



## An Outbreak of Trimethoprim/Sulfamethoxazole-Resistant *Stenotrophomonas maltophilia* Meningitis Associated with Neuroendoscopy

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Stereotactic aspiration by neuroendoscopy for treatment of deep-seated intracranial hematomas is widely accepted because this procedure is minimally invasive and thereby reduces the probability of iatrogenic brain damage. Herein, we describe an outbreak of trimethoprim/sulfamethoxazole (TMP/SXT)-resistant *Stenotrophomonas maltophilia* meningitis, possibly from a contaminated neuroendoscopy, and review the previous use of antimicrobial therapies for this condition without TMP/SXT. This is the first reported outbreak of TMP/SXT-resistant *S. maltophilia* meningitis. The discussion emphasizes the importance of adequate disinfection processes before and after endoscopic neurosurgery and the use of therapeutic options other than TMP/SXT when encountering *S. maltophilia* meningitis.

**Key words:** Trimethoprim/sulfamethoxazole resistance, meningitis, *Stenotrophomonas maltophilia*, neuroendoscopy

### INTRODUCTION

Stereotactic aspiration of an intracranial hematoma with a neuroendoscope is a feasible and effective method to prevent further brain damage.<sup>1</sup> Although outbreaks of nosocomial infections and pseudoinfections have been linked to contaminated endoscopy, outbreaks associated with contaminated neuroendoscopy have not been reported.<sup>2</sup> Herein, we report an outbreak of trimethoprim/sulfamethoxazole (TMP/SXT)-resistant *Stenotrophomonas maltophilia* meningitis. Our investigation concluded that this outbreak resulted from inadequate neuroendoscopic decontamination procedures and identified the most suitable treatment options for TMP/SXT-resistant *S. maltophilia* meningitis.

### CASE REPORT

A 73-year-old man was sent to our Emergency Department by ambulance following an acute onset of altered consciousness while at home. Upon arrival, the patient was unconscious, his

pupils were anisocoric, and he was unresponsive to painful stimulation. Computed tomography of the brain indicated an intracranial hemorrhage in the left basal ganglion, with perifocal edema and uncal herniation. The patient underwent stereotactic aspiration of the hematoma in the left frontal lobe in combination with neuronavigation and drainage of the cerebrospinal fluid (CSF) by use of an external ventricular drain. The intracranial pressure was simultaneously monitored, and he was admitted to the Neuro intensive care unit (NICU) for further treatment.

Five days after admission, the patient had a fever of 38.9°C and laboratory findings indicated a white blood cell count (WBC) of 14,620/μL, hemoglobin of 12.6 g/dL, platelet count of 135,000/μL, and C-reactive protein of 26.32 mg/dL. Analysis of a CSF sample showed a WBC of 156 cells/μL (87% neutrophils, 9% lymphocytes), glucose of 25 mg/dL, protein of 87 mg/dL, and the presence of Gram-negative bacilli. Intravenous vancomycin (2 g/day) and meropenem (6 g/day) were administered empirically. The patient remained febrile despite use of these broad-spectrum antibiotics. Ten days after admission, *S. maltophilia* was identified in the CSF. The isolate was highly drug-resistant and only susceptible to ceftazidime.

Two days after admission of this first case, a second meningitis case occurred in the same intensive care unit. The second case, a 61-year-old male, was admitted for a spontaneous intracranial hemorrhage in the left thalamus. He received stereotactic neuroendoscopy for a hematoma aspiration that employed the same neuroendoscopy and the same operation room. One week after surgery, this second patient developed

Received: March 13, 2014; Revised: May 2, 2014; Accepted: May 14, 2014

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a fever of 39.1°C. Analysis of his CSF showed a leukocyte count of 439 cells/μL (71% neutrophils, 29% lymphocytes), glucose of 35 mg/dL, and protein of 284 mg/dL. Twelve days after this second surgery, *S. maltophilia* was isolated from the CSF. This second isolate had the same antibiogram as the first isolate, and was resistant to TMP/SXT, but susceptible to ceftazidime only.

We were able to isolate *S. maltophilia* from the neuroendoscopy, but not from other environmental specimens in NICU or the operation room. A review of all medical records during one month before the first case indicated no other cases that were positive for *S. maltophilia* in the NICU, which we considered a possible source of the infection. Analysis of the records indicated that the neuroendoscopy was reprocessed using a glutaraldehyde disinfectant for sterilization, but the immersion time (1 h) was not long enough to achieve sterilization (3–10 h). Thus, after the second case, we implemented a hydrogen peroxide gas plasma sterilization procedure for neuroendoscopic instruments. In both cases, we adjusted the antimicrobial therapy to ceftazidime 6 g/day, based on the identical antibiograms.

The fever of the first case subsided gradually and after 3-week of intravenous ceftazidime treatment (6 g/day), a follow-up lumbar puncture showed acellular CSF with normal biochemistry and negative culture results. This patient was discharged from the hospital after 3-week ceftazidime treatment. The second case also resolved and was also discharged after 3 weeks of ceftazidime therapy. After switching the disinfection process, there was no new case of *S. maltophilia* meningitis at our institution.

