TMP-SMX Induced Aseptic Meningitis

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Introduction

Aspetic meningitis secondary to drug adverse effects is a rare but serious disorder, most commonly reported with non-steroidal anti-inflammatory drugs and trimethoprim and sulfamethoxazole (TMP-SMX). Early diagnosis is important, since the cessation of the problem drug leads to rapid clinical improvement. We report a case of TMP-SMX induced meningitis.

Case Report

A 24-year-old previously healthy man was admitted after a four-day history of severe headaches, neck stiffness, nausea, vomiting, and low grade fever and chills. He had been taking TMP-SMX for 18 days for a suspected community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) abscess of his right groin. In addition, he noticed sudden onset of a diffuse maculo-papular rash on the day of presentation sparing only his face and palms.

The patient denied any history of contact with infected individuals, cough, or sinus discharges. His past medical history was negative. He had never taken TMP-SMX. He smoked cigarettes, but did not report any alcohol or illicit drug use. He had no known medication allergy. On presentation, he was awake and oriented.

On physical examination, the patient showed a positive Brudzinski sign and the rash as described above, as well as a painful, 2x2 cm, right groin abscess. Vital signs were remarkable for a temperature of 103°F and a heart rate of 103 bpm.

A Complete Blood Count (CBC), Comprehensive Metabolic Profile, urinalysis, chest xray, and a brain CT scan were normal. Lumbar puncture was significant for 427 WBCs with 93% segmented neutrophils, protein of 51, normal glucose, and and no organism on gram stain. The following tests were negative: *Rickettsia rickettsi* serology, human immunodeficiency virus (HIV) antibody, *Erlichia chaffensis* serology, Lyme disease serology, herpes simplex virus polymerase chain reaction (PCR) on cerebrospinal fluid (CSF), Enterovirus PCR on CSF, Tularemia serology, cryptococcal antigen, *Bartonella* serology, venereal disease research laboratory (VDRL) test. Bacterial, viral, acid fast, and fungal cultures and stains also were negative. TMP-SMX was stopped on admission and the patient recovered within three days.

Discussion

TMP-SMX induced meningitis has been well reported in literature. The reaction is idiosyncratic.[1] The described symptoms can occur in patients naïve to TMP-SMX as well as previous users. These symptoms can occur hours to weeks following administration of the drug. Meng et al.[2] reported recurrent aseptic meningitis following TMP-

SMX use for urosepsis four times in the same patient.

The pathogenetic mechanism of this disease is still uncertain. Possible mechanisms include hypersensitivity reaction, direct drug toxicity, and immune complex deposition. Antonen et al.[3] suggested IL6 as a possible mediator.

Symptoms usually include mild headache, low grade fever, and neck stiffness, although hemodynamic compromise and respiratory failure requiring intubation and admission to the intensive care unit also have been reported.[1] Cerebrospinal fluid analysis suggestive of TMP-SMX induced meningitis includes a neutrophilic pleocytosis and mildly elevated protein along with normal glucose and negative gram stain.[1]

Some reports suggested that CSF fluid findings alone cannot differentiate between TMP-SMX induced meningitis and partially treated bacterial or viral meningitis.[4] Brain CT scan is normal in most case reports. Blumenfeld et al.[5] described MRI findings consistent with diffuse bilateral T2 signal abnormalities of the white matter of the cerebral hemispheres.

Recovery after discontinuation of the drug, and negative viral, bacterial, and fungal cultures are strongly suggestive of TMP-SMX induced meningitis. Fortunately, recovery is complete most of the time and uneventful within 3 to 11 days, even in the case of most severe symptoms.

Conclusion

The incidence of TMP-SMX induced meningitis is unknown. It does not appear to be dose or time related. Neutrophilic pleocytosis and negative cultures are essential for the diagnosis. Treatment is discontinuation of the drug. Prognosis is usually excellent.

References

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