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Case Report

Unveiling the Unforeseen: Diclofenac-Triggered Near-Fatal Rapid Onset Asthma in a Stable Asthmatic Managed by Noninvasive Ventilation: A Case Report

Risly Mohamad[1], Sahana Jawfer[2], Dinesh Weerasinghe[3]

[1]National Hospital, Kandy, Sri Lanka
[2]Teaching Hospital, Peradeniya, Sri Lanka.
[3]Teaching Hospital, Anuradhapura, Sri Lanka

Abstract

Diclofenac tablets are commonly used in Sri Lanka and rapid onset asthma triggered by them is a rare phenomenon. The use of noninvasive ventilation in status asthmaticus is still under consideration in the guidelines. We discuss a case of rapid onset acute asthma managed with noninvasive ventilation successfully. This report details a 35-year-old woman with a history of mild intermittent asthma, who presented with rapid-onset worsening severe respiratory distress shortly after ingesting oral diclofenac sodium tablets for mechanical neck pain. Despite being well-controlled with inhalers for over a year, she developed near-fatal asthma, characterised by severe hypoxia, hypercapnia with altered mental status, requiring immediate, intervention. The patient was treated with high-flow oxygen, back-to-back nebulisations, and non-invasive ventilation (bi-level positive airway pressure mode), resulting in clinical improvement. Here, we highlight the rare but severe risk of diclofenac-induced asthma exacerbations and signify the importance of prompt recognition, aggressive treatment in managing life-threatening asthmatic episodes along with consideration of noninvasive ventilation in management of acute asthmatic attacks. Clinicians should be aware about the rapid onset acute asthma which resolves completely with proper management.

***Keywords:** Near-fatal asthma, Rapid-onset acute asthma, NSAID-induced asthma, Diclofenac sodium, Noninvasive ventilation (BiPAP)

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Corresponding author: Email:risly526@gmail.com https://orcid.org/0009-0000-4743-5034

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Introduction:

Asthma is a chronic condition marked by airway inflammation and hyperresponsiveness, which can vary significantly in severity. While it's typically managed effectively with bronchodilators and anti-inflammatory medications, some asthma presentations can complicate quickly and become fatal. Among these severe complications are near-fatal asthma episodes and rapid-onset acute asthma exacerbations [1]. Near-fatal asthma is characterised by severe respiratory compromise that often mandates, unless provided with prompt treatment, can progress to respiratory failure. In contrast, rapid-onset acute asthma involves a sudden and severe deterioration of respiratory function in a

previously stable or well-controlled individual. This rapid exacerbation can be triggered similarly to anaphylaxis by various factors such as allergens, respiratory infections or, as demonstrated in this case, by ingesting certain medications. [2]

We report a case where a previously stable asthmatic patient experienced a rapid onset acute asthma with severe respiratory distress leading to near fatal asthma following the ingestion of diclofenac sodium tablets. This case exemplifies how a routine medication can precipitate a near fatal asthmatic attack.

Case presentation:

A 35-year-old woman with a history of mild intermittent asthma, well-controlled with inhalers for over a year without any exacerbation, presented to the emergency department with a sudden onset of severe shortness of breath that occurred 15 to 30 minutes after taking oral diclofenac sodium prescribed by her general practitioner.

She could not provide a coherent history when she arrived at the emergency department. A bystander reported that she had been well until visiting the general practitioner after finishing work as an accountant, experiencing mechanical neck pain possibly from prolonged screen use.

On examination, she was severely breathless, confused and unable to complete sentences. Airway was patent. Breathing effort was poor, with bilaterally reduced but equal chest expansion. The trachea was midline with a resonant percussion note. Auscultation revealed a silent chest with a high respiratory rate (36 cycles per minute). Vitals showed a pulse oximeter reading of 65%, a blood pressure of 135/85 mmHg, and relative bradycardia (55 to 65 bpm). The patient had a Glasgow coma scale (GCS) of 12 (E3V4M5). On exposure, no rashes were noted. The patient was afebrile, not hypothermic, but showed early peripheral cyanosis.

Initial arterial blood gas analysis showed acute severe respiratory acidosis with partial metabolic compensation with type two respiratory failure with tissue hypoxia (Table 1). ECG was in sinus rhythm with frequent ventricular ectopics. Bedside point of care ultrasound was normal (normal ejection fraction with A profile, no right atrial or ventricular dilatation with good inferior vena cava filling)

The patient was managed as rapid-onset near-fatal asthma. Initial treatment included high-flow oxygen via a non-rebreather mask at 15L/minute with back-to-back nebulisation with salbutamol respiratory solution. Despite these measures, the patient's condition initially worsened, with dropping GCS and a repeat arterial blood gas analysis showing worsening parameters (Table 1)

Table 1: Arterial blood gas (ABG) analysis of the patient

Parameter	Normal value	1st ABG	2nd ABG	3rd ABG
pH	7.35-7.45	7.162	7.171	7.428
pCO_2 (mmHg)	35-45	75.7	83.1	33.8
pO_2 (mmHg)	60-80	33.5	25.2	51.7
HCO^{3-} (mmol/L)	22-26	27.3	30.6	22.5
SpO_2 %	>94	46.7	40.2	92
K^+ (mmol/L)	3.5-5.0	4.08	3.33	3.23
Na^+ (mmol/L)	135-145	146.9	147.9	142.4
Lactate (mmol/L)	<1.0	3.8	5.2	3.0

Following a specialist's consultation, IV magnesium sulfate was administered. Given the severity of hypercapnia and the low GCS (a relative contraindication for noninvasive ventilation), the patient was nonetheless placed on noninvasive ventilation with bi-level positive airway pressure mode (considering the intubation and intensive care related risks in asthma along with anticipated complete and instant recovery in rapid onset acute asthma) under close monitoring with a low threshold for elective intubation.

