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Clarithromycin-Related Thrombophlebitis: A Rare yet Noteworthy Complication

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ABSTRACT

Clarithromycin, a widely used macrolide antibiotic, is generally well tolerated but can rarely cause thrombophlebitis following intravenous administration. We present a case of a 24-year-old male diagnosed with pneumonia, treated with intravenous clarithromycin and piperacillin-tazobactam. While his respiratory symptoms improved, he developed sudden-onset pain, swelling, and tenderness in his left upper limb on the third day of treatment. Doppler ultrasound confirmed cephalic vein thrombophlebitis, with patent deep veins. The patient was successfully managed with subcutaneous fondaparinux and oral antibiotics, leading to full recovery. This case highlights the need for vigilance in detecting clarithromycin-induced thrombophlebitis, as early intervention can prevent complications.

Keywords

Clarithromycin, Thrombophlebitis, Antibiotic complications, Intravenous drug reactions, Macrolide antibiotics.

Introduction

Clarithromycin, a macrolide antibiotic, is widely used for treating a variety of bacterial infections, particularly those affecting the respiratory tract, skin, and gastrointestinal system. By inhibiting protein synthesis in bacteria, it demonstrates broad-spectrum activity against both gram-positive and gram-negative pathogens. This makes it an effective treatment for common conditions such as pneumonia, bronchitis, tonsillitis, and Helicobacter pylori infections, earning it the reputation of a 'wonder drug' in modern clinical practice [1].

Despite its effectiveness, clarithromycin is not without its side effects. Common adverse effects include gastrointestinal disturbances, such as a bad taste and abdominal discomfort. While these are usually mild and self-limiting, more serious reactions although rare can include liver failure, arrhythmias, and neurotoxicity [2]. A less frequently reported but potentially serious complication is thrombophlebitis, particularly following intravenous administration. This condition, which involves inflammation and clot formation in the veins, is often underrecognized and can be mistaken for other issues [3]. This case report aims to highlight thrombophlebitis as a potential, yet overlooked, side effect of clarithromycin therapy, drawing attention to the need for vigilance in its early detection and management.

Case Description

A 24-year-old male with no significant past medical or surgical history presented to the emergency department with a four-day history of fever and productive cough. The fever had a sudden onset, was high-grade (documented at 39°C), and was associated with body aches, which were relieved by simple analgesics taken at home. The cough was productive with yellowish sputum and was accompanied by pleuritic chest pain that worsened with inspiration and improved with rest. The patient denied any history of haemoptysis, shortness of breath, night sweats, weight loss, or gastrointestinal or urinary symptoms. On assessment in the emergency room, his temperature was 39.4°C, respiratory rate 22 breaths per minute, blood pressure 116/69 mmHg, pulse 99 beats per minute, and SpO_2 99% on room air. He was conscious, alert, and oriented to time, place, and person, with a Glasgow Coma Scale (GCS) score of 15/15. Chest examination revealed coarse crepitations on the right side, with good air entry on the left.

Abdominal examination was unremarkable, with a soft, lax abdomen and no organomegaly. Cardiovascular examination showed normal heart sounds (S1, S2) without murmurs. Initial investigations included a chest X-ray, which revealed a right upper lobe opacity. Electrocardiography (ECG) showed sinus tachycardia. A complete blood count (CBC) demonstrated neutrophilic leukocytosis, while renal and liver function tests (RFTs and LFTs) were within normal ranges. The patient was admitted to the medical ward as a case of pneumonia and was started on intravenous antibiotics empirically, including Clarithromycin and Tazocin. Sputum and blood cultures were sent, and tuberculosis was ruled out based on three negative acid-fast bacilli (AFB) samples and negative gastric lavage cultures. With the administration of antibiotics, the patient showed clinical improvement; his fever subsided, and his cough improved. A repeat chest X-ray showed resolution of the initial opacity. However, on the third day of admission, the patient developed severe pain, swelling, redness, and tenderness in his left upper limb (Figure 1).

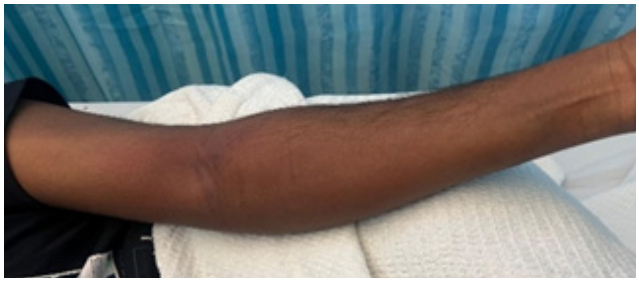

Figure 1: Edema and erythema in left upperlimb.

