

# Trimethoprim-Sulfamethoxazole Plus Topical Antibiotics as Therapy for Acute Otitis Media With Otorrhea Caused by Community-Acquired Methicillin-Resistant *Staphylococcus aureus* in Children

Baha A. Al-Shawwa, MD; Dennis Wegner, PhD

**Objective:** To report our experience in identification and treatment of acute otitis media (AOM) with otorrhea secondary to community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA), which is seen in children at increasing rates.

**Design:** Clinical and laboratory records were retrospectively reviewed between January 2003 and December 2003.

**Setting:** Primary pediatric clinic.

**Patients:** Six pediatric patients who had AOM with otorrhea caused by CA-MRSA.

**Main Outcome Measures:** Clinical resolution of AOM with otorrhea.

**Results:** All patients had acute-onset otorrhea associated with their AOM. Five patients had tympanostomy tubes and 1 had perforation of the tympanic membrane. None of the patients were responding to treatment with oral antibiotics (amoxicillin sodium–clavulanate potassium, cefpodoxime proxetil, and cefprozil) or fluoroquinolone ear drops (ofloxacin, ciprofloxacin). Specimens

were obtained from the ears for cultures, and MRSA was present in the cultures. The organisms were resistant to levofloxacin and erythromycin in all patients and resistant to clindamycin hydrochloride in 2 patients. The cultures were sensitive to trimethoprim-sulfamethoxazole, gentamicin sulfate, rifampin, and vancomycin hydrochloride. All patients were treated successfully with oral trimethoprim-sulfamethoxazole and ear drops (gentamicin sulfate or polymyxin B sulfate–neomycin sulfate–hydrocortisone [Cortisporin]).

**Conclusions:** The rising rate of CA-MRSA as a cause for many pediatric infections is a major concern. It is very important to obtain cultures from patients with nonresponsive or persistent otorrhea with AOM to look for MRSA and determine the sensitivity of the pathogen to antibacterial therapy. Trimethoprim-sulfamethoxazole is a good choice for initial, empirical therapy when combined with a topical agent for AOM with otorrhea if CA-MRSA is suspected. Further studies are needed to determine whether there is a link between the overuse of topical fluoroquinolones in pediatric patients and the recent rising rate of CA-MRSA.

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**Author Affiliations:**  
Departments of Pediatrics  
(Dr Al-Shawwa) and  
Microbiology, Collaborative  
Laboratory Services  
(Dr Wegner), Ottumwa  
Regional Health Center,  
Ottumwa, Iowa.

**A**CUTE OTITIS MEDIA (AOM) is the most common bacterial infection in children and accounts for as many as 30 million office visits to physicians annually.<sup>1</sup> Proper treatment is critical because offending pathogens become increasingly resistant to antibiotics, and the cost of managing the disorder has exceeded 3 billion dollars per year.<sup>2-4</sup> The microorganisms classically associated with AOM, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*, account for a significant percentage of AOM that occurs in an ear with a tympanostomy tube (or with a perforation), especially in children younger than 2 years. However, *Pseudomonas ae-*

*ruginosa* and *Staphylococcus aureus* also account for a significant percentage of infections (often >40%), especially in older children.<sup>5</sup>

Methicillin-resistant *S aureus* (MRSA) has been an emerging concern as a pathogen in the community in addition to hospitals and chronic care facilities and among drug abusers. Reports<sup>6,7</sup> show that as many as 3% of healthy children carry MRSA in their nasopharynxes. Most pediatric MRSA infections have been reported as skin infections. However, a few reports<sup>8,9</sup> have mentioned MRSA as a cause of AOM. A recent article by Santos et al<sup>8</sup> suggested that intravenous vancomycin hydrochloride treatment is necessary for the resolution of AOM caused by MRSA. Vancomycin is

**Table 1. Profile of Pediatric Patients With Persistent Acute Otorrhea and Acute Otitis Media Caused by Community-Acquired Methicillin-Resistant *Staphylococcus aureus***

Patient No./Sex/Age, y	T/P	Site	Treatment	Outcome
1/M/1	T	B	T-S (PO) gent (ear drops)	Resolved
2/M/2.7	T	L	T-S (PO) Cortis (ear drops)	Resolved
3/F/11.9	P	L	T-S (PO) gent (ear drops)	Resolved
4/M/3.6	T	R	T-S (PO) oflox (ear drops)	Resolved
5/M/2	T	R	T-S (PO) gent (ear drops)	Resolved
6/M/2.4	T	L	T-S (PO) Cortis (ear drops)	Resolved

Abbreviations: B, both ears; Cortis, Cortisporin (Glaxo Wellcome Inc, Research Triangle Park, NC); gent, gentamicin sulfate; L, left ear; oflox, ofloxacin; P, perforation; PO, per oral; R, right ear; T, tympanostomy tube; T-S, trimethoprim-sulfamethoxazole.

**Table 2. Resistance Profile of Community-Acquired Methicillin-Resistant *Staphylococcus aureus* in Pediatric Patients With Persistent Acute Otorrhea and Acute Otitis Media**

Patient No.	T-S	Rif	Clind	Eryth	Oxac	Vanc	Levo	Gent
1	S	S	S	R	R	S	R	S
2	S	S	R	R	R	S	R	S
3	S	S	R	R	R	S	R	S
4	S	S	S	R	R	S	R	S
5	S	S	S	R	R	S	R	S
6	S	S	S	R	R	S	R	S

Abbreviations: clind, clindamycin hydrochloride; eryth, erythromycin; gent, gentamicin sulfate; levo, levofloxacin; oxac, oxacillin; R, resistant; Rif, rifampin; S, sensitive; T-S, trimethoprim-sulfamethoxazole; vanc, vancomycin hydrochloride.

very expensive and requires 24-hour intravenous access and monitoring of its levels, which makes it inconvenient for the patient and the family. Linezolid is an oral alternative to vancomycin, but its cost, which is approximately \$120 per day, limits its use to more severe and serious infections.

