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Case Report

Adverse Drug Reactions: Trimethoprim-sulfamethoxazole Induced Myoclonus

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Abstract

A 58-year-old male presented with complaints of new-onset periodic tremors and spasms for a few days. The patient was found to have recently started a course of trimethoprim-sulfamethoxazole (TMP-SMX) due to concern for a suspected urinary tract infection found incidentally after presenting for wound dehiscence following L1-L4 laminectomies a month prior. A neurological workup revealed was unremarkable, resulting in the exploration of further potential causes. A literature review revealed a case report that reported myoclonus as an adverse effect of TMP-SMX. So, the medication was discontinued, resulting in a resolution of myoclonus. The purpose of this case report is to make clinicians aware of a rare reversible adverse drug reaction from the use of TMP-SMX.

Keywords: *trimethoprim-sulfamethoxazole, TMP-SMX, Bactrim$^{C\$}$, adverse drug reactions, myoclonus, tremor.*

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Introduction

Trimethoprim-sulfamethoxazole, or TMP-SMX, is a sulfonamide antimicrobial drug that has been widely prescribed since its introduction in 1968 due to its extensive range of effects, low cost, and familiarity among clinicians.[1] Commonly reported adverse effects include rash, photosensitivity, folate deficiency, fatigue, nausea/vomiting, and tinnitus, among others.[1] Myoclonus is defined as involuntary, brief, and "jerky" movement due to muscular contraction.[2] While TMP-SMX-induced reversible myoclonus has been reported in the literature previously, there are very few case reports on the subject,[3-6] demonstrating the rarity of this occurrence.

Case Report

A 58-year-old male with a past medical history of hypertension, hypothyroidism, and spontaneous subdural hematoma treated with L1-L4 laminectomies and no known allergies was admitted from an acute-care facility due to the development of tremors and spasms in his limbs that began a few days prior. The patient was at an acute-care facility for treatment of post-operative wound dehiscence following his spine surgery and incidentally began TMP-SMX empirically for urinary tract infection (UTI). The patient subjectively stated he was having full-body tremors and spasms that resulted in a loss of coordination and lack of control over movements. He felt he could have seizures that resolved spontaneously. He also noted milder episodes a month earlier while on TMP-SMX for a UTI, which occurred outside the hospital, yet he completed the medication course. The patient's family had video evidence of the tremors and endorsed sleep-talking episodes that were new for the patient. The patient's review of systems was negative for all symptoms except tremors. Notably, this included negative findings for dizziness, lightheadedness, and headache. The patient had no known allergies and was never a smoker. The family history was notable for rheumatoid arthritis in the patient's brother and maternal uncle, but otherwise non-contributory.

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Medications at Onset of TMP-SMX Treatment

Medication	Dose (mg)	Frequency
Amlodipine	5	Daily
Losartan	100	Daily
Tamsulosin	0.4	Daily
Tolterodine	2	Daily
Methocarbamol	750	BID
Pregabalin	50	TID
Levothyroxine	25	Daily
Butalbital-APAP-Caffeine	50-325-40	Daily
Oxycodone	10	Daily
Amitriptyline	10	Daily
Duloxetine	60	Daily

The physical examination of the patient revealed a lack of coordination and an abnormal finger-to-nose test. No other abnormalities were found on physical examination. Laboratory studies revealed no acute cause of the myoclonus at the time of admission. The summary of pertinent lab findings completed at our hospital is below:

Laboratory Test	Value (normal range)
Ammonia	39 umol/L (<72)
BUN	32 mg/dl (7-26)
Creatinine	1.23 mg/dl (0.71-1.16)
Lactic Acid	1.1 mmol/l (<2.0)

A CT head without contrast on admission revealed a known resolving subarachnoid hemorrhage without midline shift, that had been present since last admission. Follow-up MRI with and without contrast demonstrated no evidence of cerebral infarction, or acute hemorrhage, with mild ex vacuo ventricular dilation. A 21-channel EEG conducted revealed generalized slowing, consistent with encephalopathy but with no clear etiology. The rest of the neurologic workup was unremarkable. Given the onset of myoclonus symptoms with the initiation of TMP-SMX treatment, in combination with the subjective history from the patient on their experience of these symptoms in the past while on TMP-SMX, we conducted a literature review. Our literature review revealed a previous case of reversible TMP-SMX-induced myoclonus in the setting of spinal trauma, so we recommended that the patient discontinue the medication. The cessation of TMP-SMX resulted in a remarkable improvement of myoclonus within three days and the patient was safely discharged to follow up with neurology as an outpatient.

Discussion

The prevalence of adverse drug reactions (ADRs) related to TMP-SMX use is variable, with one study reporting 40-80% of HIV patients and 3-5% of the general population experiencing an ADR of any kind while on the medication.[1,6] Of all ADRs, myoclonus is not typically of primary concern for TMP-SMX.[1] This is certainly due to an unclear mechanism of how myoclonus develops in these patients as a result of this drug, although it has been proposed that it involves altered dopamine metabolism due to inhibition of dihydrofolate reductase. However, more research is warranted. While myoclonus has been related to the onset of other antibiotics, including penicillin, cephalosporins, quinolones, and carbapenems,[5,7] it is less frequently associated with TMP-SMX aside from few case reports with varying clinical backgrounds.[3-6] Of these cases, ours differs in that the patient was receiving the medication for a UTI, whereas the other cases involve treatment for upper respiratory infections or prophylaxis in the setting of HIV. Further, our case involved a recent spinal surgery, which may potentially be related to the pathophysiology of the adverse event through more accessibility to the central nervous system (CNS) in the setting of inflammation. This theory aligns with a reported case of aseptic meningitis due to TMP-SMX,[8] but is not confirmed. In all cases, including ours, the cessation of TMP-SMX resulted in the resolution of symptoms. Given the wide prevalence of TMP-SMX prescriptions in the current healthcare setting, clinicians need to remember this potential adverse. While it may not be a particularly morbid adverse effect, it can be distressing for the patient,[2] leading to further anxiety about their health as it did for our patient. In this case, TMP-SMX was identified as the likely cause due to the timing of symptom onset following its administration. However, pinpointing a drug as the culprit is not always straightforward, especially in scenarios like major trauma where multiple medication adjustments occur. Removing all drugs at once or conducting trial-and-error tests could delay treatment and compromise patient care. Therefore, clinicians encountering new onset myoclonus during or after a TMP-SMX course, without other clear causes, should consider the possibility of an adverse drug reaction.

Conclusion

Trimethoprim-sulfamethoxazole (TMP-SMX) can trigger reversible myoclonus even in patients without known sulfa allergies. Early diagnosis through comprehensive patient history and examination is key to reversing TMP-SMX-induced myoclonus.

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