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Community Acquired MRSA from Head and Neck Space Infections

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ABSTRACT

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Community acquired Methicillin-resistant *Staphylococcus aureus* (CA-MRSA) has been recognised as one of the important pathogen in head and neck infections. These infections include tonsillitis, thyroiditis, sinusitis, periorbital cellulitis, otitis, retropharyngeal abscess, cervical lymphadenitis and wounds of the neck. This review illustrates the growing prevalence of CA-MRSA, and the current therapeutic approaches to head and neck infections caused by this bacterium. Treatment of head and neck infections associated with CA-MRSA includes drainage and debridement, as well as administration of local and systemic antibiotics that provide potential coverage against these organisms and against polymicrobial infection (aerobic and anaerobic) that may be present in such wounds.

Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) has become a worldwide problem, although its prevalence varies considerably among countries. The epidemiology of MRSA is now changing; infections are no longer confined to the hospital setting, but also appear in healthy community-dwelling individuals with no established risk factors for the acquisition of MRSA. Currently, molecular epidemiological definitions, based on staphylococcal cassette chromosome mec (SCCmec) typing and phylogenetic analyses of the MRSA isolates, are considered the most reliable means to differentiate between

hospital-acquired MRSA (HA-MRSA) and CA-MRSA. Although CA-MRSA infections are usually mild, they may also be severe, and can result in hospitalisation and even death.

The prevalence of infection and colonisation with CA-MRSA is increasing in all infections, including those of the head and neck. Within head and neck infections, the highest rate of CA-MRSA infection occurs in otological infections, followed by sinusal, oropharynx and neck infections.² This review summarises and illustrates the growing prevalence of CA-MRSA. It also summarises current therapeutic approaches to CA-MRSA head and neck infections, which may include otitis, sinusitis,

periorbital cellulitis, thyroiditis, tonsillitis, cervical lymphadenitis, retropharyngeal abscess, and neck abscesses and wounds¹.

Specific head and neck infections

Ear infections

While MRSA remained mainly nosocomial in nature through the 1980's, community-acquired MRSA (CA-MRSA) emerged in the 1990's and is increasingly become common in soft tissue and otolaryngologic infections since.

In 2002, Hwang *et al.*, (3) reported >8.5% increase in CA-MRSA incidence in ear infections in Taiwan. Similarly, in 2007 a group from Hawaii noted a rapid increase in CA-MRSA head and neck infections from 21% to 64% over a five-year period.

S. aureus is considered to be the second most common pathogen in acute bacterial otitis externa, with case series identifying *S. aureus* in up to 40% of cases. Studies from Pakistan, New Zealand and Korea found rates of *S. aureus* AOE above 30%, while the most recent study in the U.S. reported rates of 7.8%. This difference could be due to changing population demographics and/or changes in the nature of strains of *S. aureus* occurring in the community. Local modifications in the external ear microbiota may also result from the selective pressure imposed by empirical antibiotic treatment. As the likely causative agent of 1 in 3 AOE cases, *S. aureus* should be considered into antimicrobial coverage decisions on initiation of empiric treatment.³

Despite the rise of MRSA soft tissue infections, few studies have examined the current clinical features and incidence patterns of MRSA in AOE. In the UK, an English 2007 study and an Irish 2001 study

have reported rates of 0.7% and 6%, respectively.^{4,5} The most recently published work on uncomplicated AOE, a 2012 study from Singapore, reported a MRSA AOE rate of 4.2%.⁶ Studies in South Africa, Pakistan and Korea found no MRSA in AOE cultures, consistent with the low levels of MRSA colonization of their populations.^{7,8}

Current guidelines for treatment of otitis external focus on *Pseudomonas* spp. and *S. aureus* because of their high incidence in AOE. Generally, empirical therapy with topical antibiotics targeting non-resistant strains of these bacteria is recommended (9). A 2014 update of the clinical practice guidelines (American Academy of Otolaryngology-Head and Neck Surgery [AAO-HNS]) identifies topical fluoroquinolones, aminoglycosides, and/or polymyxin B for empiric treatment. While most studies have found no significant difference in treatment outcomes with antiseptic or different types of antibiotic drops treating AOE, two meta analyses by Rosenfeld *et al*¹⁰ and Mo'sgen *et al.*,¹¹ suggest that quinolone drops resulted in higher rates of bacteriologic and clinical cure. At present, empiric treatment with ototopical antibiotic drops is recommended, unless there is extension of infection outside the ear canal, or the patient has concerning host factors such as immunocompromise or diabetes. In such cases, the inclusion of systemic antibiotics is appropriate.³

In the USA in 1999, Santos *et al.*, described three children with purulent otorrhea caused by community-acquired MRSA. All required intravenous antibiotics therapy.²

