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Perioperative Anaphylactic Shock Induced by Cisatracurium: A Case Demonstrating the Diagnostic and Clinical Value of Early Skin Testing

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Data Interpretation D
Manuscript Preparation E
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Patient: Male, 36-year-old
Final Diagnosis: Perioperative anaphylactic shock
Symptoms: Shock
Clinical Procedure: —
Specialty: Anesthesiology

Objective: Unusual clinical course

Background: Perioperative anaphylaxis is a life-threatening anesthetic emergency most commonly triggered by neuromuscular blocking agents (NMBAs). Although international guidelines recommend performing skin testing 4 to 6 weeks after the event, this delay is often impractical for patients requiring semi-urgent surgery. Delaying surgery can risk disease progression, while unguided re-exposure poses life-threatening allergic recurrence. This case report illustrates the diagnostic utility and clinical relevance of early skin testing in guiding anesthetic management when timely reoperation is necessary.

Case Report: A 36-year-old man scheduled for laparoscopic resection of a splenic lesion experienced immediate cardiovascular collapse following administration of cisatracurium (15 mg) during anesthesia induction. He developed profound hypotension (62/34 mm Hg), tachycardia (139 bpm), and a diffuse erythematous maculopapular rash over the chest. Rapid intravenous epinephrine administration led to prompt hemodynamic stabilization. Considering the need for timely surgical completion, skin prick testing was conducted on postoperative day 6, which revealed a positive reaction to cisatracurium and a negative response to rocuronium, indicating absence of cross-reactivity. Rocuronium was subsequently used for reinduction on postoperative day 7, allowing successful completion of surgery without further adverse reactions.


Conclusions: This case report shows that early skin testing following perioperative anaphylaxis can be both feasible and clinically informative in urgent surgical settings. It offers a time-efficient diagnostic solution to balance safety and surgical urgency in high-risk patients. Prompt identification of the causative NMBA enables safe substitution, minimizes surgical delay, and facilitates evidence-based anesthetic management decisions.

Keywords: anaphylaxis • perioperative period • skin tests
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Introduction

Perioperative anaphylaxis (POA) is a rare but potentially life-threatening complication in anesthesia practice. Reported incidence rates vary considerably from approximately 1 in 18 600 to as high as 1 in 1250 procedures, reflecting differences in patient populations, diagnostic criteria, and regional reporting systems [1,2]. Characterized by abrupt onset and rapid hemodynamic collapse, POA can manifest as severe hypotension, bronchospasm, or cardiovascular arrest, posing major challenges for anesthetic management. Among the known triggers, NMBAs remain the leading cause, followed by antibiotics and antiseptic agents such as chlorhexidine [3,4]. Although cisatracurium is generally considered less immunogenic than other NMBAs, it can nonetheless provoke severe hypersensitivity reactions when anaphylaxis occurs [5,6].

Timely and accurate identification of the offending agent is essential for safe perioperative management and for preventing recurrence during subsequent anesthetic exposures. Current international guidelines recommend deferring allergy testing for 4 to 6 weeks following an anaphylactic episode to allow immune effector cell recovery and to minimize false-negative results [7,8]. However, this recommended delay poses a clinical dilemma for patients requiring urgent or semi-urgent surgery. Proceeding without identifying the causative agent risks inadvertent re-exposure to the allergen, whereas postponing surgery can adversely affect patient outcomes. Notably, existing studies and guidelines have not yet addressed this dilemma effectively—there is a lack of practical diagnostic strategies for patients who cannot wait the recommended 4 to 6 weeks due to semi-urgent surgical needs, leaving clinicians with no clear guidance on how to balance diagnostic accuracy and surgical timeliness. Notably, existing studies and guidelines have not effectively addressed this dilemma.

Practical diagnostic strategies are lacking for patients who cannot wait 4 to 6 weeks due to semi-urgent surgery, leaving clinicians without clear guidance to balance diagnostic accuracy and surgical timeliness. To address this challenge, early skin testing performed within days to 2 weeks after the reaction has been proposed as a pragmatic alternative. Although its diagnostic sensitivity and specificity are still under investigation, emerging evidence indicates that early positive results are generally reliable for identifying the offending agent, whereas negative results should be interpreted with caution and in conjunction with clinical findings [9,10]. Nevertheless, most previous studies on early skin testing focused only on its diagnostic accuracy in general perioperative settings, failing to specifically explore its applicability, safety, and optimal timing in patients with semi-urgent surgical needs. This gap means that clinicians lack evidence-based support when deciding whether to perform early skin testing for such patients,

and there is no clear consensus on how to adjust testing protocols to ensure both safety and effectiveness in time-sensitive scenarios.

