CASE REPORT

Trimethoprim/Sulfamethoxazole Induced Encephalopathy

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Abstract

Aim: To describe a rare case of encephalopathy induced by sulfonamide.

Background: Antibiotic-induced neurotoxic side effects can have a multitude of neurologic presentations. Patients with previous central nervous system (CNS) disease, renal disease, and advanced age are at an increased risk. Treatment mainly consists of discontinuation of the offending agent, use of antiepileptic drugs in the case of seizures or status epilepticus, and hemodialysis if necessary. The risk of CNS toxicity can be reduced with dosage adjustments in high-risk populations.

Case description: We present to you the case of a 63-year-old male patient, who was diagnosed to develop Bactrim-induced encephalopathy, which is not a common presentation of the neurological side effects of the drug. The patient was treated supportively and educated about his diagnosis to prevent future recurrences and well on to recover well from the episode without any deficits.

Conclusion: Sulfonamide-induced encephalopathy is an extremely rare presentation of the neurological side effects of sulfonamide. It should be kept in the differential in relevant cases and treated vigilantly as it is preventable and simpler to treat once correctly identified.

Clinical significance: Bactrim is a drug combination of trimethoprim and sulfamethoxazole. It is a drug that is used widely for bacterial infections of varied types. The side effects associated with it are generally due to the sulfa component. Encephalopathy is an extremely rare side effect with about eight cases reported in the literature as of now.

Keywords: Altered mental status, Antibiotics, Bactrim, Case report, Drug-induced encephalopathy, Encephalopathy, Sulfonamide.

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Background

Delirium is a well-known complication of hospitalization. Although medications are an appreciated cause of delirium, antibiotics are an under-recognized cause. Trimethoprim/sulfamethoxazole (TMP/SMX) is a sulfonamide that is routinely used in clinical practice for the treatment and prophylaxis of several infections. While the neurotoxic effects are theorized to be at least in relation to the excellent CNS penetration of TMP/SMX, the precise mechanism of neurotoxicity is not established.[1] TMP/SMX has reportedly been associated with encephalopathy, transient psychosis, and aseptic meningitis. About eight cases are reported in the literature. Our case developed encephalopathy due to the use of Bactrim, a commonly used antibiotic containing a combination of sulfamethoxazole and trimethoprim.

Case Description

A 63-year-old white male presented to the emergency department with complaints of altered mental status vomiting, fever, slurred speech, ataxia, fever, chills, and decreased level of consciousness, since a day. He had been prescribed a course of the antibiotic Bactrim for a day for right upper limb bursitis. He had no known previous allergies. Vitals on presentation were blood pressure of 134/84 mm Hg, a pulse of 89 bpm, respiratory rate of 17/minute, a temperature of 99.4°F, and SpO_2 of 95% on room air.

Upon examination, his neck was supple, with negative Kerning's and Brudzinski's signs. He was found to be oriented to person, situation, and time but not place. He responded to name, knew the hospital and year, but did not state the month or day. He could not recall three words after 3 minutes, couldn't spell the word "word" backward, nor could perform serial seven subtraction beyond 93. He identified and repeated objects but had difficulty following instructions crossing the midline. All other system examinations were normal.

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An initial diagnosis of an ischemic cerebral vascular accident was established.

Computed tomography (CT) brain without contrast showed no specific findings, and CT angio of the head and neck also did not show any acute findings. A carotid Doppler did not reveal any stenosis. Magnetic resonance imaging could not be done due to patient agitation. Chest X-ray showed no acute cardiopulmonary changes. The echocardiogram showed an ejection fraction of 68% and no vegetation or thrombus. His complete blood count and differential counts were normal, he was found to have a high D-dimer of 550 and an increased C-reactive protein level of 44.5 while the procalcitonin was normal with a level of 0.005. The ammonia level was <10. Cerebrospinal fluid (CSF) showed elevated protein of 84 mg/dL, with inflammatory cells.

Blood cultures were negative.

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A diagnosis of viral/autoimmune encephalitis was established, and the patient was treated with cefepime and vancomycin, and went on to improve with no deficits from the event.

A month later, he was prescribed Bactrim for phlebitis post intravenous line insertion in hand, and after the first dose, he soon developed altered mental status, vomiting, and pain in the abdomen and was again rushed to the emergency department.

His vitals on presentation were blood pressure of 132/94 mm Hg, a pulse of 123 beats/minute, respiratory rate of 20/minute, a temperature of 100.3°F, and SpO_2 of 93% on room air.

He appeared ill, was awake and obeyed commands, could answer questions but continued on a tangent, and was not oriented to person or place. His neck was supple and had a full range of motion. He had normal muscle tone and reflexes.

A diagnosis of TMP/SMX-induced encephalopathy was established considering the temporality of the present event and past history of a similar event after taking Bactrim.

The medication was stopped, supportive care was provided, and the patient went on to recover well from the event.

A list of all sulfa-containing medications was provided to him and he was educated about his diagnosis.

Discussion

The sulfamethoxazole component of SMX/TMP is responsible for most of its side effects.

Trimethoprim/sulfamethoxazole (TMP/SMX) induced encephalopathy is an unusual but salient diagnosis. The use of TMP/SMX had been approved by the United States Food and Drug Administration in 1973. It was authorized to be used as a combination drug due to its synergistic effect causing sequential blockade of bacterial dihydrofolate reductase. TMP/SMX is widely distributed in the body, also in the CSF. The half-life of TMP is 8–10 hours and that of SMX is 10 hours.[2] The drug is usually used to treat various infections like urinary tract infections, traveler's diarrhea, methicillin-resistant *Staphylococcus* skin, and soft tissue infections.

The most commonly reported side effects from the medication are gastrointestinal upset and skin rashes.

There have been only about eight reported cases of TMP/SMX-induced encephalopathy. The incidence remains unrevealed as most cases are not reported or remain unrecognized. The mechanism of development is not established. Recognition and treatment of the condition are important as stopping the offending agent can treat it and prevent the recurrence. The outcome is generally good, with no long-term sequel.

Clinical Significance

Neurotoxicity is recognized among several groups of antibiotics, particularly in high-risk patients. It ranges from ototoxicity, neuropathy, and neuromuscular blockade to confusion, nonspecific encephalopathy, aseptic meningitis, transient psychosis, seizures, and status epilepticus. Patients at a higher risk of neurotoxicity associated with various groups of antibiotics include those with extremes of age, suffering critical illness, renal dysfunction, and prior neurological disease. Information on neurotoxic effects is necessary in order to avoid this preventable complication. Sulfonamide-containing drugs are associated with causing encephalopathy and should be considered in the differential in relevant scenarios.

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