gangrene

Abbreviations

NMBDs: Neuromuscular Blocking Drugs; TOF: Tetralogy of Fallot; CPB: Cardiopulmonary Bypass; SpO₂: Pulse Oxygen Saturation; ECG: Electrocardiogram; SBP: Systolic Blood Pressure; ETCO₂: End-Tidal Carbon Dioxide; TEE: Trans Esophageal Echocardiography; MAP: Mean Arterial Pressure; DIC: Disseminated Intravascular Coagulation

Introduction

Anaphylaxis during the perioperative period is one of the major life-threatening risk factors for patients undergoing surgery and is a significant concern for anesthesiologists [1]. The incidence of perioperative anaphylaxis associated with anesthetics is approximately 1:5000-1:2000, with neuromuscular blocking drugs (NMBDs) being the most commonly involved [2]. Among all non-depolarizing NMBDs used

for anesthesia, rocuronium has the highest incidence rate of histamine release and anaphylaxis [3]. Vecuronium has been promoted as the NMBD least likely to cause anaphylaxis due to its low histamine-releasing potential [4]. We report a case of a patient with TOF who experienced symmetrical peripheral gangrene after undergoing catecholamine-refractory anaphylactic shock in response to perioperative vecuronium administration.

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Case Presentation

A 42-year-old woman (weight, 46 kg; height, 156 cm) with tetralogy of Fallot (TOF) came to our hospital seeking surgery treatment for cyanosis and dyspnea with general anesthesia. She had no history of allergies and had never been exposed to anesthetic drugs before.

The patient was monitored for oxygen saturation (SpO_2), ECG (DII and V5), and invasive blood pressure when she presented to the operating room. A low arterial oxygen saturation (79%) was detected by the basal blood gas analysis and oxygen was given to the patient. Midazolam (2 mg), sufentanil (60 μg), and propofol (100 mg) were successively administered for induction of general anesthesia, and vecuronium (8mg) was given after the patient fell asleep. After approximately 3 minutes, the patient experienced difficulty of breathing with mask-assisted ventilation, oxygen desaturation, worsening cyanosis, tachycardia and impalpable radial artery pressure. Successive administration of metaraminol 0.2mg, norepinephrine 20 μg and epinephrine 3 μg within a few minutes did not significantly improve the blood pressure (Fig-1). Endotracheal intubation and mechanical ventilation (VT: 400ml, Paw: 20mmHg) were performed

immediately. The heart rate soared from 60 to 120 beats/min, SpO_2 varied between 60% and 70%, end-tidal carbon dioxide (ETCO_2) fluctuated within a low range (0-15 mmHg). Then trans esophageal echocardiography (TEE) probe was inserted, and the TEE result showed that the heart atriums and ventricles of the patient were empty (Fig-2). Systolic arterial pressure (SBP) remained around 40mmHg and was poorly responsive to catecholamine drugs. Under the guidance of TEE monitoring, 1000 ml crystalloids were fast infused for anti-shock therapy. Hydrocortisone and calcium gluconate were also administered for antianaphylaxis, but the blood pressure remained unimproved.

Then emergency thoracotomy was performed, and a full dose of heparin (138mg) was given. About 27 minutes later the CPB started to work and the mean arterial pressure (MAP) increased to 60 mmHg in a short time. After aggressive antianaphylaxis treatment and continuous intravenous pumping of norepinephrine ($0.03\text{--}0.12 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$), the MAP was barely maintained from 50 to 60 mmHg. Intraoperative cerebral oxygen monitoring was performed, and its value fluctuated between 57% and 76%.