Here, we present a case of severe anaphylaxis induced by cisatracurium during induction of general anesthesia for an elective laparoscopic procedure. Owing to the need for timely surgical intervention, early multi-agent skin testing was conducted on postoperative day 6. The results informed a revised anesthesia plan that enabled safe reinduction and successful completion of surgery. This case underscores the potential role of early allergy assessment in time-sensitive perioperative settings and may guide future strategies when adherence to standard diagnostic timelines is impractical.

Case Report

A 36-year-old man (height: 174 cm, weight: 73 kg) was admitted for elective surgical management of a splenic mass that had been incidentally detected 2 years earlier. Abdominal computed tomography revealed a well-defined space-occupying lesion within the spleen, and laparoscopic partial splenectomy combined with cholecystectomy was planned. Preoperative laboratory and imaging evaluations were unremarkable.

On the day of surgery, the patient arrived in the operating room at 08:00 AM and was placed under standard monitoring, including electrocardiography, noninvasive blood pressure (NBP), heart rate (HR), and pulse oximetry. Baseline measurements were: NBP 131/86 mm Hg, HR 93 bpm, EtCO₂ 36 mm Hg and SpO₂ 98%. At 08:45 AM, a radial arterial line was established, revealing an invasive blood pressure (IBP) of 137/79 mm Hg.

General anesthesia was induced with intravenous dexamethasone (8 mg), sufentanil (20 µg), remimazolam (15 mg), propofol (60 mg), and cisatracurium (15 mg). After successful anesthesia induction, endotracheal intubation was performed on the patient. Within 3 minutes of cisatracurium administration, the patient developed abrupt and profound hypotension (nadir: 62/34 mm Hg), EtCO₂ decreased to 22 mm Hg, with marked sinus tachycardia (peak: 139 bpm), accompanied by diffuse erythema and a maculopapular rash over the chest.

Immediate treatment was initiated with an intravenous bolus of epinephrine (0.05 mg), resulting in partial hemodynamic improvement. A second bolus (0.05 mg) promptly restored blood pressure to 140/75 mm Hg. Continuous norepinephrine infusion (0.05 µg/kg/min) was started to maintain circulatory stability. Transient hypotensive episodes (IBP 105/65 mm Hg) 5 minutes after the second epinephrine bolus indicated persistent vasodilation secondary to anaphylactic mediator release. As vital signs normalized and cutaneous manifestations subsided,

Table 1. Timeline of management and vital signs during the anaphylactic shock episode.

Time	Intervention/management	Vital signs
8:00	Patient entered operating room; oxygen administration, ECG, noninvasive blood pressure (NBP), heart rate (HR), pulse oximetry, and respiratory rate (RR) monitoring initiated	NBP 131/86 mm Hg; HR 93 bpm; SpO ₂ 98%; RR 14 bpm
8:45	Radial arterial catheterization for invasive blood pressure (IBP) monitoring	IBP 137/79 mm Hg; HR 95 bpm; SpO ₂ 99%; RR 14 bpm
8:50	Induction of anesthesia: dexamethasone 8 mg, sufentanil 20 µg, remimazolam 15 mg, propofol 60 mg, cisatracurium 15 mg administered	IBP 62/34 mm Hg; HR 139 bpm; SpO₂ 95%; RR 22 bpm (severe hypotension, tachycardia, skin flushing and maculopapular rash observed)
8:51	Epinephrine 0.05 mg IV bolus administered	IBP 90/67 mm Hg; HR 115 bpm; SpO ₂ 97%; RR 19 bpm (partial hemodynamic improvement)
8:53	Second epinephrine 0.05 mg IV bolus administered	IBP 140/75 mm Hg; HR 101 bpm; SpO ₂ 99%; RR 16 bpm (vital signs stabilized)
9:00	Continuous norepinephrine infusion initiated at 0.05 µg/kg-min	IBP 137/89 mm Hg; HR 97 bpm; SpO ₂ 99%; RR 16 bpm (circulation maintained)
9:05	Patient transferred to intensive care unit (ICU) for observation	IBP 142/93 mm Hg; HR 90 bpm; SpO ₂ 99%; RR 16 bpm (stable condition)

Note: Severe anaphylactic shock occurred immediately after cisatracurium administration during induction. Prompt epinephrine boluses and continuous norepinephrine infusion rapidly restored and maintained hemodynamic stability.

anesthesia was discontinued. Surgery was cancelled despite rapid hemodynamic correction because the anaphylactic reaction occurred during anesthesia induction, prior to airway securement and surgical incision, proceeding with surgery at this stage would have exposed the patient to ongoing risk of recurrent hypersensitivity, airway compromise, and hemodynamic instability. The patient was extubated and transferred to the intensive care unit for monitoring and subsequently returned to the general ward the following day (Table 1).

