



CASE REPORT

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Pantoprazole–Induced Acute Interstitial Nephritis: A Case Report

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Introduction: Proton pump inhibitors (PPIs), such as pantoprazole, are widely prescribed for managing acid-related gastrointestinal disorders due to their efficacy and safety. However, despite their generally favorable profile, PPIs have been associated with rare but serious adverse effects, including Acute Interstitial Nephritis (AIN). AIN is an immune-mediated condition that can lead to significant renal dysfunction if not promptly recognized and treated.

Case Details: We present the case of a 73-year-old male with a history of ischemic heart disease, who developed AIN following a brief course of intravenous and oral pantoprazole. The patient presented with shortness of breath, bilateral leg swelling, and worsening renal function. Laboratory investigations revealed a marked increase in serum creatinine, and urine analysis showed proteinuria and hematuria. Abdominal ultrasound indicated bilateral grade 1 renal parenchymal disease. Following the cessation of pantoprazole and the initiation of corticosteroid therapy, the patient's renal function improved, confirming the diagnosis of pantoprazole-induced AIN.

Conclusion: This case highlights the need for heightened clinical awareness of PPI-induced AIN, particularly in elderly patients with recent PPI use. Although rare, this adverse drug reaction can lead to significant renal impairment if not promptly recognized and managed. Clinicians should consider AIN in the differential diagnosis of acute kidney injury in patients on PPIs to prevent irreversible damage.

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Introduction

Proton pump inhibitors (PPIs) are widely prescribed medications, primarily used to manage conditions such as gastroesophageal reflux disease (GERD), peptic ulcer disease, and other acid-related disorders. Pantoprazole, one of the most commonly used PPIs, is valued for its potent acid suppression and favorable safety profile (Ahmed A et al., 2023). However, despite their broad utility, PPIs have been increasingly associated with a

range of adverse effects, including electrolyte imbalances, bone fractures, and infections. Among these, drug-induced Acute Interstitial Nephritis (AIN) is a particularly concerning yet under-recognized complication (Finnigan NA et al., 2023).

AIN is an immune-mediated inflammatory condition affecting the renal interstitium, often triggered by medications. While antibiotics, nonsteroidal anti-



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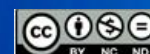
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inflammatory drugs (NSAIDs), and certain diuretics are well-known culprits, the role of PPIs in inducing AIN has gained attention in recent years (Moledina DG et al., 2017). The first report of PPI-induced AIN surfaced in 1992, and since then, the number of documented cases has been rising. Despite this, the condition remains rare, and its non-specific clinical presentation often leads to delayed diagnosis (Sampathkumar K et al., 2013).

This case report presents an instance of pantoprazole-induced AIN in an elderly patient, highlighting the need for heightened clinical awareness of this serious adverse reaction. Early identification and prompt management are crucial to preventing irreversible renal damage and ensuring patient safety.

Case Description

A 73-year-old male presented to the outpatient department (OPD) with symptoms of shortness of breath and bilateral leg swelling persisting for one week. The patient reported that the dyspnea, accompanied by wheezing, was exacerbated by exertion and lying supine, and graded as II to III on the Modified Medical Research Council (MMRC) scale. Additionally, the patient had developed painless, pitting pedal edema over the past week, along with worsening gastritis over the previous day.

The patient had a significant medical history of ischemic heart disease and had undergone Percutaneous Transluminal Coronary Angioplasty (PTCA) three years prior. He was on a regimen of TAB. NOVASTAT GOLD (a combination of aspirin, clopidogrel, and rosuvastatin).

On physical examination, the patient was found to have stable vital signs, with occasional bilateral ronchi. He was treated with antibiotics, steroids, nebulization, and diuretics. Intravenous (IV) pantoprazole was administered at a dose of 40 mg for six days, followed by oral administration for an additional three days. Concurrently, the patient received Inj. Lasix 20 mg IV and Inj. Methylprednisolone 40 mg IV.

