Toxic Delirium and Myoclonus from Amantadine and Trimethoprim-Sulfamethoxazole Interaction in a Stroke Patient

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INTRODUCTION

- Amantadine is a neurostimulant commonly used after stroke to help improve cognitive and functional recovery.
- This is a rare case of myoclonus and toxic delirium that developed after trimethoprim-sulfamethoxazole (TMP-SMX) was started to treat a urinary tract infection (UTI) in a stroke patient who had been on a stable dose of amantadine.
- The drug interaction illustrated in this case can help guide clinicians when choosing an antibiotic for a patient who is already on amantadine.

CASE PRESENTATION

- The patient is an 80 year old previously independent woman who presented to inpatient rehabilitation hospital with dense left hemiplegia and neglect following an aneurysm rupture of the posterior communicating artery, complicated by a right middle cerebral artery infarct.
- Amantadine was started to help increase attention and initiation.
- She later developed urosepsis requiring IV piperacillin-tazobactam, which was transitioned to oral TMP-SMX.
- Following the second dose of TMP-SMX, she acutely developed confusion that progressed to florid visual hallucinations and generalized myoclonus.
- A stat MRI and MRA were stable, and EEG suggested diffuse encephalopathy without epileptiform discharges. Given the time course, medication toxicity was presumed, and TMP-SMX was discontinued.
- Within two days, her hallucinations subsided, and mental status returned to baseline.

IMAGING

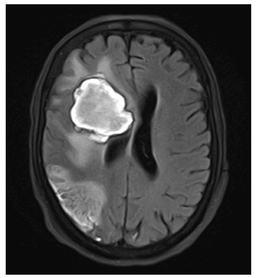
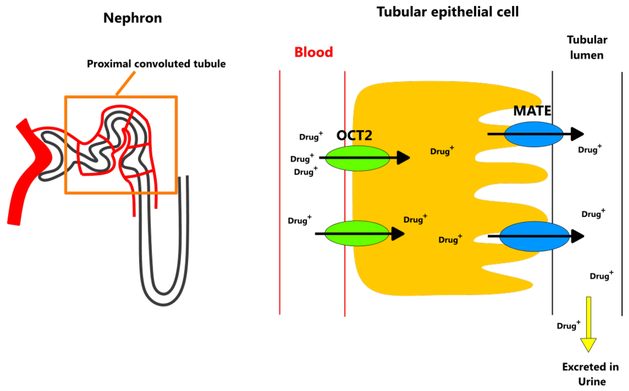


Figure 1. T2 FLAIR Axial MRI without contrast. MRI during the time of myoclonus demonstrated evolving large subacute lobulated intraparenchymal hematoma centered in the right frontal lobe with surrounding edema and associated mass effect and evolving large subacute right MCA territory infarct involving parietal, posterior temporal and occipital lobes. No new acute changes were noted.

PHARMACOLOGY OF DRUG INTERACTION



OCT2-MATE illustration. 2021. Retrieved from: https://www.straighthealthcare.com/oct2-mate-illustration.html

Figure 2. Organic cation transporter 2 (OCT2). OCT2 is a transport protein found in the kidney, and is located in the membrane of tubular epithelial cells in the proximal convoluted tubule. OCT2 transports drugs such as amantadine that have a positive charge from the blood supplying the proximal tubule to the inside of the tubular epithelial cell. Trimethoprim is an inhibitor of OCT2, and inhibits the elimination of medications that are cleared by OCT2. When when used together, TMP can increase serum concentration of amantadine by inhibiting the renal clearance.

DISCUSSION

- This episode of myoclonus caused setback in her functional progress, prolongation of her rehabilitation course, and costly workup to rule out structural causes.
- Previous case reports concluded that the use of drugs that inhibit the organic cation transporter-2 in the tubule, such as trimethoprim, metformin, or imipramine, may interfere with elimination and subsequently lead to drug accumulation of medications such as amantadine and memantine (Figure 2).
- Another previous case report demonstrated that TMP-SMX alone contributed to myoclonus in a patient with hypoxic ischemic brain injury.
- Understanding this interaction can help guide providers to choose antibiotics with a safer profile and to monitor patients for adverse reactions.

CONCLUSION

- This is a unique case of TMP-SMX induced amantadine toxicity leading to myoclonus and delirium.
- Considering the common use of amantadine in stroke recovery and the high prevalence of UTI in patients with stroke, it is important to be cognizant of this interaction in the neurorehabilitation setting.

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