



NEAR-FATAL ANAPHYLACTIC REACTION TO INTRAMUSCULAR DICLOFENAC INJECTION: EARLY RECOGNITION AND EMERGENCY MANAGEMENT

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ABSTRACT

Diclofenac is one of the most widely used nonsteroidal anti-inflammatory drugs (NSAIDs) in clinical practice, yet it remains a significant cause of drug-induced hypersensitivity reactions, including life-threatening anaphylaxis. We report the case of a 21-year-old previously healthy male who developed fulminant anaphylactic shock following intramuscular administration of diclofenac for acute abdominal pain. Shortly after injection, he experienced rapidly progressive generalized itching, followed by diffuse erythematous maculopapular rashes and worsening restlessness. Within hours, he deteriorated to a drowsy and poorly responsive state. On arrival to the emergency department, he was hypotensive with non-recordable blood pressure, bradycardic, and had a Glasgow Coma Scale score of 12/15. Systemic examination revealed widespread rash and mild wheeze, with no evidence of alternative causes for shock. Immediate resuscitative measures were initiated, including high-flow oxygen, aggressive intravenous fluid therapy, intramuscular adrenaline administered in repeated doses, antihistamines, corticosteroids, bronchodilator nebulisation, and eventual intravenous adrenaline infusion. Serum tryptase levels were elevated, supporting the diagnosis of anaphylaxis. Over the next 24 hours, the patient responded well to treatment, stabilized hemodynamically, and was transferred to the MICU for continued monitoring. He was subsequently shifted to the ward and discharged in stable condition after counseling on strict lifelong avoidance of diclofenac and related NSAIDs, with advice regarding emergency preparedness and follow-up with an allergy specialist. This case underscores the unpredictability and severity of diclofenac-induced anaphylaxis, even in individuals without prior drug allergy. It highlights the importance of early recognition, prompt administration of intramuscular adrenaline, and escalation to vasopressor therapy when needed. Comprehensive patient education and proper documentation play vital roles in preventing recurrence. Awareness of NSAID-induced anaphylaxis among clinicians remains essential for improving outcomes in emergency settings.

Keywords: Diclofenac, Anaphylaxis, Intramuscular injection, Drug hypersensitivity, Emergency management, NSAID allergy, Adrenaline therapy

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most widely prescribed and over-the-counter medications globally for their analgesic, antipyretic, and anti-inflammatory properties. Diclofenac, a phenylacetic acid derivative NSAID, ranks among the top analgesics used in India because of its rapid onset of action, cost-effectiveness, and versatility across a wide range of medical conditions. Despite its widespread use and overall safety profile, diclofenac is also recognized as one of the NSAIDs most frequently implicated in severe hypersensitivity reactions, including anaphylaxis, urticaria, angioedema, and bronchospasm [1]. Although NSAID-induced hypersensitivity is relatively uncommon, accounting for approximately 0.3–6% of all adverse drug reactions, the sheer volume of NSAID consumption means that clinicians frequently encounter such reactions in emergency settings [2].

Anaphylaxis is an acute, potentially fatal, multisystem hypersensitivity reaction that can occur within minutes to hours after exposure to an allergen. Drug-induced anaphylaxis is responsible for a growing proportion of emergency department visits and hospital admissions worldwide. NSAIDs rank second only to antibiotics as leading causes of drug-induced anaphylaxis in several epidemiological studies [3]. Diclofenac, in particular, has been consistently reported as a trigger for both IgE-mediated and non-IgE-mediated anaphylactic reactions. The exact mechanism by which diclofenac induces anaphylaxis is variable and complex. IgE-mediated responses may occur following prior sensitization, while non-IgE-mediated mechanisms typically involve cyclooxygenase-1 (COX-1) inhibition, leading to an imbalance in arachidonic acid metabolism and excessive release of inflammatory mediators such as leukotrienes and prostaglandins [4].

Several studies have highlighted that diclofenac-induced anaphylaxis tends to be rapid, severe, and unpredictable, even in young patients with no prior history of drug allergy or atopy [5]. Intramuscular (IM) administration, although generally safe, may facilitate a more rapid systemic absorption of the drug, potentially accelerating the onset of an anaphylactic reaction compared to oral formulations. Case reports have documented that IM diclofenac may precipitate fulminant anaphylaxis characterized by hypotension, tachycardia or bradycardia, respiratory compromise, and altered mental status, necessitating immediate resuscitative measures [6]. The index patient in this report developed profound hypotension, drowsiness, widespread maculopapular rash, and cardiovascular instability—hallmark features of severe anaphylactic shock.

