

## Reversible isolated thrombocytopenia: a rare adverse effect of diclofenac infusion

Divya G. Krishnan<sup>1\*</sup>, Anukesh V. Keloth<sup>2</sup>, Mohammed Faiz Akram<sup>1</sup>

<sup>1</sup>Department of Pharmacology,  
KMCT Medical College,  
Calicut, Kerala, India,  
<sup>2</sup>Department of Surgery,  
KMCT Medical College,  
Calicut, Kerala, India

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**\*Correspondence to:**

Dr. Divya G. Krishnan,  
Email: dgkindia@gmail.com

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### ABSTRACT

Diclofenac infusion is prescribed for acute painful and inflammatory conditions in intensive care. Thrombocytopenia is a very rare adverse effect of diclofenac infusion. We report a case of thrombocytopenia due to diclofenac infusion, occurring in a 32-year-old male treated conservatively for acute appendicitis. The thrombocytopenia recovered completely with the discontinuation of the drug. The rarity, clinical importance, and the diagnostic difficulty associated with this case prompted us to report it here.

**Keywords:** Adverse effect, Isolated thrombocytopenia, Reversible, Diclofenac infusion

### INTRODUCTION

Diclofenac is a commonly prescribed non-steroidal anti-inflammatory drug. Diclofenac infusion is prescribed for acute painful and inflammatory conditions in intensive care. Thrombocytopenia is a very rare (<1/10,000) adverse effect of diclofenac.<sup>1</sup> During the literature review, we identified a limited number of reports of thrombocytopenia induced by oral diclofenac.<sup>2,3</sup> However, we did not find any report of thrombocytopenia induced by diclofenac infusion. In this paper, we present the case of a male patient, diagnosed with acute appendicitis, who developed thrombocytopenia during treatment with diclofenac infusion which recovered completely on discontinuation of the drug.

### CASE REPORT

A 32-year-old male with no significant previous medical history presented to the outpatient clinic with complaints of acute onset lower abdominal pain, low-grade fever and two episodes of

vomiting. On abdominal examination, there was right iliac fossa tenderness with mild guarding. Vital parameters and other systems were unremarkable. A provisional diagnosis of acute appendicitis was made which was confirmed by abdominal ultrasound. Laboratory investigations (complete blood count, urine routine, blood urea, serum creatinine, and serum electrolytes) were within normal limits.

As the total leukocyte count was not elevated, a decision was taken to manage the patient conservatively with parenteral antibiotics (cefoperazone+sulbactam 1.5 g every 12 hrs, metronidazole 500 mg every 8 hrs) and analgesic (diclofenac (aqueous) 75 mg/3 ml administered as intravenous infusion every 12 hrs). Patient improved over the next 12 hrs with a resolution of abdominal signs. Hence, conservative line of management was continued with the same drugs.

On day 3 of hospitalization, patient developed a febrile episode for which complete blood count was repeated. The blood test revealed a low platelet count (55,000/ $\mu$ L).

In view of the incidental thrombocytopenia and the fever, blood investigations (immunoglobulin M (IgM) dengue, IgM leptospira, spot test for malarial parasite, peripheral smear) were done to rule out possible causes of thrombocytopenia. All the tests were negative while the peripheral smear inferred mild thrombocytopenia only. Repeated abdominal ultrasound revealed resolving appendicitis. On day 4, the patient had no further episodes of fever. However, the platelet count further reduced to 29,000/ $\mu$ L. It was then that the possibility of drug-induced thrombocytopenia (DIT) was considered. Suspecting diclofenac to be the most likely one among all the medications administered to the patient to have caused thrombocytopenia, it was discontinued.

Platelet count increased to 37,000/ $\mu$ L on the next day following the stoppage of diclofenac. On the subsequent days, platelet count continued to increase and finally became 1.5 lakhs/ $\mu$ L within 4 days of stopping diclofenac. As the patient's appendicitis too had resolved by now, he was discharged and was advised to review after 3 days. The patient's platelet count on the day of review was 2.2 lakhs/ $\mu$ L. The adverse drug reaction causality assessment done using the WHO scale showed a "probable" association of the reaction with diclofenac infusion.

## DISCUSSION

DIT presents a diagnostic and management challenge because of the extensive differential diagnosis of thrombocytopenia and absence of rapid and reliable laboratory tests to confirm the diagnosis of DIT. It often remains a diagnosis of exclusion.<sup>4</sup>

Diclofenac and many other drugs have been associated with thrombocytopenia.<sup>5</sup> Diclofenac induced thrombocytopenia is said to be mediated through an immune mechanism that involves the non-covalent interaction between the drug and a platelet membrane glycoprotein. Antibodies then react with the resulting drug-glycoprotein complex, resulting in thrombocytopenia.<sup>6</sup>

Our literature review showed that all forms of DIT demonstrated a 9% rate of major bleeding and 67% rate of less severe forms of bleeding in reported cases.<sup>7</sup> Contrary to this, our patient remained asymptomatic even at a platelet count of 29,000/ $\mu$ L and thrombocytopenia thus happened to be an unexpected finding.

Several reports have shown that once the drug is withdrawn the prognosis of DIT is excellent and the platelet count recovery to >1 lakh/ $\mu$ L is generally within 1-10 days of

stopping the offending drug.<sup>8</sup> This was true in our case too with the platelet count reaching the said value within 4 days of stopping diclofenac.

To summarize, diclofenac infusion is safe and widely used but severe thrombocytopenia may occur with its use. As the thrombocytopenia can be asymptomatic as in our case, it can be easily missed leading to serious complications. Hence, clinicians must be cautious against the possibility of thrombocytopenia when using diclofenac infusion and platelet count should be monitored in such cases for rapid identification and timely patient care.

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