## DISCUSSION

Meningitis due to *S. maltophilia* is rarely encountered. Nosocomial *S. maltophilia* meningitis usually occurs after neurosurgical procedures.<sup>3</sup> Clinicians should consider the possibility of *S. maltophilia* infection in patients who present with meningitis after neurosurgery, particularly in those who respond poorly to broad-spectrum antibiotics and who have Gram-negative bacilli in the CSF. There were very few previous cases of *S. maltophilia* meningitis in our institute, with only four TMP/SXT-susceptible *S. maltophilia* meningitis in the past 5 years. The two isolates of *S. maltophilia* meningitis described here were both TMP/SXT-resistant and had identical antibiogram with susceptibility to ceftazidime and ciprofloxacin, prompting an outbreak investigation.

We found that the sterilization procedures used for the neuroendoscope in these two cases did not adhere to decontamination guidelines.<sup>4</sup> Use of an inadequate disinfectant immersion period may result in persistent *S. maltophilia*

colonization on the surface of a neuroendoscope, and transmission to subsequent cases. Although our investigation was unable to identify the initial contaminated source, we believe that the use of an inappropriate disinfection process is the likely reason for this outbreak. With the widespread use of endoscopic neurosurgery, it is important to use adequate sterilization processes for neuroendoscopic instruments. Unlike other endoscopes, neuroendoscopes should be sterilized because they enter sterile tissue. Glutaraldehyde has been most commonly used as a high-level chemical disinfectant, if medical instruments were immersed for 30 min and may function as a chemical sterilant if prolonged immersion of medical instruments with Glutaraldehyde (3–12 h). However, a previous study indicated that even with the use of valid endoscope reprocessing protocols, microbial accumulation can lead to the development of a mature biofilm inside endoscope channels, resulting in subsequent infections.<sup>5</sup> More effective sterilization processes, as provided by hydrogen peroxide gas plasma, is probably better for neuroendoscopy sterilization.<sup>4</sup>

Currently, TMP/SXT is recommended for the treatment of *S. maltophilia* meningitis.<sup>6</sup> The recent emergence of TMP/SXT-resistant *S. maltophilia* isolates presents a therapeutic dilemma for clinicians, because there has been minimal testing of the few available cases.<sup>7,8</sup> Recent literature on the treatment of *S. maltophilia* infections suggests that a fluoroquinolone is indicated when there is documentation of resistance or allergy to TMP/SXT.<sup>9</sup> A review of previous *S. maltophilia* meningitis cases who required treatment other than TMP/SXT indicated that ciprofloxacin and ceftazidime were used most cases, and that the clinical success rates were 100% [Table 1]. Despite of the *in vitro* activity of quinolones and ceftazidime to *S. maltophilia* and above clinical reports, ciprofloxacin use should be cautious because some studies revealed that brain distribution of several quinolones is restricted by the operation of multiple efflux transporters of the brain and may limit its therapeutic effect in treating CNS infection<sup>10</sup> In contrast, ceftazidime, a 3<sup>rd</sup> generation of cephalosporin, may be the drug of choice in such cases for its good penetration into the CSF and had recommended in treating bacterial meningitis, especially in patient after neurosurgery.<sup>11,12</sup>

The present report emphasizes the importance of proper sterilization procedures for neuroendoscopes and our review of the limited number of clinical reports indicate that ciprofloxacin and ceftazidime (alone or in combination with other antibiotics) may be considered as alternatives to TMP/SXT for treatment of *S. maltophilia* meningitis. Additional published cases and clinical trials are required to formulate a more evidence-based approach for the treatment of patients with *S. maltophilia* meningitis when TMP/SXT cannot be used.

Table 1: Cases of *S. maltophilia* meningitis treated with regimen other than trimethoprim-sulfamethoxazole

| Age/sex                | Comorbidity                                 | Neurosurgery                                             | Initial therapy                | Outcome |
|------------------------|---------------------------------------------|----------------------------------------------------------|--------------------------------|---------|
| 55/female <sup>6</sup> | Brain metastasis secondary to breast cancer | Ommaya reservoir placement                               | Chloramphenicol and gentamicin | Died    |
| 28/female <sup>6</sup> | CP angle tumor                              | Tumor removal                                            | Ciprofloxacin                  | Cured   |
| 49/male <sup>6</sup>   | Hepatic steatosis                           | NR                                                       | Ceftazidime and amikacin       | Cured   |
| 48/male <sup>3</sup>   | Traumatic ICH                               | Craniectomy                                              | Ciprofloxacin                  | Cured   |
| 61/male <sup>3</sup>   | Traumatic ICH and ICA aneurysm              | Craniotomy                                               | Ceftazidime                    | Cured   |
| Present case           |                                             |                                                          |                                |         |
| 73/male                | ICH                                         | Navigator assistance stereotactic aspiration of hematoma | Ceftazidime                    | Cured   |
| 61/male                | ICH                                         | Navigator assistance Stereotactic aspiration of hematoma | Ceftazidime                    | Cured   |

CP = cerebral-pontine; ICH = intracranial hemorrhage; ICA = internal carotid artery; TMP/SXT = trimethoprim/sulfamethoxazole; NR = not reported;  
*S. maltophilia* = *Stenotrophomonas maltophilia*

## DISCLOSURE

The authors declare this study has no conflict of interest.

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