Timely recognition and management of anaphylaxis are crucial for preventing mortality. Adrenaline (epinephrine) administered intramuscularly into the anterolateral thigh remains the first-line and most effective treatment for anaphylaxis, with delayed administration strongly associated with fatal outcomes [7]. Guidelines recommend that clinicians maintain a high index of suspicion for anaphylaxis in any patient presenting with sudden-onset skin manifestations accompanied by airway, breathing, or circulatory compromise. However, studies indicate that adrenaline continues to be underused, particularly in LMIC emergency settings, often due to diagnostic uncertainty or fear of side effects [8]. The present case underscores the importance of immediate administration of adrenaline, repeated IM dosing when initial response is inadequate, and transition to intravenous adrenaline infusion in refractory cases under strict monitoring conditions.

The emergency department management of drug-induced anaphylaxis requires a multifaceted approach, including airway support, supplemental oxygen, aggressive fluid resuscitation due to profound vasodilation and capillary leakage, and adjunctive pharmacotherapy such as H1 antihistamines, corticosteroids, and nebulised bronchodilators. In severe cases, vasopressors such as noradrenaline may be required to maintain adequate perfusion pressure, particularly in distributive shock unresponsive to initial therapy [9]. The index patient required multiple IM doses of adrenaline, prompt fluid resuscitation, and subsequent vasopressor support, reflecting the severity of the reaction.

Serum tryptase measurement is often useful in supporting the diagnosis of anaphylaxis, particularly when levels are elevated within 1–3 hours of symptom onset. While a normal tryptase level does not rule out anaphylaxis, elevated levels provide strong evidence of mast cell activation and are valuable for medicolegal documentation [10]. In this case, serum tryptase was elevated, further confirming the diagnosis. Additionally, ECG, ABG, and biochemical evaluation aid in ruling out alternative causes such as cardiogenic shock, metabolic disorders, or infectious etiologies, especially when neurological symptoms such as drowsiness are present.

NSAID hypersensitivity reactions can be classified into cross-reactive and selective types. Diclofenac-induced anaphylaxis is typically a selective NSAID hypersensitivity, meaning the reaction is specific to diclofenac or structurally related agents, rather than all NSAIDs. However, due to potential cross-reactivity within the same chemical group, patients are generally advised lifelong avoidance of diclofenac and related NSAIDs until formal allergy evaluation can be completed [11]. Given the risk of recurrence and the unpredictable nature of anaphylaxis, patient education is paramount, including strict avoidance of diclofenac, wearing medical alert identification, informing healthcare providers of the allergy, and carrying an epinephrine auto-injector if available.

Biphasic anaphylaxis—recurrence of symptoms after initial resolution—remains an important consideration, especially in severe reactions. Monitoring patients for at least 12–24 hours after stabilization is recommended by major international guidelines such as WAO and AAAAI. The index patient was appropriately monitored in MICU for one day and subsequently observed in the ward prior to discharge, reflecting adherence to evidence-based practice [12].

This case is significant for several reasons. First, it highlights that even a previously healthy young adult with no history of drug allergy can develop sudden, life-threatening anaphylactic shock from a commonly used analgesic. Second, it demonstrates the classical progression of NSAID-induced anaphylaxis from cutaneous symptoms to cardiovascular collapse. Third, it reinforces the life-saving importance of early IM adrenaline, aggressive fluid therapy, vasopressor support, and vigilant monitoring for complications. Finally, it emphasizes the importance of discharge counseling, prevention strategies, and the need for systematic allergy documentation to prevent accidental re-exposure.

In summary, diclofenac-induced anaphylaxis, though rare, represents a medical emergency requiring rapid identification and evidence-based management. This case contributes to the growing body of literature emphasizing the severity, unpredictability, and potential fatality of NSAID-induced anaphylaxis and underscores the critical role of prompt treatment, multisystem monitoring, and patient education in improving outcomes.