Although the splenic mass was incidentally discovered 2 years ago, imaging studies confirmed potential malignant features (irregular margins and heterogeneous enhancement); therefore, semi-urgent surgical removal was required to rule out malignancy and prevent complications such as rupture or local invasion. This semi-urgent situation (not a strict medical urgency, but a need to avoid delay beyond 1 to 2 weeks to prevent disease progression) justified the decision to proceed with early skin testing rather than waiting the recommended 4 to 6 weeks. Because the patient strongly desired to proceed with definitive surgery without delay and was reluctant to wait the recommended 4 to 6 weeks for intradermal allergy testing, early allergy evaluation was undertaken on postoperative day 6. Skin prick testing was performed in the post-anesthesia care unit against a panel of commonly used anesthetic agents (drug concentrations are listed in Table 2 and results are shown in Figure 1). Skin testing was performed as a combination of skin prick testing followed by intradermal testing (for agents with negative prick test results), in accordance with

published guidelines [9,10]. For cisatracurium, testing was initiated with a lower dilution (1: 1000, 2 µg/mL) to minimize the risk of false-positive reactions [10], followed by the standard concentration (20 µg/mL) when the dilute test was negative. All test concentrations were within published non-irritant thresholds for anesthetic agents [10], and the chosen concentrations are supported by guidelines from the Australian and New Zealand Anaesthetic Allergy Group and the EAACI [9,10]. A pronounced wheal reaction was elicited by cisatracurium, whereas rocuronium testing was negative, indicating absence of cross-reactivity.

On postoperative day 7, the patient underwent laparoscopic partial splenectomy and cholecystectomy under a revised anesthesia plan. Rocuronium replaced cisatracurium as the neuromuscular blocking agent, and remimazolam was omitted. The surgery proceeded uneventfully, and the patient was discharged in stable condition on postoperative day 10.

Discussion

Perioperative Anaphylaxis: Epidemiology and Mechanisms

POA is a rapid-onset, potentially life-threatening systemic hypersensitivity reaction triggered by pharmacologic or chemical agents administered during the perioperative period. Clinical manifestations range from mild cutaneous symptoms to profound cardiovascular and respiratory compromise.

Table 2. Intradermal Test (IDT) agents, concentrations, reactions, and wheal diameters.

Drug	Test concentration	Reaction	Wheal diameter (mm)
Normal saline (negative control)	—	Negative (-)	5
Morphine (positive control)	10 µg/mL	Positive (+, papule enlargement with erythema)	10
Propofol 1%	1 mg/mL	Negative (-)	5
Propofol 2%	1 mg/mL	Negative (-)	5
Remimazolam	10 µg/mL	Negative (-)	7
Cisatracurium	20 µg/mL	Positive (+, papule enlargement with erythema)	10
Rocuronium	50 µg/mL	Negative (-)	5
Sufentanil	0.5 µg/mL	Negative (-)	5
Remifentanil	5 µg/mL	Negative (-)	5
Dexamethasone	400 µg/mL	Negative (-)	7
Palonosetron	5 µg/mL	Negative (-)	5

Note: A positive reaction was defined as a wheal ≥ 3 mm larger than the negative control, accompanied by erythema. Testing was performed on postoperative day 6 under standard monitoring conditions.



Figure 1. Intradermal injection test results.

Epidemiological studies consistently identify neuromuscular blocking agents (NMBAs), antibiotics, antiseptics, particularly chlorhexidine and latex, as the most common culprits. However, reported incidence rates and causative profiles vary across regions and populations due to differences in diagnostic criteria, exposure patterns, and reporting systems [1,3,11].

The immunopathogenesis of POA is multifaceted and not fully elucidated. Approximately 60% of cases are mediated by classic

type I hypersensitivity reactions involving allergen-specific IgE. The remaining cases arise from non-IgE-mediated mechanisms such as direct mast cell or basophil activation, complement activation, bradykinin pathway dysregulation, or IgG-mediated immune responses [4,5]. This heterogeneity complicates diagnosis and shows the need for a systematic, multidisciplinary approach to identifying the offending agent.

Diagnostic Role of Skin Testing

Skin testing remains the cornerstone of perioperative drug allergy evaluation owing to its rapid turnaround, cost-effectiveness, and high clinical relevance. The procedure typically involves intradermal or prick administration of diluted test agents. In IgE-mediated reactions, allergen binding to cell bound IgE on mast cells triggers degranulation, producing a wheal (≥ 3 mm) with surrounding erythema. A positive result strongly implicates the tested drug as the causative agent and provides actionable diagnostic guidance.

Timing of Skin Testing: Conventional Versus Early Approaches

International guidelines recommend performing skin testing 4 to 6 weeks after an anaphylactic event [7-10]. This interval allows for recovery of mast cell and basophil reactivity, thereby minimizing the likelihood of false-negative results due to temporary immune cell refractoriness. However, this delay can be problematic in patients requiring urgent or semi-urgent

surgery, where deferring testing can lead to significant procedural or clinical consequences.

