

UNCOMMON COMPLICATION: ANALGESIC-INDUCED PLATELET DYSFUNCTION - A CASE REPORT

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DOI: [10.5281/zenodo.12619322](https://doi.org/10.5281/zenodo.12619322)

Abstract

Platelet dysfunction is an uncommon complication associated with analgesic usage, particularly with drugs like piroxicam, leading to dysfunction in secondary haemostasis. Platelet dysfunction refers to abnormalities in the function of blood platelets, which play a crucial role in blood clotting. We report a case of platelet dysfunction caused by piroxicam in an elderly male with no comorbidities. The patient in this case had no other underlying health conditions. However, after discontinuing the use of piroxicam, his condition was managed conservatively, meaning it was treated without aggressive intervention such as surgery or other invasive procedures. The implication here is that simply stopping the use of the medication was sufficient to address the platelet dysfunction. This underscores the importance of proper drug usage monitoring. It suggests that using medications, especially those with potential side effects like piroxicam, should be done under the guidance and supervision of a healthcare professional. This case serves as a reminder of the risks associated with self-medication and the importance of seeking medical advice before starting or stopping any medication regimen.

Keywords: Platelet Dysfunction, Secondary Haemostasis, Analgesic-Induced, Piroxicam.

INTRODUCTION

Platelets, essential for blood clotting [1], are minute cell fragments originating from megakaryocytes and characterized by their small size. Dysfunction of these platelets, a rare occurrence, results in platelet dysfunction [2]. This impairment can be attributed to either intrinsic platelet defects or external factors interfering with normal platelet function. Platelet dysfunction may manifest as either hereditary conditions, such as von Willebrand disease or hereditary intrinsic platelet disorders, or acquired disorders, often associated with diseases or the usage of drugs like aspirin and antibiotics. In countries like India, where drugs are readily available without prescription, improper and unwarranted drug usage can lead to unforeseen complications. Efforts are underway to mitigate this issue through preventive measures. It is crucial to recognize that platelet dysfunction is a significant concern that warrants attention and should not be overlooked.

Due to the advent of the internet, there is lot of medication available for the people to browse. With the rise in applications of mobile phones and laptops there is lot of information available for the same. Sometimes this information may be misleading as everything is not disclosed on the internet. Symptoms can be searched online, and medication can be bought over the counter for the same. The use of the same medication can always be helpful to alleviate the symptoms, but it is never the cure.

As the patients do not consult a doctor and rely on the internet and over the counter medication there is always rise a risk of side effects. If the drug in question is an antibiotic it can cause antibiotic resistance, abuse of certain steroidal drugs can cause detrimental effects to the bone, metabolism, and overall general function of the body. So constant vigilance is needed to prevent the abuse of medications and the people should be educated for the same.

Case Report:

A 62-year-old male patient, with persistent blackish discoloration and swelling in his left forearm and arm for three days, visited the hospital on 25/11/2022.

The onset of symptoms followed a fall at his workplace, during which his left hand made direct contact with the ground. Despite the fall, there was no reported open wound. The patient noticed mild swelling in his left hand immediately after the incident, which gradually worsened over time. There is no history of experiencing pain or itching associated with the swelling. Additionally, he reported blackish discoloration of his left forearm and arm during the same period, without any discharge or fever.

The patient's medical history revealed a six-month episode of left knee pain, for which he sought treatment from an orthopedician. Piroxicam and prednisolone were prescribed for this condition. Although the patient discontinued prednisolone after one month, he continued taking piroxicam without further consultation. Additionally, he underwent hernioplasty on the right side fifteen years prior. He had no history of diabetes, hypertension, or previous hospitalization.

Upon examination, the patient appeared moderately built, well-nourished, afebrile, conscious, and oriented to time, place, and person. There were no signs of anaemia, jaundice, cyanosis, or clubbing noted during systemic examination. Local examination of the left arm and forearm revealed swelling below the elbow, accompanied by blackish discoloration of the skin. A 2 x 1 cm healed ulcer was observed on the dorsal aspect of the forearm, with no apparent dilated veins or sinuses. The patient reported slight tenderness upon palpation of the affected area.



Fig 1: Blackish discoloration on the patient's left forearm and arm, initially observed upon admission to the hospital. It also demonstrates the improvement in discoloration following conservative management and offending drug discontinuation

The patient was admitted to the surgical ward, and investigations were conducted as detailed in **Table 1**. Consultations were sought from the General Medicine and Transfusion Medicine departments. Since we suspected platelet dysfunction we conducted special platelet investigations, including the Platelet function test, were performed on the second day, as outlined in **Table 2**. The blood test involved the addition of collagen to the sample. Normally functioning platelets would exhibit a decrease in platelet count following collagen addition. However, in our patient, there was no decline in platelet count after collagen addition, indicating platelet dysfunction. This observation supported the diagnosis of platelet dysfunction, as evidenced by the absence of the expected decrease in platelet count from 2.68 lakhs.

The patient was managed conservatively, with discontinuation of piroxicam on the day of the platelet function test (26/11/2022). Diclofenac, another medication known to cause platelet dysfunction, was also discontinued the following day, on 27/11/2022. Instead, the patient was initiated on alternative pain relief with paracetamol and administered the antibiotic Augmentin. Subsequently, the patient's condition improved following cessation of the offending drugs, and upon complete recovery, he was discharged on 30/11/2022.