CASE DESCRIPTION

A 21-year-old male student, resident of Nagpada, Mumbai, with no known comorbidities, was brought by relatives to the Emergency Department (ED) of GGMC & JJ Hospital, Mumbai, in a drowsy condition. The primary complaint was the sudden onset of generalized rashes that had developed earlier that afternoon.

The patient was reportedly well until the morning, when he developed abdominal pain that was insidious in onset, gradually progressive, and mild to moderate in intensity. The pain was non-radiating, not related to meals, and not relieved or aggravated by any specific factors. There was no associated nausea, vomiting, diarrhea, or constipation.

Due to persistent abdominal discomfort, he visited a local hospital around 11:30 AM, where he received a single intramuscular injection of diclofenac for symptomatic relief. Shortly after

administration, he developed generalized itching, initially involving the upper limbs but rapidly spreading to the face, trunk, abdomen, and lower limbs. This was quickly followed by the appearance of diffuse erythematous maculopapular rashes across the entire body.

Figure 1: Diffuse maculopapular rash over bilateral arms and abdomen



By mid-afternoon, he became increasingly restless and progressively drowsy. Over the next 20–30 minutes, his responsiveness deteriorated significantly. Family members reported that he initially responded only when shaken and later only to painful stimuli. He was unable to converse normally and had poor cooperation.

There was no history of seizures, syncope, loss of consciousness, altered sensorium prior to this episode, fever, headache, neck stiffness, urinary symptoms, cough, dyspnea, chest pain, fall, or head injury. Past history was unremarkable, with no known history of diabetes, hypertension, tuberculosis, asthma, thyroid disease, drug allergy, or prior similar episodes. Family and personal histories were non-contributory, and he denied addictions.

Examination in Emergency

On arrival, the patient's general condition was poor.

- GCS: E3V4M5 (12/15)
- Temperature: Afebrile
- Blood Pressure: Not recordable
- Pulse: 48/min
- Respiratory Rate: 22/min
- SpO₂: 95% on room air
- RBS: 145 mg/dL

Local examination revealed widespread maculopapular rash over the upper limbs and abdomen (Figure 1).

Systemic Examination

- CVS: S1, S2 audible; no murmurs
- RS: Bilateral AEBE; mild wheeze present; no rhonchi or crepitations
- CNS: Drowsy but arousable
- PA: Soft and non-tender

Given the constellation of findings—diffuse rash, profound hypotension, bradycardia, altered sensorium—severe anaphylactic shock secondary to intramuscular diclofenac was suspected.

Differential diagnoses included:

- Anaphylactic shock (most likely)
- Severe acute urticaria
- Viral exanthem with shock (less likely)
- Toxic/metabolic encephalopathy secondary to shock

Family members were counseled regarding the high-risk condition and poor initial prognosis.

Emergency Department Management: The emergency team initiated immediate resuscitative measures.

Airway and Breathing

- Oxygen supplementation @ 10–15 L/min via non-rebreathing mask.
- Nebulisation with salbutamol (5 mg) and ipratropium (0.5 mg) in repeated cycles for bronchospasm.

Circulation

- Two wide-bore (16G) IV cannulas were secured.
- IV fluid resuscitation: 2 L Normal Saline bolus.
- BP reassessed every 10 minutes.
- IM Adrenaline 0.5 mg (0.5 mL of 1:1000) administered promptly, repeated twice at 10–15-minute intervals due to persistent non-recordable BP.
- IV Adrenaline infusion: 1 mg adrenaline in 100 mL NS, titrated at 0.05–0.1 µg/kg/min to maintain MAP ≥65 mmHg.

Medications

- Inj Pheniramine maleate (Avil) 22.75 mg IV
- Inj Hydrocortisone 200 mg IV
- Inj Pantoprazole and Inj Ondansetron
- Bronchodilator nebulisation as above

Monitoring

- Foleys catheter inserted for urine output monitoring
- Continuous monitoring of BP, HR, RR, SpO₂, temperature, urine output
- Strict input-output charting

- Observation for biphasic reaction

Investigations: Blood samples and tests sent immediately included: CBC, ECG, RFT, LFT, serum electrolytes, coagulation profile, ABG, serum tryptase, and chest X-ray. (Table 1)