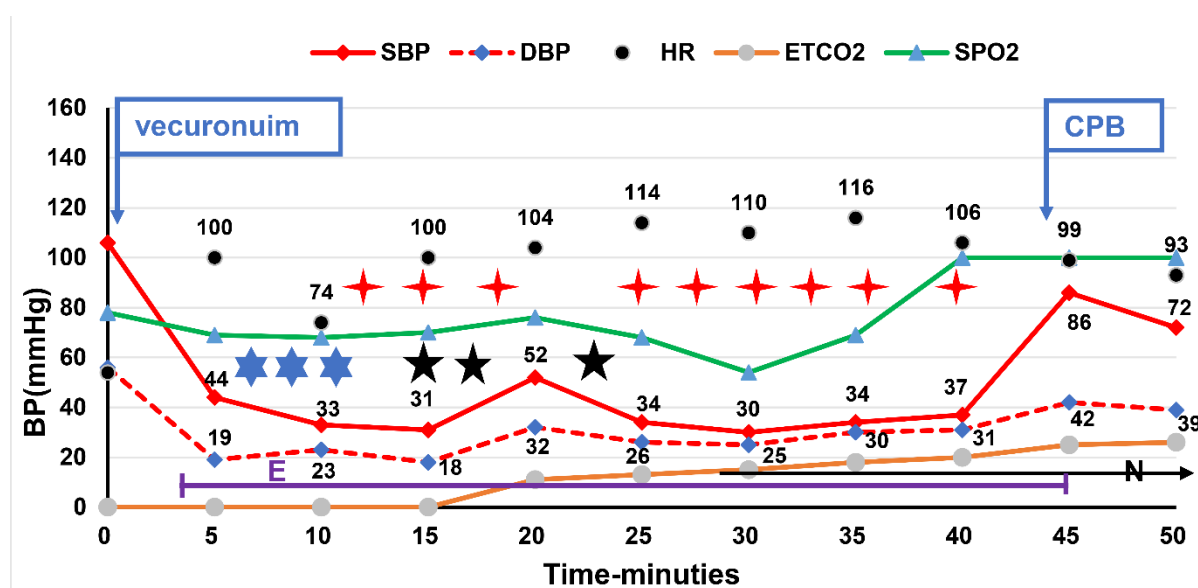


Fig-1: Vital Signs during the Anesthesia Induction

CPB, Cardiopulmonary Bypass; BP: Blood Pressure; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; E: Epinephrine ($0.1 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$); N: Norepinephrine ($0.1 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$); ★: epinephrine (3 μg bolus); ★: metaraminol (0.2mg bolus); ★: norepinephrine (20 μg bolus).

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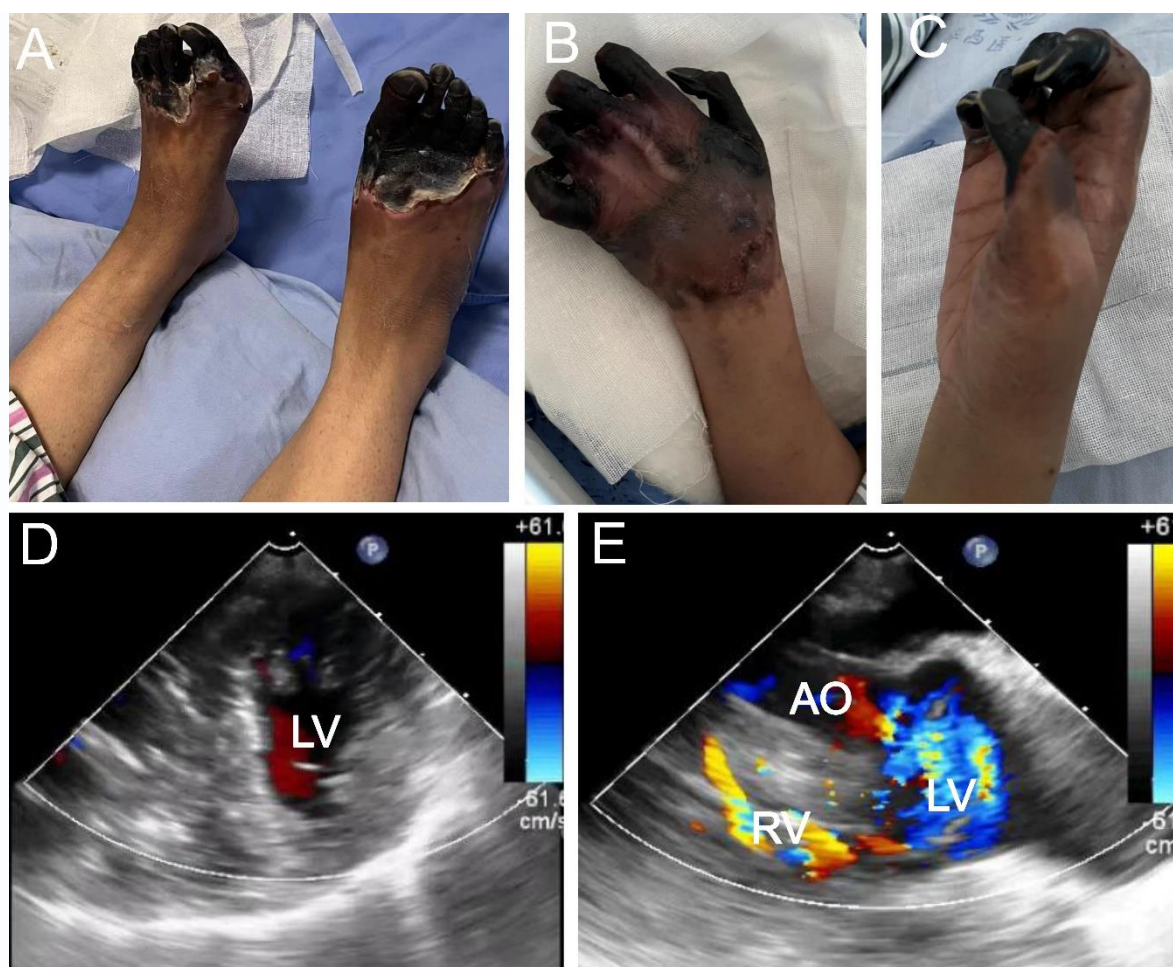


