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Diagnosis and Management of a Patient with Methicillin-resistant Staphylococcus aureus Conjunctivitis

Abstract

Background : Methicillin-resistant Staphylococcus aureus (MRSA) infections are becoming more common. These infections can cause various ocular conditions including conjunctivitis. Conjunctival cultures are an important tool to assist with proper diagnosis and treatment of these infections. **Case Report :** A 61-year-old African American male presented with the complaint of redness and drainage from his eyes. With the assistance of conjunctival cultures, he was diagnosed with MRSA conjunctivitis. Treatment with vancomycin ultimately led to resolution of the condition. **Conclusion :** MRSA conjunctivitis should always be considered when a conjunctivitis is not responding to empirical therapy. Eye care professionals should be aware of the susceptibility profiles of these microorganisms in order to appropriately manage patients with the proper medications.

Keywords

MRSA, bacterial conjunctivitis, vancomycin, MRSA conjunctivitis

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Introduction:

Methicillin-resistant *Staphylococcus aureus* (MRSA) infections are a common cause of bacterial conjunctivitis.¹ Originally thought of as a hospital acquired condition, MRSA is now spread through the community as well, in younger and healthier people.² As antibiotic susceptibility profiles change, ongoing surveillance studies can help clinicians appropriately and effectively treat these infections. Recognizing the characteristics of MRSA infections will help clinicians know when to culture to help treat the infection earlier, with better results.

Case Report:

A 61-year-old African American male presented to the eye clinic with a consultation request from his primary care provider for an evaluation of conjunctivitis, with the patient having a complaint of “increasing drainage and redness.” He had previously been given tobramycin 0.3% ophthalmic solution QID OU and subsequently levofloxacin 0.5% ophthalmic solution QID OU by his primary care provider, with proper compliance reported by the patient. He reported redness, mucous, and itching for a few weeks in both eyes, which had worsened despite reporting compliance with the eyedrops. All ocular medication treatment had completed one week prior to his presentation. There was no pertinent ocular history, but his medical history was positive for anemia, myocardial infarction, impaired fasting glucose, hypercholesterolemia, obesity, erectile dysfunction, coronary atherosclerosis, hypertension, prostate cancer, and history of nasal MRSA infection. He was known to be allergic to sulfa medications.

Entering corrected visual acuities were 20/20 in each eye. Pupil testing, confrontation visual fields and extraocular motility testing were all normal. There were no palpable or tender pre-auricular lymph nodes. The anterior segment evaluation with biomicroscopy revealed normal eyelids in both eyes, moderate bulbar conjunctival hyperemia in both eyes, and mild palpebral conjunctival papillae in both eyes. There was significant mucopurulent discharge, and trace amounts of superficial punctate staining noted in both eyes. Intraocular pressures were 15 mm Hg OD and 16 mm Hg OS by Goldmann applanation. The evaluation of the fundus was normal in both eyes. **Table 1** lists differential diagnoses.

Given the history of systemic MRSA infection, along with the absence of palpable preauricular lymph nodes and corneal involvement, the bilateral appearance of signs, and the presence of purulent discharge and conjunctival papillae, the diagnosis was presumed to be MRSA conjunctivitis. Conjunctival culture swabs were taken on each eye using the BBL™ CultureSwab™ Collection and Transport System (Becton Dickinson, Franklin Lakes, NJ) while the patient had been off drops for about a week, and culture and susceptibility tests were ordered. While waiting for these laboratory results to return, the patient was prescribed polymyxin B/bacitracin ophthalmic ointment twice daily in both eyes,

polymyxin B/trimethoprim ophthalmic solution four times daily in both eyes, and generic preservative free artificial tears as needed. The patient was instructed to return for re-evaluation in 3 days or sooner if the condition worsened.

Conjunctival culture results were available at the 3-day follow-up and were positive for methicillin-resistant *Staphylococcus aureus*. The susceptibility results revealed resistance to cephalothin, ciprofloxacin, clindamycin, erythromycin, levofloxacin, penicillinase resistant penicillin, and penicillin. The pathogen was shown to be susceptible to rifampin, tetracycline, trimethoprim-sulfamethoxazole, and vancomycin. The patient reported minimal relief at this time, and all ocular findings were consistent with the first visit. Because the patient was diagnosed with MRSA conjunctivitis, he was instructed to continue polymyxin/bacitracin ointment twice daily in both eyes, and prescribed polymyxin B/trimethoprim and vancomycin ophthalmic solution 50 mg/ml prepared onsite at our pharmacy, alternating every 2 hours while awake in both eyes, and to use preservative free artificial tears as needed. The patient was educated on drop spacing and instructed to return to the clinic 1 week later for follow-up, or sooner if the condition worsened.