Table 1: Investigation Summary	
Test	Result
Hb	13.8 g/dL
TLC	9,000/mm ³
Platelets	2.6 lakh/mm ³
Total Bilirubin	0.8 mg/dL
AST/ALT	37/40 IU/L
Creatinine/Urea	0.9 mg/dL / 25 mg/dL
PT/INR	13 sec / 1.1
Na/K	142/4.1 mEq/L
RBS	156 mg/dL
Serum Tryptase	25 µg/L (elevated)
ABG	pH 7.46, SpO ₂ 95%, PaO ₂ 90, PaCO ₂ 36, HCO ₃ 21, Lactate 1.1
Chest X-ray (PA)	Normal (Figure 2)

Figure 2: Chest X-ray (PA) showing no acute pathology.



The patient improved significantly in the ED, with stabilization of vital parameters over the next several hours.

MICU and Ward Course

Day 1 – MICU: The patient was shifted to MICU for further monitoring.

Vitals:

- GC: Good
- GCS: 15/15
- BP: 100/60 mmHg
- Pulse: 70/min

- RR: 18/min
- SpO₂: 97% on facemask @ 6 L/min

Management in MICU included:

- Oxygen at 6 L/min
- Inj Hydrocortisone 100 mg IV TDS
- Inj Pheniramine IV BD
- Noradrenaline infusion (0.05–1 µg/kg/min) titrated to MAP ≥65 mmHg
- IVF: 2 L NS + 1 L RL over 24 hours
- Dermatology consultation: advised Levocetirizine, calamine lotion
- Continuous monitoring of vitals and urine output

Day 2–3 – Ward: After stabilization, the patient was shifted to the medicine ward and later discharged in stable condition.

Discharge Summary

Medications:

- Tab Levocetirizine 5 mg once daily for 5 days
- Tab Paracetamol 500 mg SOS
- Topical calamine lotion BD

Strict Advisory:

- Absolute lifelong avoidance of diclofenac
- Avoid aceclofenac, ibuprofen, naproxen, ketorolac until formal testing
- Always inform treating physicians about this allergy
- Advised epinephrine auto-injector for emergency use (if available)
- Follow-up in OPD in 5 days

Education: Patient and family counseled extensively regarding drug allergy precautions, avoidance of self-medication, and emergency preparedness.

DISCUSSION

Diclofenac-induced anaphylaxis, though rare, remains a critical cause of sudden cardiovascular collapse in emergency settings. NSAIDs are among the top drug groups responsible for hypersensitivity reactions worldwide, and diclofenac ranks prominently due to its widespread use, potent COX-1 inhibition, and rapid systemic absorption when administered intramuscularly [1,4]. The present case illustrates a classic example of fulminant, life-threatening NSAID-induced anaphylactic shock in a previously healthy young adult with no prior known allergies. This aligns with published evidence that NSAID anaphylaxis often occurs without a preceding sensitization history and may present abruptly following therapeutic dosing [5,13].

The rapid progression from itching and maculopapular rash to circulatory collapse in this case is characteristic of severe anaphylaxis. Cutaneous symptoms are often the earliest warning signs, reported in up to 90% of cases, followed by respiratory and cardiovascular manifestations [3]. However, the absence of early respiratory symptoms in this patient underscores that anaphylaxis can present with predominant cardiovascular compromise, especially with parenteral drug administration, which increases bioavailability and onset speed [6,14]. Profound hypotension with bradycardia, as seen in this case, is consistent with the “cardiovascular phenotype” of anaphylaxis, often associated with severe mast-cell mediator release, vasodilation, and capillary leak [10].

The elevated serum tryptase level in this patient provided strong diagnostic support. Tryptase rises within 1–3 hours of symptom onset and is considered a marker of mast cell activation. Although

normal tryptase does not exclude anaphylaxis, elevated levels significantly increase diagnostic certainty, especially in cases with predominant cardiovascular symptoms or altered sensorium [10,15]. Early measurement, as performed here, is essential for medicolegal documentation and future allergy evaluation.