Fig-2:

Symmetrical peripheral gangrene on the feet (a) and hands (b,c); Trans esophageal echocardiography findings after induction of anesthesia (d,f)

Finally, the patient underwent radical operation of TOF and pulmonary valve replacement, with a 56-minute intra-operative aortic blockade. The intraoperative CPB was maintained for 160 minutes at a flow rate of $3 \text{ L}^{-1} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ and shut down smoothly with an hourly urination of $6 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$.

The SBP of the patient remained difficult to maintain at 80-90 mmHg with a high dose of catecholamines for 12 hours after surgery. The dose of epinephrine was gradually reduced until discontinuation after five days., and the endotracheal tube was successfully removed after seven days. Gastrointestinal bleeding occurred in the patient on the first day postoperatively. Then the plasma, human fibrinogen and prothrombin complex were transfused to stop bleeding. Postoperative coagulation function monitoring showed that the activity of coagulation was stronger than that of fibrinolysis, and the endothelial

system was damaged. On the fifth postoperative day, the patient was found to have multiple peripheral thrombosis, as well as cyanosis and swelling in the distal wrists and feet on both sides. The ischemia of the extremities did not improve after the treatments including keeping the peripheral limbs warm, anticoagulation with heparin, and improvement of microcirculation. Black dry gangrene with infection and symmetrical peripheral gangrene (SPG) gradually emerged (**Fig-2**).

Two weeks later, skin prick test (SPT) and intradermal test (IDT) for anesthetics which has been used during the operation revealed a strongly positive allergy to vecuronium, while the results for other general anesthetics such as sufentanil, midazolam, cis-atracurium, and propofol were negative. The patient was discharged 1.5 months after the surgery without any neurologic or cardiac sequelae, and was followed

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up regularly in orthopedic clinic for SPG. After three months, the patient was again hospitalized for fingers/toes amputation due to SPG. Vecuronium was replaced with cis-atracurium as a NMDB, along with other anesthetics used in the previous general anesthesia protocol, with no complications. The timeline lists important events in the patient's course in chronological order (**Fig-3**).

Discussion

Anaphylaxis, also known as acute systemic hypersensitivity, involves multiple organ systems, especially the skin, respiratory, cardiovascular, gastrointestinal and digestive systems [5]. Severe anaphylactoid reactions can lead to refractory shock, circulatory collapse, bronchospasm or even death. According to previously reports, NMDBs, antibiotics, gelatin, protamine, latex, and blood products are the

most often implicated allergens [6,7]. The most prevalent clinical signs of perioperative allergic anaphylaxis include hypotension, bronchospasm, tachycardia, oxygen desaturation, bradycardia and reduced or absent ETCO₂ [8].