In this article, we report our experience in treating AOM with otorrhea caused by community-acquired MRSA (CA-MRSA) with oral trimethoprim-sulfamethoxazole and topical antibiotics.

## METHODS

This study was conducted in a primary pediatric clinic in a rural community in the United States. We reviewed the laboratory and medical records for all patients younger than 18 years with cultures positive for MRSA between January and December 2003. Collected data included demographic information, anatomical sites of infection, clinical symptoms, treatment modalities, and the results of treatment. The sensitivity results of the antibiotic treatment were collected from the original laboratory records. Only patients who had cultures positive for CA-MRSA and who had AOM were included.

Swabs from the ears of patients were obtained for culture on sheep's blood agar plates. Susceptibility testing of the *S aureus* isolates was performed using the Vitek 1 Legacy model automated instrument (BioMerieux Inc, Durham, NC), according to manufacturer's instructions. Quality control of the instrument and susceptibility cards was conducted according to Clinical and Laboratory Standards Institute regulations. Confirmation of resistance to methicillin was accomplished by using the Kirby-Bauer cefoxitin disk (Remel Inc, Lenexa, Kan) diffusion method specified by the Clinical and Laboratory Standards Institute.

## RESULTS

Eleven patients were found to be MRSA positive; 5 had soft tissue and skin infections rather than otitis media and therefore were excluded from the study. The remaining 6 patients did have otitis media (**Table 1**). None had been recently hospitalized, and all of the infections appeared to be community-acquired infection.

Five patients had tympanostomy tubes, and 1 patient had a preexisting tympanic membrane perforation. All patients had new onset of otorrhea that was not responding to oral antibiotics (amoxicillin sodium-clavulanate, cefpodoxime proxetil, cefprozil) and fluoroquinolone ear drops (ofloxacin, ciprofloxacin). Ear culture specimens were obtained only when there was no response to these antibiotics. The organisms were sensitive to trimethoprim-sulfamethoxazole, gentamicin sulfate, rifampin, and vancomycin in all patients (**Table 2**). All patients were treated successfully (ie, the otorrhea resolved within the treatment period of 10-14 days) with oral trimethoprim-sulfamethoxazole (8-10 mg/kg per day) plus a topical agent. The topical agents used were gentamicin sulfate (3 patients), polymyxin B sulfate-neomycin sulfate-hydrocortisone (2 patients), and ofloxacin (1 patient). The patient who received ofloxacin ear drops carried an MRSA isolate that was resistant to levofloxacin, which suggests that trimethoprim-sulfamethoxazole alone may have cleared the infection. Follow-up examinations were conducted after 2 to 3 weeks to document resolution of ear drainage. None of the patients needed tympanostomy tube removal or irrigation because they had new onset of drainage and responded to modified treatment.

The pathogen MRSA is increasingly found in children. Most of the reported cases of CA-MRSA in children are soft tissue and skin infections and rarely have been reported<sup>8-12</sup> as a cause of AOM. In this study, we report CA-MRSA as a causative bacteria for AOM with persistent tube or perforation otorrhea. All patients were treated successfully with trimethoprim-sulfamethoxazole oral antibiotics and with either topical gentamicin sulfate or polymyxin B sulfate-neomycin-hydrocortisone (Cortisporin; Glaxo Wellcome Inc, Research Triangle Park, NC). Trimethoprim-sulfamethoxazole has lost its role in treating AOM empirically<sup>13,14</sup> because of the resistance profile of *S pneumoniae* and *H influenzae*. However, most of the recent studies<sup>7,10,12,15-17</sup> and our sensitivity testing data show that CA-MRSA remains sensitive to trimethoprim-sulfamethoxazole.

One observation in our study is that all the patients were initially treated with ciprofloxacin or ofloxacin ear drops. Because of their safety profiles, fluoroquinolone ear drop preparations are replacing other otic antibiotics (ie, gentamicin sulfate, tobramycin, and polymyxin B sulfate-neomycin) in the treatment of otorrhea.<sup>5,18-22</sup> A recent study by Weber et al<sup>23</sup> concluded that the exposure to ciprofloxacin and levofloxacin is a significant risk factor for increasing the prevalence of MRSA. Although ciprofloxacin and other fluoroquinolones are rarely used parenterally in pediatric patients, the topical use of these agents has been increasing. Further studies are needed to determine whether the recent rise of CA-MRSA in pediatric patients is linked to the overuse of fluoroquinolones as topical agents.

Community-acquired methicillin-resistant *S aureus* infection presents an increasing challenge in treating AOM with otorrhea. We have had success with oral therapy with trimethoprim-sulfamethoxazole plus topical gentamicin sulfate or Cortisporin. We are aware of studies showing that oral rifampin could be combined with trimethoprim-sulfamethoxazole in treating MRSA infection.<sup>15,24</sup> However, to date, no studies have been performed in which this combination has been used to treat AOM with otorrhea.

This report identifies the importance of culturing otorrhea in any patient with persistent otorrhea (nonresponsive acute or chronic) because of the possibility of MRSA, a pathogen that may not come to mind and that may necessitate modifying therapy. Also, this study supports the use of trimethoprim-sulfamethoxazole with a topical antibiotic as initial, empirical therapy in suspected cases of CA-MRSA.

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**Correspondence:** Baha A. Al-Shawwa, MD, Ottumwa Regional Health Center, 931 E Pennsylvania Ave, Ottumwa, IA 52501 (balshawwa@hotmail.com).

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