Within 30 minutes, the patient's GCS improved, and the appearance of bilateral rhonchi on auscultation indicated a positive response. A bedside chest X-ray was normal. After 40 minutes of intensive treatment, repeat blood gas analysis showed improved parameters (Table 1). The patient was gradually weaned from noninvasive ventilation and oxygen over the next 2 hours with significant clinical improvement. By discharge from the emergency department to the medical unit, the patient had normal vitals, a clear chest on auscultation and did not require oxygen support.

In recounting the patient's experience after recovery, from her perspective, the situation was both frightening and overwhelming as she couldn't talk and provide a detailed history. She was happy about the medical team's prompt, aggressive intervention stabilising her condition.

Discussion

Although asthma is generally manageable with appropriate medications and lifestyle modifications, specific episodes can emerge unexpectedly and pose life-threatening challenges, as in our case, which

highlighted a marked deviation from her usual asthma control.

Rapid onset acute asthma attacks are infrequent manifestations of asthma, mainly observed in individuals with a history of severe life-threatening asthma. Yet, our patient had a history of mild intermittent asthma, which was well-controlled with inhalers [1]. Evidence suggests that rapid-onset acute asthma is a rare but distinct presentation in emergency departments, often more common in male patients. Although various triggers are recognised, contrary to the common notion, Upper Respiratory Tract Infections are not typically significant in these cases. Rapid-onset acute asthma patients generally experience a rapid decline followed by a quicker response to treatment, resulting in lower hospital admission rates compared to those with slow-onset acute asthma [2]. The only identified trigger in this case was the oral diclofenac sodium tablets.

Diclofenac is a nonsteroidal anti-inflammatory drug (NSAID) commonly prescribed to alleviate pain, inflammation, and swelling. It inhibits substances that cause these effects and is available in various forms, including tablets and topical applications. NSAIDs can induce severe asthma through the inhibition of cyclooxygenase-1, leading to increased release of cysteinyl leukotrienes [3, 4]. This pathway results in lower production of prostaglandin E2 due to down-regulation of cyclooxygenase-2, alongside increased expression of leukotriene C4 synthase in bronchial inflammatory cells. Aspirin and NSAIDs further elevate cysteinyl leukotriene synthesis, which, along with genetic factors and receptor overexpression, enhances the inflammatory response [5]. Understanding the pathogenesis of NSAID-induced asthma could improve treatment strategies.

Although fatal asthma from oral diclofenac is extremely rare, the occurrence in this case is worthwhile reporting. While oral diclofenac is not commonly reported as a trigger for near-fatal asthma, there have been rare instances of severe reactions. Reports include fatal anaphylactic reactions to oral diclofenac [6] and acute asthmatic attacks from diclofenac sodium eye drops [7, 8, 9]. This case appears unique in demonstrating oral diclofenac sodium as a trigger for rapid onset acute asthma.

In managing this patient, noninvasive ventilation was employed due to hypercapnia and low GCS, aiming to avoid intubation and its associated complications. The management of near fatal asthma involves a comprehensive approach, including optimising asthma control, addressing adherence and socioeconomic issues, and recognising the limitations of pharmacotherapy [10]. Early and aggressive treatment is crucial to maintain oxygenation, relieve airflow obstruction, and reduce airway oedema and mucus plugging. Emergency physicians must consider potential asthma-related complications, intubation admission to intensive care and risks in severe asthma management [11, 12]. Patient education on asthma as a chronic condition and treatment adherence is also of vital concern [13].

Noninvasive ventilation has been explored as a treatment for near fatal asthma. Studies suggest that it may reduce the need for endotracheal intubation and improve outcomes compared to invasive mechanical ventilation [14]. Noninvasive ventilation is safe and effective in patients with severe respiratory acidosis or altered mental status [15]. However, its use in severe acute asthma remains controversial, lacking specific randomised controlled trials or national guidelines [16]. Further research is needed to define the optimal application of noninvasive ventilation in near fatal asthma cases. The limited evidence and variability in critical asthma care practices highlight the need for additional research to establish the best care strategies for near fatal asthma [17].

Conclusion

This case signifies the potential for seemingly routine medications, such as diclofenac sodium, to precipitate rapid onset acute asthma, ending up as near fatal asthma. Despite its controversial status, the effective use of noninvasive ventilation in this scenario exemplifies the need for innovative approaches in handling severe asthma exacerbations.

Conflicts of Interest: Authors find no conflict of interest.

Consent: Written informed consent was obtained from the patient's spouse.

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