Tetralogy of Fallot (TOF) is a cyanotic congenital heart disease with ventricular septal defect, pulmonary artery stenosis, aortic riding and right ventricular hypertrophy [9]. Perioperative hypoxemia due to anaphylactic reactions in patients with TOF is often and easily misdiagnosed as anoxic spells. Even though, there still are differences between anoxic spells and anaphylactic shock in terms of clinical manifestations and treatments (**Table-1**). In our case, after the anesthesia induction, airway resistance increased, blood pressure decreased rapidly, heart rate increased, blood oxygen desaturated, and the result of TEE

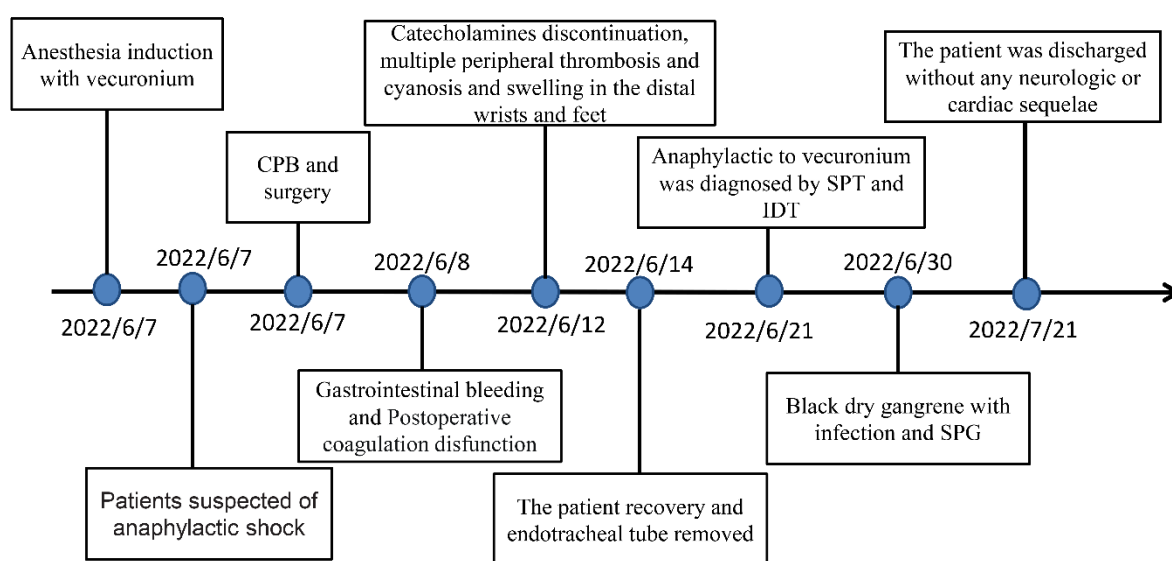


Fig-3: The Timeline for Diagnosis, Treatment and Prognosis

Table-1: Comparison of Anoxic Spells and Anaphylactic Shock [1,15]

	Anoxic spells	Anaphylactic shock
Airway Resistance	-	±
Blood Pressure	↓↓↓	↓↓↓
Heart Rate	↓	↑
Central Venous Pressure	↑	↓
Oxygen Saturation	↓↓↓	±
Skin Rashes	-	±
Cardiac Echocardiography	right-to-left shunt	cardiac emptiness

“—” : negative results; “+” : positive results; “↑” : increasing; “↓” : decreasing

showed cardiac emptiness, indicating the significant decrease of the effective circulating blood volume in a short time. Severe anaphylactic reaction rather than anoxic spells was first considered. When she had a catecholamine-refractory anaphylactic reaction, the systemic hypoxia in the patient worsened and the pulmonary artery pressure rose, resulting in a complete right-to-left shunt, a low pulmonary blood flow, oxygen desaturation, and a decreased ETCO_2 . Refractory anaphylactic shock also caused cardiac emptiness and peripheral hypotension because it lowered the peripheral vascular resistance, increased the vascular permeability, decreased the returned blood volume, and decreased the volume of efficient blood circulation.