A D-dimer test was requested and was elevated to 836 ng/ml. Doppler ultrasound revealed patent and compressible axillary, brachial, radial, and ulnar veins, with no evidence of deep vein thrombosis. The deep veins exhibited normal phasic flow, spectral waveform, and an intact response to distal compression (positive augmentation test). However, the cephalic vein was dilated, non-compressible, and demonstrated intraluminal echogenicities with no flow on color Doppler mode, leading to the diagnosis of left cephalic vein thrombophlebitis. IV Clarithromycin was stopped. The patient was started on subcutaneous Fondaparinux 2.5 mg twice daily for two weeks, along with oral antibiotics and an antitussive syrup. He was subsequently discharged and reviewed in the medical outpatient department after two weeks, showing remarkable clinical improvement (Figure 2).

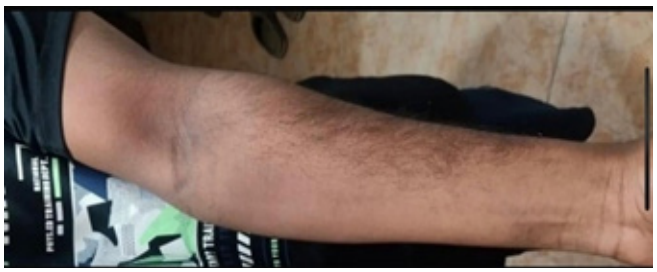

Figure 2: Resolution of symptoms after two weeks.

Discussion

Thrombophlebitis is a known but underreported complication of intravenous antibiotic therapy, particularly with macrolides such as clarithromycin. While clarithromycin is widely used for respiratory and soft tissue infections due to its broad-spectrum antibacterial activity, its intravenous administration has been associated with local venous irritation and, in rare cases, thrombophlebitis. This case highlights an uncommon but significant adverse effect of clarithromycin that clinicians should be aware of, especially in hospitalized patients receiving intravenous therapy. The development of cephalic vein thrombophlebitis in our patient, despite the absence of traditional risk factors for venous thromboembolism, suggests a direct association with intravenous clarithromycin administration. The pathophysiology of clarithromycin-induced thrombophlebitis is not entirely understood, but it is believed to be related to the drug's irritant properties, endothelial damage, and subsequent inflammatory response leading to thrombus formation. Previous studies have reported similar findings, with intravenous macrolides causing varying degrees of venous inflammation and clot formation [3]. A case report by Kuçukbayrak et al. described a vesiculobullous eruption with venous thrombosis following intravenous clarithromycin, reinforcing the potential for severe local adverse reactions and emphasizing the importance of careful intravenous administration.

Diagnosis of superficial thrombophlebitis is primarily clinical, characterized by pain, redness, swelling, and tenderness over the affected vein. However, imaging techniques such as Doppler ultrasound play a crucial role in confirming the presence of intraluminal thrombi and assessing the patency of deeper veins. In our patient, Doppler ultrasound confirmed thrombosis of the cephalic vein while ruling out deep vein involvement, an important distinction as superficial vein thrombosis carries a lower risk of pulmonary embolism compared to deep vein thrombosis (DVT) [4]. Management of clarithromycin-related thrombophlebitis is supportive and includes discontinuation of the offending agent, anti-inflammatory measures, and anticoagulation in select cases. Our patient was successfully treated with subcutaneous Fondaparinux for two weeks, leading to complete resolution of symptoms. The use of anticoagulation in superficial thrombophlebitis remains a topic of debate, but it is generally recommended in cases where there is significant thrombus burden, progression towards deep veins, or severe symptoms [1,4].

This case underscores the importance of careful intravenous administration techniques to minimize complications. Slow infusion rates, adequate dilution, and frequent monitoring of IV sites can help reduce the risk of thrombophlebitis. Additionally, clinicians should maintain a high index of suspicion for thrombotic complications in patients receiving intravenous macrolides, particularly those presenting with unexplained limb pain and swelling.

Conclusion

Clarithromycin-related thrombophlebitis is a rare but clinically significant complication that can lead to morbidity if not promptly recognized and managed. Our case highlights the need for vigilance when administering intravenous macrolides and emphasizes the role of Doppler ultrasound in confirming the diagnosis. Early identification and appropriate treatment, including discontinuation of the offending agent and anticoagulation when indicated, can lead to favourable outcomes. Further research is needed to establish the exact incidence and risk factors for macrolide-associated thrombophlebitis, as well as to develop guidelines for prevention and management.

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