In this case, the need for timely definitive surgery necessitated deviation from the conventional diagnostic timeline. Recent studies suggest that early skin testing performed within days to 2 weeks after the event can yield reliable diagnostic information, especially when test results are positive [12,13]. In our patient, early skin testing on postoperative day 6 demonstrated strong reactivity to cisatracurium and a negative response to rocuronium, with no evidence of cross-reactivity. These results enabled rapid modification of the anesthesia plan, allowing safe surgical completion on postoperative day 7 without further complications. Early identification of the causative agent prevented unnecessary surgical delay and mitigated the clinical risk and psychological stress for the patient.

If early skin testing had been negative, we would have proceeded with a graded challenge using an alternative NMBA (rocuronium) under close hemodynamic monitoring in the operating room, in accordance with EAACI guidelines [9]. This approach balances the need for timely surgery with patient safety, minimizing the risk of recurrent anaphylaxis while avoiding unnecessary delay.

Limitations and Optimization Strategies for Early Skin Testing

Despite its diagnostic value, early skin testing has inherent limitations, chiefly its uncertain negative predictive value. A negative result obtained within the early testing window cannot definitively exclude hypersensitivity; therefore, cautious interpretation in conjunction with clinical context is essential. To improve diagnostic confidence, early skin testing should be complemented by adjunctive assays such as serum tryptase and histamine measurements, drug specific IgE testing, basophil activation tests (BAT), and histamine release tests (HRT) [9].

Ensuring technical rigor and methodological standardization is vital for accurate results. For concentration control, test agents must be prepared at validated concentrations consistent with published safety thresholds (Table 2). Overly-dilute preparations can yield false-negative results, whereas excessive concentrations risk irritant or false-positive reactions [10,14]. For procedural precision, correct intradermal technique and the inclusion of both positive (histamine) and negative (saline) controls are mandatory to maintain internal validity. Regarding clinical correlation, in certain cases wheal diameters < 3 mm are accompanied by consistent erythema or pruritus. Although such responses fall short of standard positivity criteria, they can be classified as “suspected positive” when supported by clinical history, warranting cautious avoidance of the agent in future anesthetic exposures.

The limitation of this study is that serum tryptase was not performed during the optimal period. Although we recommend consideration of auxiliary examinations (BAT, HRT, IgE testing), these tests were not carried out in this patient because our hospital could not provide them, which may have limited the comprehensiveness of the diagnostic work. Overall, this case reinforces that, when performed under appropriate conditions, early skin testing can provide timely, clinically meaningful guidance for anesthetic management in urgent surgical settings.

Conclusions

This case represents a classic presentation of severe perioperative anaphylaxis characterized by profound hypotension, tachycardia, and a diffuse maculopapular rash occurring immediately after cisatracurium administration during anesthesia induction. Skin prick testing performed on postoperative day 6 confirmed cisatracurium as the offending agent, while rocuronium produced no hypersensitivity reaction. Based on these findings, rocuronium was safely used as an alternative neuromuscular blocking agent on postoperative day 7, enabling successful completion of surgery without further complications.

This case underscores the diagnostic and practical value of early skin testing in patients who develop perioperative anaphylaxis and require timely reoperation. When adherence to the conventional 4- to 6-week testing interval is impractical, early allergy assessment can yield reliable diagnostic information, guide safe anesthetic planning, and facilitate prompt surgical management without compromising patient safety.

The successful management of this case also shows the importance of collaboration between anesthesiologists and allergy specialists, who together can optimize the diagnostic workup (including skin testing and laboratory monitoring) and develop safe anesthesia plans. Our patient received comprehensive education regarding his cisatracurium allergy, including written documentation of the allergy in his medical record and a medical alert bracelet. For future anesthetic exposures, he was advised to avoid cisatracurium and other potential cross-reactive NMBAs, with rocuronium identified as a safe alternative based on our testing results.

Future Perspectives

Although the outcome in this case was favorable, the broader adoption of early skin testing in perioperative anaphylaxis requires further validation through robust, evidence-based research. Future large scale, high-quality prospective studies should aim to clarify several critical aspects, including diagnostic sensitivity and specificity of skin testing performed at different intervals following an anaphylactic reaction, negative

predictive value of early skin testing within the initial post reaction period, and optimal timing and test concentrations for various anesthetics [12,13]. Addressing these questions will enable anesthesiologists to establish more precise and standardized approaches for identifying culprit agents, refine perioperative pharmacologic protocols, and further strengthen patient safety frameworks in anesthesia practice.

Institution Where Work Was Done

The Central Hospital of Wuhan, Wuhan, Hubei, PR China.

Patient consent

The study was approved by the Ethics Committee of Tianyou Hospital affiliated to Wuhan University of Science and Technology, with the ethics approval number TY-IEC2025-037. Written informed consent was provided by the patient.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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