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# A RARE NSAID-INDUCED PULMONARY REACTION: DICLOFENAC AND PLEURAL EFFUSION

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**ABSTRACT**

Non-steroidal anti-inflammatory drugs (NSAIDs) such as diclofenac are extensively used for their analgesic and anti-inflammatory effects. However, long-term use may lead to rare adverse reactions including drug-induced pleural effusion. Drug-induced pleural effusion is a diagnosis of exclusion and is often under-recognized. Regular review of chronic medications, especially NSAIDs, is essential in elderly and polymedicated patients to avoid under diagnosed drug-induced pulmonary complications.

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## Introduction

Drug-induced pleural effusion is an uncommon but important clinical entity, often overlooked due to its non-specific presentation and the broad range of potential causes. Non-steroidal anti-inflammatory drugs (NSAIDs), including diclofenac, are among the widely used agents known to cause adverse drug reactions affecting the respiratory system, albeit rarely. Diclofenac works by inhibiting cyclooxygenase (COX-1 and COX-2), leading to reduced prostaglandin synthesis, which can disrupt normal inflammatory and immune responses.

Pleural effusion associated with NSAID use is hypothesized to occur due to hypersensitivity reactions or direct pleural inflammation.

## Case report

A 58-year-old female presented with complaints of breathlessness for the past 15 days. She had a known history of hypertension for the last two years and type 2 diabetes mellitus for the past eight months. Her regular medications included Telmisartan 40 mg, Metformin 500 mg, and Diclofenac 50 mg. On general examination, the patient was febrile, with an elevated blood pressure of 170/90 mmHg, a pulse rate of 84 beats per minute, and a respiratory rate of 16 breaths per minute at the time of admission. Systemic examination revealed that her respiratory system was bilaterally clear, and auscultation findings were normal. The patient was advised to undergo various laboratory tests including complete blood count (CBC), liver function tests (LFT), renal function tests (RFT), serum electrolytes and a chest X-ray. Based on the investigation reports, she was found to have a pleural effusion of unknown origin.

Taking into account her clinical presentation and diagnostic findings, she was prescribed a combination of medications for three days. These included Amoxicillin with Clavulanic acid 1 gram intravenously twice a day as a broad-spectrum antibiotic, Furosemide 40 mg intravenously twice a day as a loop diuretic, and Pantoprazole 40 mg intravenously once a day as a proton pump inhibitor. Additionally, she was continued on Telmisartan 40 mg once daily, Amlodipine 5 mg once daily, and Metformin 500 mg twice daily. Nebulization therapy with a combination of Duolin and Budecort was also administered to support respiratory function.

During a ward round interaction, the patient mentioned that she had been taking diclofenac 50 mg orally once a day, along with Telmisartan and Metformin, for the past eight months. It was observed that diclofenac was not indicated in her current treatment plan and might have been continued either due to a healthcare provider's assumption or due to the patient's lack of understanding regarding the appropriate use an indication of the medication.

## Discussion

Non-steroidal anti-inflammatory drugs (NSAIDs), such as diclofenac, are widely used for their analgesic, antipyretic, and anti-inflammatory properties. However, their use is not devoid of adverse effects, particularly those involving the gastrointestinal, renal, cardiovascular, and, rarely, respiratory systems. This case highlights an uncommon but significant adverse effect—pleural effusion—associated with long-term oral use of Diclofenac.

Our case involved a 58-year-old female with a history of hypertension and type 2 diabetes mellitus, who presented with breathlessness and was ultimately diagnosed with pleural effusion. The patient had been taking oral diclofenac 50 mg once daily for eight months. No other apparent causes for pleural effusion were identified during diagnostic work-up, including infection, malignancy, cardiac dysfunction, or hepatic disease.

A similar rare case was documented by Kumar V et al., where the authors reported acute onset of respiratory symptoms and pleural effusion following diclofenac exposure. Their findings support the hypothesis of

diclofenac-induced pulmonary complications, possibly through hypersensitivity reactions or direct alveolar-capillary membrane injury, leading to non-cardiogenic pulmonary edema and pleural fluid accumulation [2].

Additionally, Singh. R et al. reported an anaphylactic reaction to intravenous diclofenac, highlighting the drug's potential to induce severe systemic and pulmonary hypersensitivity reactions [1]. Though our case involved chronic oral use rather than acute IV administration, it underscores the unpredictable nature of diclofenac-related adverse events across various routes of administration.

Unlike acute hypersensitivity or anaphylaxis seen in Singh et al.'s report [1], our case suggests a more insidious onset of pulmonary involvement, possibly immune-mediated or due to chronic inflammation of the pleura. Long-term use might trigger delayed-type hypersensitivity, consistent with drug-induced pleuritis, leading to fluid accumulation.

The pathophysiological mechanisms underlying NSAID-induced pleural effusion are multifaceted. One proposed mechanism involves the inhibition of cyclooxygenase (COX) enzymes, particularly COX-1, leading to a decrease in protective prostaglandin E2 (PGE2) levels. This reduction may result in unopposed leukotriene activity, promoting bronchoconstriction, increased vascular permeability, and eosinophilic infiltration, culminating in pleural inflammation and effusion [4].

Furthermore, NSAIDs may impair the resolution phase of inflammation by inhibiting COX-2-mediated production of anti-inflammatory lipid mediators such as lipoxins. This disruption can prolong the inflammatory response, leading to persistent pleural inflammation and effusion [5].

It is worth noting that NSAID-induced pleural effusion remains a diagnosis of exclusion, especially in patients with multiple co-morbidities. However, the resolution of symptoms upon cessation of diclofenac would have further supported the causality, which could be assessed using tools like the Naranjo scale for adverse drug reaction probability [3].

This case, therefore, raises awareness among clinicians and pharmacists regarding the long-term safety profile of diclofenac, emphasizing the need for periodic review of medication necessity, particularly in elderly patients or those on polypharmacy. Monitoring for subtle respiratory symptoms and early imaging might help identify drug-induced pulmonary adverse events before severe complications arise.

## Conclusion

This case illustrates a rare but clinically significant adverse reaction—pleural effusion—linked to long-term use of oral diclofenac. The absence of other identifiable causes and the patient's prolonged unsupervised use of the medication strengthen the association. Importantly, this outcome highlights the consequences of inadequate patient counseling and lack of regular medication review. It underscores the vital role of clinical pharmacists in ensuring appropriate drug use, educating patients about potential adverse effects, and conducting routine medication reconciliation. By actively participating in the healthcare team, clinical pharmacists can help prevent such preventable drug-induced complications, especially in patients with co-morbidities and polypharmacy.

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