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Meropenem and metronidazole-induced neuropsychiatric and gastrointestinal adverse effects in an elderly patient with diabetic foot infection: A case report

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Abstract
A 78-year-old male with Type 2 Diabetes Mellitus (T2DM) and Systemic Hypertension (SHTN) presented with bilateral diabetic foot ulcers, sepsis, and left foot gas gangrene. He was treated with intravenous meropenem and metronidazole, later followed by cefoperazone-sulbactam. During treatment, he developed tremors, insomnia, anorexia, and dry mouth. Serial laboratory monitoring showed resolution of leukocytosis and persistent anemia. The adverse effects were suspected to be related to prolonged antibiotic therapy. This case highlights the importance of monitoring for drug-induced toxicities, especially in the geriatric population.

Keywords: Diabetic foot infection, meropenem, metronidazole, adverse drug reaction, neurotoxicity

Introduction
Diabetic foot infection (DFI) is a serious and frequent complication in patients with long-standing diabetes and is often associated with high morbidity and mortality [1]. Management requires prolonged courses of broad-spectrum antibiotics to control infection and prevent systemic sepsis. Meropenem, a carbapenem antibiotic, is widely used in severe DFIs due to its broad antibacterial spectrum and ability to penetrate infected tissues. However, its capacity to cross the blood-brain barrier may predispose elderly patients to neurotoxicity, manifesting as tremors, confusion, or seizures [3].
Metronidazole is frequently co-administered with carbapenems for its potent activity against anaerobic bacteria. While generally well tolerated, prolonged use has been associated with central and peripheral neurotoxicity, including tremor, insomnia, anorexia, and xerostomia [4, 5]. Elderly patients are particularly vulnerable to such adverse drug reactions (ADRs) because of altered pharmacokinetics, comorbid conditions, and polypharmacy [2].
Here, we present a case of an elderly male with DFI who developed neuropsychiatric and gastrointestinal ADRs during prolonged treatment with meropenem and metronidazole, highlighting the importance of early recognition and careful monitoring.

Case Summary
A 78-year-old male was admitted on 24 June 2025 with a known history of Type 2 Diabetes Mellitus and Systemic Hypertension for the past 15 years. The patient reported poor adherence to his prescribed medications for 5 days before admission. He presented with bilateral lower limb pain and swelling for 6 days, associated with purulent discharge from the wound sites and persistent pain over the affected areas.

Laboratory interpretation:
The patient's laboratory profile demonstrated profound leukocytosis at admission (WBC $54.1\times10^3/\mu L$), which was consistent with severe infection and sepsis [1]. Serial monitoring revealed a progressive decline in leukocyte counts, indicating an adequate microbiological response to the administered antibiotics.

Despite the resolution of leukocytosis, the patient's hematological profile revealed persistent normocytic anemia with gradual reductions in red blood cell and haemoglobin levels. This hematological pattern may be attributed to chronic inflammation [8], age-related marrow reserve decline [2], or a potential adverse drug reaction such as meropenem-associated cytopenia, although this remains a rare event [6]. Notably, there were no clinical or laboratory signs suggestive of hemolysis or overt bleeding, thereby excluding common alternative causes of anemia. Importantly, the onset of neuropsychiatric manifestations—including tremors and insomnia—occurred despite infection control, suggesting a non-infective etiology. The temporal association with prolonged antibiotic therapy strengthens the likelihood of adverse drug reactions [3, 5], rather than sepsis-related encephalopathy, as the underlying cause.

Diagnosis

The patient was diagnosed with bilateral diabetic foot infection, complicated by left foot gas gangrene and sepsis, on a background of Type 2 Diabetes Mellitus and systemic hypertension. Additionally, during treatment, he developed antibiotic-induced neuropsychiatric and gastrointestinal adverse drug reactions.

Treatment Course

The patient received intravenous meropenem 1 g BD from 24 June 2025 to 11 July 2025 (18 days) and metronidazole 500 mg BD from 24 June 2025 to 13 July 2025 (20 days). Following the discontinuation of meropenem, cefoperazone-sulbactam 1.5 g BD was initiated as a step-down therapy.

Observed Adverse Drug Reactions

Around day 10-14 of therapy, the patient developed tremors, insomnia, anorexia, and xerostomia. These manifestations occurred in the absence of metabolic or renal dysfunction and subsided gradually after withdrawal of meropenem and completion of metronidazole, supporting the likelihood of antibiotic-induced adverse effects.

Causality Assessment: Using the Naranjo Scale, the ADRs scored "Probable" (score: 6), based on time correlation, symptom resolution, and exclusion of alternative causes [7].

Results

The patient's infection improved with meropenem and metronidazole, as shown by resolution of leukocytosis. By the second week, he developed tremors, insomnia, anorexia, and xerostomia, which resolved after stopping meropenem and completing metronidazole. Persistent anemia remained despite infection control. Naranjo assessment indicated the adverse reactions were "probable."

Discussion

Meropenem can cross the blood-brain barrier and cause neurotoxic effects, particularly in elderly patients [3]. Metronidazole is known for central and peripheral neurotoxicity, including tremor, insomnia, anorexia, and mouth dryness [4, 5]. In this case, the onset of symptoms correlated with prolonged antibiotic exposure and improved upon cessation, supporting a diagnosis of drug-induced ADRs. The serial falls in WBC reflected infection control, but the persistence of anemia without other systemic involvement suggests a possible chronic inflammatory response or marrow suppression, which may be potentiated by antibiotic therapy in elderly patients [6, 8].

Conclusion

This case highlights that prolonged use of meropenem and metronidazole in elderly patients with DFI may lead to neuropsychiatric and GI ADRs even in the presence of improving infection markers. Careful patient selection, dose adjustment, and early recognition of ADRs are crucial in antimicrobial stewardship, especially in the elderly.

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