Ertapenem-Associated Encephalopathy and Myoclonus Despite Preserved Renal Function

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"Making Waves"
25th Annual Pain Medicine Meeting
November 5-7, 2026 | Tampa, Florida
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INTRODUCTION

Carbapenem antibiotics are widely used for the treatment of serious infections because of their broad-spectrum activity and favorable clinical efficacy. However, β-lactam antibiotics, including carbapenems, are associated with neurologic adverse effects that can range from mild confusion and somnolence to encephalopathy, seizures, and myoclonus. Although these complications are uncommon, they may be difficult to recognize in hospitalized or postoperative patients because altered mental status and abnormal movements frequently have multiple potential causes.

Ertapenem-associated neurotoxicity is particularly challenging to identify because its clinical presentation is nonspecific and may mimic other common causes of postoperative encephalopathy. Reported manifestations include confusion, delirium, altered level of consciousness, hallucinations, seizures, and myoclonus. The risk of β-lactam–associated neurotoxicity has traditionally been associated with advanced age, underlying neurologic disease, high medication exposure, and impaired renal clearance. Because ertapenem is predominantly eliminated by the kidneys, renal dysfunction is often considered an important predisposing factor for accumulation and subsequent neurotoxicity.

Importantly, however, neurologic toxicity can occur even when renal function is preserved. This may create a diagnostic challenge when clinicians rely heavily on renal impairment as a risk factor. In postoperative patients, the differential diagnosis is further complicated by exposure to opioids, sedatives, gabapentinoids, and other central nervous system–active medications, as well as infection, metabolic disturbances, sleep disruption, and postoperative delirium.

Drug-induced myoclonus may also be difficult to distinguish from epileptic activity. Myoclonic movements occurring predominantly during drowsiness or sleep may prompt evaluation for seizures or other primary neurologic disorders. Neuroimaging, electroencephalography, and cerebrospinal fluid analysis may therefore be required to exclude structural, infectious, inflammatory, or epileptic etiologies. When these evaluations are unrevealing, careful review of medication exposure and the temporal relationship between drug initiation and symptom onset becomes particularly important.

MATERIALS AND METHODS

This retrospective, single-patient case report was based on review of the electronic medical record, including medical history, medication exposures, neurologic examinations, laboratory studies, neuroimaging, electroencephalography, lumbar puncture, treatment, and clinical course. The evaluation focused on the temporal relationship between ertapenem initiation and onset of encephalopathy and myoclonus, while assessing renal function and alternative causes including infection, metabolic abnormalities, structural neurologic disease, and other central nervous system–active medications. The patient's response following ertapenem discontinuation was also assessed. The case was de-identified using the HIPAA Safe Harbor method, and institutional policy determined that Institutional Review Board review was not required. Verbal authorization for case report submission was obtained by telephone and documented in the medical record.

CASE PRESENTATION

An older adult with a medical history significant for diabetes mellitus and atrial fibrillation was initially hospitalized for left prosthetic knee septic arthritis due to *Serratia marcescens*. The patient underwent surgical intervention for management of the infected prosthetic joint and was subsequently discharged on intravenous ertapenem for continued antimicrobial therapy. At the time of discharge and prior to initiation of ertapenem, there was no documented history of encephalopathy, significant altered mental status, or abnormal involuntary movements.

Within several days of starting ertapenem, the patient developed a progressive change in mental status. Family members noted increasing drowsiness, confusion, decreased interaction, and abnormal behaviors during sleep. He subsequently developed intermittent involuntary jerking movements that occurred primarily during periods of drowsiness and while transitioning from wakefulness to sleep. Because these symptoms represented a change from his baseline and continued to progress, the patient was readmitted for further evaluation of altered mental status and abnormal movements.

During readmission, the patient demonstrated fluctuating levels of alertness, ranging from periods of significant somnolence to improved wakefulness. The myoclonic movements were intermittent and were most consistently observed during drowsiness or sleep rather than during sustained wakefulness. Given the recent hospitalization, surgical procedure, active treatment for a serious infection, and exposure to multiple medications, the differential diagnosis included postoperative or infectious encephalopathy, medication-induced delirium, metabolic abnormalities, opioid-related neurotoxicity, seizure activity, and other central nervous system processes.

Renal function remained preserved throughout the evaluation, with a serum creatinine of 0.62 mg/dL and estimated glomerular filtration rate of 100 mL/min/1.73 m^2. This was clinically relevant because ertapenem is predominantly renally eliminated and renal impairment is a recognized risk factor for accumulation and β-lactam–associated neurotoxicity. The absence of significant renal dysfunction made the development of neurologic toxicity less expected and increased the diagnostic challenge.

A comprehensive neurologic evaluation was performed to investigate alternative causes. Computed tomography and magnetic resonance imaging of the brain demonstrated no acute intracranial abnormality or structural lesion to explain the patient's encephalopathy or abnormal movements (Figure 1). Electroencephalography demonstrated nonspecific generalized cerebral dysfunction but did not demonstrate reported epileptiform activity or an electrographic correlate to suggest an active seizure disorder. Lumbar puncture was also performed, with cerebrospinal fluid studies showing no acute abnormality or evidence of an infectious or inflammatory central nervous system process (Figure 2).