The immediate administration of intramuscular adrenaline remains the cornerstone of anaphylaxis management. Guidelines worldwide emphasize that adrenaline should not be delayed, as delays of even minutes significantly increase the risk of biphasic reactions, hospitalization, and mortality [7,8,16]. In this case, the patient required repeated IM doses due to persistent non-recordable blood pressure, which is consistent with recommendations that repeat doses be given every 5–15 minutes if symptoms persist [7]. The subsequent need for IV adrenaline infusion reflects the severity of shock and is appropriate only in settings with continuous cardiac monitoring, as performed in the ED and MICU. Such escalation is recommended in adrenaline-refractory anaphylaxis, particularly when distributive shock persists despite adequate IM dosing and fluid resuscitation [9,17].

Aggressive fluid resuscitation is another essential component of therapy. In severe anaphylaxis, intravascular volume depletion can exceed 30% within minutes due to vascular permeability changes induced by histamine, platelet-activating factor, and cytokines [4,10]. Administration of 1–2 L of isotonic crystalloid, as provided in this case, is recommended rapidly to restore perfusion. The subsequent requirement of noradrenaline infusion further highlights the profound vasodilatory shock state, and its use is supported by current evidence in refractory cases [9,17].

Bronchospasm in anaphylaxis is mediated by leukotriene-driven smooth muscle contraction; thus, nebulized bronchodilators such as salbutamol and ipratropium provide symptomatic relief but are not substitutes for adrenaline [7]. Steroids and antihistamines remain adjunctive therapies that reduce prolonged symptoms and prevent protracted reactions but do not treat life-threatening manifestations [8].

One of the important teaching points in this case is the risk of biphasic anaphylaxis, a recurrence of symptoms after apparent recovery. Biphasic reactions occur in up to 20% of severe cases and may appear within 1–72 hours, though most occur within 12 hours [12]. The decision to admit the patient to MICU for 24 hours, followed by observation in the ward, was therefore appropriate and adheres to WAO and AAAAI recommendations.

Another important dimension is NSAID hypersensitivity classification. Diclofenac typically triggers selective NSAID-induced anaphylaxis, meaning the reaction is specific to diclofenac or its structurally similar agents, rather than all COX-1 inhibitors [11]. However, due to possible cross-reactivity within the phenylacetic acid group, patients must avoid related agents such as aceclofenac, ibuprofen, ketorolac, and naproxen until formal allergy evaluation is performed. The discharge counseling provided—strict avoidance, medical alert information, and education on epinephrine auto-injector use—is consistent with best practices for the long-term prevention of accidental re-exposure [16,18].

Furthermore, the case highlights an important public health concern: injudicious prescription and administration of NSAIDs at local clinics, often without proper assessment or documentation of drug allergy history. NSAIDs remain one of the most common medications involved in preventable drug-induced emergencies in India and other LMICs, underscoring the need for community and clinician education [19]. Emergency physicians must remain vigilant, as early recognition and timely adrenaline administration are the most decisive factors in survival.

Overall, this case reinforces essential clinical principles:

- Anaphylaxis can occur in any patient, at any time, even with commonly used drugs.
- Early IM adrenaline saves lives.
- Escalation to IV adrenaline and vasopressors is sometimes necessary.
- Observation for biphasic reactions is mandatory.
- Documentation and patient education are critical to preventing recurrence.

The dramatic improvement in this patient after prompt intervention demonstrates how adherence to evidence-based protocols can be lifesaving. This case adds to the global literature by highlighting the severity of diclofenac-induced anaphylaxis and demonstrating optimal emergency and critical care management in a resource-limited, high-volume urban hospital setting.

CONCLUSION

This case highlights the potential for rapid, severe, and life-threatening anaphylaxis following intramuscular diclofenac, a commonly used NSAID. The patient, a previously healthy young adult, developed fulminant anaphylactic shock characterized by widespread rash, profound hypotension, bradycardia, and altered sensorium within a short time of drug administration. Prompt recognition, immediate intramuscular adrenaline, aggressive fluid resuscitation, and early initiation of vasopressor support were crucial in reversing the shock state and preventing multiorgan failure. Elevated serum tryptase supported the diagnosis of anaphylaxis, and vigilant monitoring helped avert potential biphasic reactions. This case reinforces the importance of maintaining a high index of suspicion for anaphylaxis even with routinely prescribed medications, ensuring timely adrenaline use, and adhering to guideline-based emergency management. Comprehensive discharge counseling, strict drug avoidance, and patient education remain essential to prevent recurrence and ensure long-term safety. It underscores the need for increased awareness of NSAID-induced hypersensitivity among clinicians.

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