Catecholamine-refractory anaphylactic shock to vecuronium is rare. Yagi *et al.* reported a anaphylactoid reaction to vecuronium with bronchospasm and skin rashes [10]. Duman *et al.* reported an anaphylactoid reaction to vecuronium during intradermal testing with respiratory difficulties, angio-oedema, and hypotension [11]. The occurred anaphylactic reactions recovered quickly with the use of catecholamines in the previous reports. The patient in our report initially manifested an allergic reaction during anesthesia induction manifested as a catecholamine-refractory hypotension. Anoxic cyanosis concealed the skin rashes when severe allergic reaction happened in the patient with TOF. The patient suffered from severe anaphylactic shock, and the high doses of catecholamine drugs failed to improve the blood pressure consistently. Emergency thoracotomy to establish CPB was used as it turned out that CPB was an effective treatment for the refractory shock in patients with congenital heart disease. The results of intraoperative monitoring of cerebral oxygen saturation and urine volume were in the normal range, indicating good perfusion of brain and kidney.

Approximately 95% of NMBD-induced reactions appeared within 5 minutes [1]. The patient in our case report developed refractory shock 3 minutes after intravenous induction, and we strongly suspected that she was allergic to the vecuronium; postoperative intradermal test result confirmed our speculation. Tests used to diagnose anaphylaxis include basophil

activation assays, SPT and IDT, serum tryptase levels, and drug-specific IgE levels. These test sensitivity and specificity of a skin test for NMBDs are over 95%.

There are several possible reasons for the poor prognosis of the patient. First, it was reported to have decreased endothelial function and impaired fibrinolysis in adults with TOF due to the long-term hypoxemia [12]. The patient with TOF in this case was more prone to endothelial injury and coagulation dysfunction. Second, hypercoagulability can occur after severe shock, the risk can change from bleeding to thrombosis during the complicated, dynamic process of responding to tissue injury caused by shock [13]. In our case, the high-dose heparinization blocks the thrombotic pathway during the surgery, and the dose of heparin was reduced after surgery because of bleeding tendency. In the early stage, hypoperfusion induced hypocoagulability and hyperfibrinolysis and bleeding tendency. Then heparin was discontinued, and the transfusion of plasma, human fibrinogen and prothrombin complex were performed to stop bleeding. In the later stage, continuous hypoperfusion and oxygen shortage triggered vascular endothelial damage, platelet dysfunction, and massive release of procoagulant, disseminated intravascular coagulation (DIC), and the activity of coagulation turned to be stronger than that of the fibrinolytic which promoted blood clotting. The DIC occurred in this case may be responsible for the intravascular thrombosis and infarction of the skin and SPG. Third, long-term use of high doses of vasoactive drugs to improve blood pressure can lead to intense constriction of peripheral vessels, which exacerbates peripheral vascular occlusion. The ensuing low blood flow condition may result in thrombus blockage of the microcirculation in the affected peripheral extremities. SPG is a complication that has been reported in septic shock patients treated with vasoconstrictor drugs, most patients with SPG eventually require amputation for therapy [14]. Early vasodilation, local nerve blocks, and physical therapy may be helpful to achieve a favorable prognosis in this case.

Conclusion

Perioperative hypoxemia in patients with tetralogy of Fallot (TOF) due to anaphylactic reactions can be

easily misdiagnosed as anoxic spells. catecholamine-refractory anaphylactic shock to vecuronium has been rarely reported in the past, CPB is the most effective support for catecholamine-refractory anaphylactic shock. Preoperative intradermal test screening for anaphylaxis to common anesthetics is an effective approach for prevention and diagnosis of anaphylaxis and also helps to figure out which drugs will be safe to use if future anesthesia is necessary.

Patient's Perspective

An unexpected severe allergic reaction can be fatal. Fortunately, I was able to save my life through timely and effective treatment. However, I developed the complication of ischemic necrosis of limbs, which may require a second operation in the future. Preoperative screening of allergens was necessary to ensure surgical safety.

Conflict of Interest

The authors have read and approved the final version of the manuscript. The authors have no conflicts of interest to declare.

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