Laboratory investigations revealed a total creatinine level of 6.10 mg/dL, with serum creatinine initially at 1.4 mg/dL. Abdominal ultrasonography indicated bilateral grade 1 renal parenchymal disease with calcified specks in both kidneys and mild benign prostatic hyperplasia (BPH). Urine analysis demonstrated the presence of protein and red blood cells (RBCs), while serum creatinine levels increased from 1.4 to 1.53 mg/dL.

In response to these findings, pantoprazole was discontinued and replaced with ranitidine 150 mg. The patient was started on pulse methylprednisolone or oral prednisolone based on the severity of interstitial infiltrations. A repeat renal function test (RFT) performed two days later showed an improvement in creatinine

levels, suggesting a favorable response to the treatment modification.

Discussion

Proton pump inhibitors (PPIs) are among the most commonly prescribed drugs worldwide, primarily for the treatment of acid-related gastrointestinal conditions. While generally considered safe, PPIs have been increasingly implicated in rare but significant adverse effects, including Acute Interstitial Nephritis (AIN) (Savarino V et al., 2020; Geevasinga N et al., 2006). This case highlights pantoprazole, a widely used PPI, as the trigger for AIN, underscoring the need for clinicians to remain vigilant for this potentially serious complication.

AIN is an immune-mediated condition characterized by inflammation of the renal interstitium and tubules. The exact pathogenesis of PPI-induced AIN is not entirely understood but is believed to involve a delayed hypersensitivity reaction. This reaction can be triggered by the parent drug or its metabolites, leading to interstitial inflammation and subsequent renal dysfunction (Härmark L et al., 2007; Raghavan R et al., 2017; Ruffenach SJ et al., 1992). In this case, the rapid onset of AIN following a relatively short duration of pantoprazole therapy suggests a strong temporal relationship between the drug exposure and the onset of renal impairment.

Several reports and case series have documented the association between PPIs and AIN. The first case of PPI-induced AIN was reported in 1992 by Ruffenach et al., involving omeprazole, another member of the PPI class. Since then, numerous cases have been reported globally, contributing to a better understanding of this adverse drug reaction (Geevasinga N et al., 2006). A notable study by Myers et al. highlighted that the onset of AIN typically occurs after an average of 2.7 months of PPI use (Myers RP et al., 2006). However, our case demonstrates that AIN can develop even after a brief exposure to pantoprazole, suggesting that individual susceptibility may play a role.

The clinical presentation of PPI-induced AIN is often non-specific, making diagnosis challenging. Symptoms such as nausea, vomiting, loin pain, and fever are common but not definitive. In our case, the patient presented with worsening renal function, evidenced by rising creatinine levels and abnormal urine analysis, in the context of recent pantoprazole use. The resolution of symptoms and improvement in renal function following the discontinuation of pantoprazole and the initiation of corticosteroids further supports the diagnosis of drug-induced AIN.

Causality assessment using the WHO-UMC system classified this case as "Probable," based on the temporal relationship between drug administration and the onset of symptoms, as well as the positive response to dechallenge.

While rechallenge was not performed due to ethical considerations, the improvement observed after stopping pantoprazole strongly implicates it as the cause of AIN in this patient.

This case contributes to the growing body of evidence suggesting that PPI-induced AIN, although rare, is an important clinical entity that warrants attention. Given the widespread use of PPIs, even a small risk of AIN could have significant public health implications. Therefore, it is crucial for healthcare providers to recognize the signs and symptoms of AIN, particularly in patients with unexplained renal dysfunction who are taking PPIs. Early detection and prompt management, including drug discontinuation and corticosteroid therapy, are essential to prevent permanent renal damage.

In conclusion, while PPIs like pantoprazole are effective and commonly prescribed, their potential to cause serious adverse effects such as AIN should not be underestimated. This case underscores the importance of considering drug-induced AIN in the differential diagnosis of acute kidney injury, especially in the context of recent PPI use. Clinicians should be aware of this rare but significant complication to ensure timely diagnosis and appropriate management.

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Conflict of Interest

Authors declared no conflict of interest.

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