The patient returned for follow-up one week later, reporting that his eye condition had subjectively improved significantly since the previous visit. He reported good compliance with the current ocular medications. Visual acuities were stable at 20/20 OD and OS with his current eyeglasses. Entrance testing remained normal. Anterior segment evaluation with a slit lamp revealed normal eyelids in both eyes, trace conjunctival hyperemia in both eyes, and trace palpebral conjunctival papillae in both eyes. There was no longer any mucopurulent discharge in either eye. The anterior chambers were deep and quiet in both eyes. The corneas were clear with no staining in either eye. Intraocular pressures were 13 mm Hg in each eye by Goldmann applanation. As the condition was improving, the patient was instructed to discontinue polymyxin B/trimethoprim and polymyxin/bacitracin ointment and continue vancomycin QID until the bottle was finished. The patient was instructed to return 1 week later for follow-up, at which time he reported complete resolution of the ocular condition. He had finished the vancomycin therapy the day before. All ocular findings were normal at this last visit.

Discussion:

Staphylococcus aureus is a catalase-negative gram-positive coccus, typically isolated on blood agar.³ Resistance to methicillin by *S. aureus* strains became evident not long after its introduction in 1959.⁴ While methicillin use has diminished over the years, the term “MRSA” now refers to any strain of *S. aureus* that is resistant to β -lactam antibiotics.⁵ MRSA is endemic in many hospital settings,⁶ and about 25-35% of otherwise healthy individuals may be carriers of *S. aureus* worldwide.⁷ Risk factors for MRSA infection in the eye include a history of healthcare exposure, ocular surface disease, immunodeficiency, and post-operative refractive and cataract surgery cases.^{4,8} MRSA is a common cause of conjunctivitis; MRSA caused 3.7% of *S. aureus* conjunctivitis infections in 2000

and increased to 13.16% of *S. aureus* conjunctivitis infections in 2009.¹ Recent data shows that there may be a decrease in the prevalence MRSA infections after a peak from 2005 to 2015.⁹

MRSA was originally thought to be a hospital acquired infection, however more recently, community acquired MRSA infections have emerged.¹⁰ Hospital acquired MRSA (HA-MRSA) is defined as infection after 48 hours of admission to the hospital, or with a history of hospitalization within 1 year of infection, or in a patient with a permanent medical device or catheter. All other MRSA infections can be considered to be community acquired MRSA (CA-MRSA).^{2,4} These two types of MRSA are genetically different, with CA-MRSA strains reportedly slowly replacing HA-MRSA strains in hospitals. CA-MRSA also tends to occur in younger patients, likely due to the mode of transmission.² The evolution of strains of MRSA illustrate the importance of continuously updating management and treatment plans based on current data.

MRSA infections of the eye have been reported to cause corneal ulcers, conjunctivitis, dacryocystitis, scleritis, endophthalmitis and, rarely, cerebral abscess.¹¹ Signs and symptoms of bacterial conjunctivitis include purulent white-yellow discharge, papillae, chemosis, redness, foreign body sensation and discharge.¹² If the findings are bilateral with a purulent discharge, it is most likely to be bacterial.¹³ Patient history is important in determining the differential diagnosis, including sexual and social history, history of medication use and contact lens wear.¹⁴ Diagnosis of bacterial conjunctivitis is often made based on symptoms and clinical signs alone, however if the conjunctivitis is severe, recurrent, or does not respond to topical antibiotic therapy, then culture and sensitivity testing on blood and chocolate agars are indicated.^{12,14}

Recently, studies have been conducted to monitor the antibiotic resistance and susceptibility of ocular microbial infections. The Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) study showed that 39% of *S. aureus* isolates were resistant to methicillin or oxacillin, and most of the MRSA isolates were also resistant to azithromycin and ciprofloxacin. Almost two-thirds of isolates were susceptible to clindamycin, and close to half of the isolates were susceptible to tobramycin. All isolates tested in the ARMOR study were found to be susceptible to vancomycin. Notably, age greater than 80 years was identified as a risk factor for MRSA.¹⁵ After 8 years, an update to the ARMOR results revealed that antibiotic resistance rates have not increased, and some may have actually decreased. Chloramphenicol was added to the panel of medications tested for *S. aureus* in the ongoing study, showing a high rate of MRSA susceptibility to chloramphenicol. All isolates were susceptible to vancomycin.¹⁶ A 2018 update to the ARMOR study also showed geographic variations in resistant *S. Aureus* strains, with greater resistance from some organisms collected in the South and Midwest regions of the United States.¹⁷ A recently published review showed that ARMOR findings were consistent with local and regional data in other studies as well.¹⁸ Chloramphenicol was found to be efficacious against MRSA in another recent study,²⁰ however chloramphenicol is not