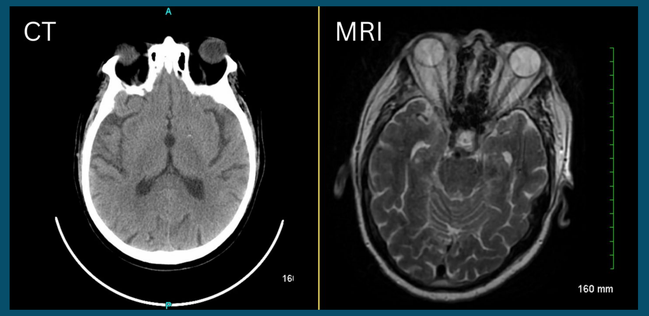


Figure 1: CT and MRI of the brain demonstrated no acute intracranial abnormality, including no acute infarction, hemorrhage, mass effect, or other structural finding to explain the patient's encephalopathy and myoclonus.



Figure 2: Electroencephalography demonstrated generalized cerebral dysfunction without reported epileptiform activity.

Other potential contributors were also considered, including opioid and other central nervous system–active medications, infection, and electrolyte abnormalities. These factors complicated the assessment because several could independently contribute to postoperative delirium or abnormal movements. However, the timing of symptom onset shortly after initiation of ertapenem, the absence of a clear structural, infectious, or epileptic etiology, and the patient's preserved renal function prompted consideration of ertapenem-associated neurotoxicity.

Given the clinical presentation and temporal relationship to ertapenem exposure, ertapenem was discontinued and antimicrobial therapy was transitioned to cefepime to allow continued treatment of the underlying *Serratia marcescens* infection. Supportive management included delirium precautions, medication minimization, correction of electrolyte abnormalities, and close neurologic monitoring. Following discontinuation of ertapenem, the patient demonstrated progressive improvement in alertness and orientation, with resolution of the sleep-associated myoclonic movements.

The patient ultimately returned to his baseline mental status following withdrawal of ertapenem. The combination of symptom onset shortly after ertapenem initiation, preserved renal function, unrevealing neuroimaging and cerebrospinal fluid studies, absence of reported epileptiform activity on electroencephalography, and clinical improvement after discontinuation of ertapenem supported suspected ertapenem-associated encephalopathy and myoclonus. This case illustrates that ertapenem-associated neurotoxicity may occur even in the setting of preserved renal function and should remain part of the differential diagnosis when new encephalopathy or abnormal movements develop during carbapenem therapy.

DISCUSSION

Ertapenem-associated neurotoxicity is an uncommon but clinically important adverse effect of carbapenem therapy that may present with confusion, delirium, somnolence, encephalopathy, seizures, hallucinations, or myoclonus. β-lactam–associated neurotoxicity is thought to involve disruption of γ-aminobutyric acid (GABA)–mediated inhibitory neurotransmission, although the exact mechanism remains incompletely understood. Because these manifestations are nonspecific, medication-related neurotoxicity can be difficult to distinguish from postoperative delirium, infection, metabolic abnormalities, opioid effects, or primary neurologic disease, particularly in medically complex patients receiving multiple medications.

This case is notable for the development of progressive encephalopathy and sleep-associated myoclonus shortly after initiation of ertapenem despite preserved renal function. Renal impairment is a recognized risk factor for carbapenem-associated neurotoxicity because reduced clearance may increase systemic and central nervous system drug exposure. However, preserved renal function does not eliminate the possibility of neurotoxicity. Other factors, including older age, acute illness, recent surgery, concomitant central nervous system–active medications, and individual susceptibility, may contribute to neurologic adverse effects.

The diagnostic evaluation was important because the patient had several potential alternative explanations for altered mental status and abnormal movements. Neuroimaging demonstrated no acute intracranial abnormality, lumbar puncture revealed no acute infectious or inflammatory process, and electroencephalography demonstrated generalized cerebral dysfunction without reported epileptiform activity. These findings, together with the absence of another clear structural, infectious, or epileptic etiology, supported consideration of a medication-induced process.

The close temporal relationship between ertapenem initiation and symptom onset, followed by progressive improvement after ertapenem discontinuation and transition to alternative antimicrobial therapy, further supported suspected ertapenem-associated neurotoxicity. The resolution of both encephalopathy and sleep-associated myoclonus following withdrawal of ertapenem strengthened the clinical association. This case emphasizes the importance of reviewing both analgesic and nonanalgesic medications when evaluating postoperative encephalopathy and abnormal movements. Ertapenem-associated neurotoxicity should remain in the differential diagnosis even when renal function is preserved, particularly when neurologic symptoms develop soon after antimicrobial initiation. Early recognition and discontinuation of the offending medication may lead to clinical improvement and help avoid unnecessary neurologic interventions or prolonged diagnostic evaluation.

REFERENCES

Rissardo, J. P., Fornari Caprara, A. L., Bhat, N., Repudi, R., Zlatin, L., & Walker, I. M. (2025). Drug-Induced Myoclonus: A Systematic Review. Medicina (Kaunas, Lithuania), 61(1), 131. https://doi.org/10.3390/medicina61010131

Wang, C., Zhou, Y., Zhou, Y., & Ye, C. (2023). Ertapenem-Induced Neurotoxicity: A Literature Review of Clinical Characteristics and Treatment Outcomes. Infection and drug resistance, 16, 3649–3658. https://doi.org/10.2147/IDR.S406852

Millar Vernetti, P., Dalamo, K., Khan, Z., Gonzalez-Duarte, A., Frucht, S., & Kaufmann, H. (2023). Meropenem-Induced Facial Myoclonus. Movement disorders clinical practice, 10(Suppl 3), S21–S23. https://doi.org/10.1002/mdc3.13777

Deshayes, S., Coquerel, A., & Verdon, R. (2017). Neurological Adverse Effects Attributable to β-Lactam Antibiotics: A Literature Review. Drug safety, 40(12), 1171–1198. https://doi.org/10.1007/s40264-017-0578-2