Table 1: Investigations Conducted at the Time of Admission (25/11/2022)

Parameter	Obtained counts
Haemoglobin	12.6%
Total WBC count	14,100
Platelets	2.75 lakhs/mm ³
Bleeding time	4.3 secs
Clotting time	5.00 secs
APTT	29.6

Table 2: Platelet Function Test Results after Collagen Addition (26/11/2022) - Pre-count

Parameter	Obtained counts
Haemoglobin	12.3%
Total WBC count	13,500
Platelets	2.55 lakhs/mm ³

Table 3: Post count after addition of collagen to same sample.

Parameter	Obtained counts
Haemoglobin	12.1%
Total WBC count	12,800
Platelets	2.64 lakhs/mm ³

DISCUSSION

Platelets play a crucial role in the clotting of blood, [1] aiding in the formation of a haemostatic plug during primary haemostasis. This process involves several key steps. First, arteriolar vasoconstriction occurs, reducing blood flow to the injured site. Then, the sub-endothelial extracellular matrix is exposed, triggering the activation of platelets. Tissue factor is released, initiating the coagulation cascade, leading to the formation of a permanent plug. Platelets are integral to both primary and secondary hemostasis, performing functions such as adhesion, activation, secretion, and aggregation. Platelet dysfunction, although rare, can occur at any of these steps.

Prolonged drug usage, like piroxicam, can induce platelet inhibition by interfering with platelet collagen. Collagen, acting as a potent agonist, binds to GpVI and GpIa/IIa receptors on platelets, triggering granule release, thromboxane A2 generation, and sustained GPIIb-IIIa activation. The GpIa/IIa receptor facilitates platelet adhesion, while GpVI receptors are crucial for platelet signaling and thromboxane A2 generation. Understanding the intricate mechanisms of platelet function and dysfunction is essential for managing conditions associated with hemostasis and thrombosis.

A lag phase is typically observed with collagen upon addition to platelet-rich plasma (PRP), usually lasting less than one minute. In the case of the patient, their self-administration of piroxicam without medical consultation led to reaching therapeutic concentrations easily, resulting in an excess of the drug in circulation. Crossing the therapeutic threshold inhibited thromboxane A2 activation in platelets, leading to the patient's development of easy bruising following a fall on an outstretched hand. Despite no resolution of the bruising after three days, prompting hospital consultation, cessation of the problematic drug and conservative management resulted in the patient's recovery. Subsequently, alternative painkillers were initiated, and the patient was discharged.

In a study by Koytchev R *et al.*, piroxicam was found to exhibit similar effects on platelet dysfunction in patients with rheumatoid arthritis and ankylosing spondylitis, consistent with the findings observed in this case [3].

In a study by Gaynor *et al.*, piroxicam was observed to inhibit the aggregation of human and dog platelets induced by collagen, but not by adenosine diphosphate (ADP). Piroxicam also inhibited the release of platelet ADP [4].

Study performed by Cronberg S *et al.*, platelet aggregation was examined in platelet-rich plasma obtained from normal volunteers before and at different time intervals following the ingestion of ten analgesic drugs, including aspirin, piroxicam, naproxen, indomethacin, diclofenac, ibuprofen, diflunisal, paracetamol, and oxyphenbutazone. It was observed that piroxicam inhibited the second wave of platelet aggregation [5].

CONCLUSION

In conclusion, this case highlights the importance of careful monitoring and proper management of platelet dysfunction, particularly in patients taking medications that can affect platelet function. The importance of patient education for the correct use of therapeutic drugs is emphasized, particularly in areas where over-the-counter dispensing is common. Increasing awareness and ensuring compliance with pharmaceutical guidelines might decrease the likelihood of negative effects such as platelet dysfunction and enhance patient outcomes. Continuous efforts in patient education and healthcare professional training are necessary to enhance drug safety and improve patient care. Platelet dysfunction can be either inherited, as shown in von Willebrand disease, or acquired as a result of factors such as sickness or drug use. Inadequate medical insurance and improper distribution of pharmaceuticals can lead to platelet dysfunction, particularly in countries like India where drugs are easily accessible without the requirement of a prescription. The proliferation of internet-driven self-medication intensifies this problem, frequently resulting in misuse and potentially grave side effects such as antibiotic resistance and systemic health consequences from steroid addiction. Hence, it is imperative to provide the people

with knowledge about the hazards of self-administered medication and enforce strict oversight of drug consumption.

Comprehending the functioning of platelets and the effects of medications such as piroxicam on platelet activity is crucial for the prevention and management of disorders associated with blood clotting and the formation of blood clots. Research has shown that piroxicam has the ability to prevent platelet aggregation and activation, highlighting the importance of medical supervision in pain management and medication usage. This example also exemplifies the wider problem of pharmaceutical usage and its repercussions, underscoring the imperative for public education and stringent drug regulation to avert such incidents. In order to effectively manage platelet dysfunction, it is crucial to understand the intricate equilibrium of platelet activity in the process of blood clotting, the possibility of drug-related disruptions, and the significance of seeking expert medical advice for therapy. By implementing education, regulation, and monitoring healthcare practices, it is possible to reduce the hazards associated with platelet dysfunction and pharmaceutical misuse. This will lead to improved patient outcomes and better overall public health.

Declaration of Patient Consent

The authors confirm that they have obtained all necessary patient consent forms. The patient has provided consent for the publication of images and other clinical information in the journal. The patient understands that their name and initials will not be disclosed, and every effort will be made to conceal their identity. However, complete anonymity cannot be guaranteed.

Financial Support and Sponsorship

None

Conflicts of Interest

The authors declare no conflicts of interest.

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