commonly used in the United States due to possible side effects, and is also not available at our pharmacy.²¹ Another large study, the Ocular Tracking Resistance in U.S. Today (TRUST) study, was developed to evaluate the susceptibility of *S. aureus*, *S. pneumoniae*, and *H. influenzae* isolates to a panel of antimicrobial agents.²² These are the three most common pathogens causing bacterial conjunctivitis.²³ Trimethoprim was the only medication on the panel that was highly effective against MRSA, while azithromycin, penicillin, polymyxin B, tobramycin, and all fluoroquinolones that were tested were not found to be efficacious against MRSA. Vancomycin was not included in the panel of antibiotics tested.²² This is consistent with other studies that have shown that while many providers consider using fluoroquinolones for treatment of bacterial conjunctivitis, they are not very effective in the treatment of MRSA infections of the eye.¹⁹ Trimethoprim is the only topical antibiotic available on our pharmacy's formulary that showed significant effectivity against MRSA in this study, which is why polymyxin B/trimethoprim was chosen in this case. Vancomycin was only available to our patient after receiving culture results and receiving pharmacy approval.

Vancomycin remains the treatment of choice for most MRSA infections, with a highly effective susceptibility profile.¹⁵ Vancomycin can be formulated in a compounding pharmacy: fortified vancomycin of 50 mg/mL is formulated by adding 500 mg of vancomycin dry powder to enough sterile water to form 10 mL of solution. Dosages typically vary from 25 mg/mL to 50 mg/mL, depending on the severity of the infection.¹² In this case, the higher dosage was selected because the condition was bilateral and a copious amount of discharge was noted. Although rare, the first strain of vancomycin-resistant *S. aureus* (VRSA) was found in 2002, however VRSA has not been reported in the eye to date. Other options for treating MRSA which may have better coverage for vancomycin-resistant strains include linezolid, tigecycline, and daptomycin.²⁴

The patient in this case had conjunctival cultures positive for MRSA that were resistant to many of the antibiotics tested on the susceptibility panel, except for tetracycline, trimethoprim-sulfamethoxazole, and vancomycin. This is consistent with the literature of most common susceptibility profiles of MRSA ocular isolates. Topical vancomycin was added after receiving susceptibility panel results, as clinical signs were not significantly improving with polymyxin B/trimethoprim. This proved effective, as the condition resolved quickly with the addition of this treatment. Due to the severe nature of this bacterial infection, along with a history of MRSA infection, it was important to obtain a culture as soon as possible so that appropriate therapy could be initiated. Adding an oral antibiotic was considered, however tetracycline and rifampin were not in stock at the pharmacy, and the patient was allergic to sulfa medications. Since the clinical findings were limited to the conjunctiva, it was decided to treat the condition topically and reconsider oral or intravenous therapy if the condition worsened or did not resolve.

Conclusion:

New antimicrobial resistance profiles will continue to emerge over time. Although ocular resistance has not changed in recent years, it is important to review current literature so that evidence based clinical decisions are implemented. Culture and susceptibility testing remains important in cases that are severe, recurrent, or non-responsive to empirical therapy; however empirical treatment can often be done based on the information from surveillance studies. This information is also important to guide treatment while waiting for culture and susceptibility results to become available. Proper hand hygiene and disinfection of equipment is also important. Consultations with primary care providers as well as infectious disease providers may be indicated when MRSA is isolated, particularly in non-resolving cases or new diagnoses of MRSA.

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Table 1: Differential diagnoses and clinical signs found with each differential diagnosis.

* clinical signs present in this case

Differential Diagnosis	Clinical signs
Allergic conjunctivitis	<ul style="list-style-type: none"> • Watery • Itching* • History of allergies • Eyelid edema • Conjunctival papillae (without palpable preauricular lymph node)*
Viral conjunctivitis (including epidemic keratoconjunctivitis)	<ul style="list-style-type: none"> • Itching* • Burning • Palpebral conjunctival follicles • Tender and/or palpable preauricular lymph nodes • Watery discharge • Eyelid edema • Subepithelial infiltrates
Herpes simplex conjunctivitis	<ul style="list-style-type: none"> • Unilateral signs • Palpable preauricular lymph node • Conjunctival follicles • Herpetic skin vesicles • Corneal dendrite
Vernal conjunctivitis	<ul style="list-style-type: none"> • Itching* • Thick discharge* • Seasonal recurrence • “Shield” ulcer • Large conjunctival papillae superiorly • Young patient age
Bacterial conjunctivitis (including MRSA and gonococcal conjunctivitis)	<ul style="list-style-type: none"> • Purulent discharge* • Conjunctival papillae* • Chemosis • No palpable preauricular lymph node (except in cases of gonococcal conjunctivitis) *