In Taiwan, Hwang *et al.*, (2) noted that *S. aureus*, including MRSA, had become more common than *Pseudomonas aeruginosa* in acute otitis externa, granular myringitis and chronic otitis media. They studied 161

patients with otorrhoea and recovered 177 isolates: 77 (43.5 %) of *S aureus* and 29 (18%) of *pseudomonas* species. The prevalence of community-acquired MRSA infections in discharging ears was 14% (22/161), and these isolates were susceptible to vancomycin, teicoplanin, minocycline and fusidic acid.

in South Korea, Kim *et al.*, in 2005 recovered 3251 *S aureus* isolates, 1900 (58 %) of which were MRSA. Community-acquired infection accounted for 112 (5.9%) of these MRSA infections; of these, 27 were pathogens and 33 colonisers. Most community-acquired MRSA patients had skin, soft tissue or acute ear infections. A new strain of community-acquired MRSA, ST72-SCCmec type IVa without the Pantone-Valentine leukocidin gene, was the commonest type identified.²

Sinusitis

Rutar *et al.*,¹² described a patient with cavernous sinus thrombosis, bilateral orbital cellulitis, pan-sinusitis and permanent, bilateral blindness due to community-acquired MRSA infection.

Huang and Hung¹³ isolated CA-MRSA from 16 of 601 patients (2.7%) with acute sinusitis. Multiple pathogens were more frequently found in children with MRSA, and eight of nine children with multiple pathogens had previously received antibiotics. Five of seven adults with MRSA had undergone previous nasal procedures. All patients' symptoms resolved following oral antibiotics guided by culture sensitivities.

Several authors have described their experience in using oral and topical antibiotics to treat MRSA sinusitis. Gerencer¹⁴ studied 28 patients who tested positive for CA-MRSA sinusitis, for a period of 12 months. Twelve infectious episodes of MRSA

were treated with oral antibiotics alone and 16 were treated with a combination of oral and topical antibiotics. It was found that oral antibiotics alone (12 patients) or a combination of oral and topical antibiotics (16 patients) were equally effective in treating community-acquired MRSA sinusitis.

Tabaee *et al.*,¹⁵ showed that intravenous antibiotics administered on an out-patient basis were effective in treating CA-MRSA sinusitis. Five of the six patients studied (83.3 per cent) had negative MRSA cultures after such therapy.

Periorbital cellulitis

CA-MRSA has been associated with abscess formation, increased severity of disease, and treatment failure. Much of this virulence has been attributed to the production of Pantone-Valentine leukocidin, a leukocyte-lysing cytotoxin that has been increasingly found in some MRSA strains.^{16,17}

A five-year (2001-2006) analysis of a national microbiologic database discovered 21,009 pediatric *S. aureus* head and neck infections, of which 21.6% were MRSA in etiology.¹⁰ This same study also found that nearly 60% of the MRSA infections were probably attributable to CA-MRSA.¹⁸

Huang *et al.*, described a 6 yr old child with bilateral, MRSA-positive, sub-periosteal abscesses and multiple brain abscesses complicating acute sinusitis, who was successfully treated with vancomycin and rifampicin.¹⁹

McKinley *et al.*,²⁰ studied paediatric orbital cellulitis associated with sinusitis. Fifteen patients required only medical management, whereas 23 needed medical and surgical intervention. Methicillin resistant *S aureus* represented 73% of *S aureus* isolates.

Cervical lymphadenitis

Guss and Kazahaya²¹ studied antibiotic-resistant *S. aureus* in community-acquired pediatric neck abscesses on 62 children with suppurating cervical lymph glands. The commonest infective organism was *S. aureus* (63% of 49 positive cultures). Among the *S. aureus* isolates, 27% were MRSA. All MRSA strains were susceptible to clindamycin and cotrimoxazole; 63% were susceptible to ciprofloxacin and 25% to erythromycin. All MRSA isolates were identified during the latter half of the study period (2003–2006); none were identified prior to 2003.

Tonsillitis

The rate of recovery of MRSA from tonsils removed from 44 children infected with recurrent group A b-haemolytic streptococci, was investigated by Brook and Foote¹⁶, between 1998 and 2003. Methicillin resistant *S. aureus* was isolated from 16 % of the tonsils. Of the 26 *S. aureus* isolates recovered from the tonsillar cores, seven (27 %) were MRSA, and of the 16 isolates isolated from the tonsillar surface, two (12.5 %) were MRSA. Five of the seven isolates from tonsillar core and all two of the surface isolates were also b-lactamase producers. All MRSA isolates were resistant to penicillin, oxacillin and erythromycin, and were susceptible to clindamycin, cotrimoxazole, and vancomycin. The emergence of MRSA in the tonsils of children with recurrent group A b-haemolytic streptococcal tonsillitis may contribute to the difficulty in eradicating such streptococci with penicillins, as most of the MRSA isolated in this study were also beta-lactamase producers. Beta-lactamase-producing MRSA can survive treatment with b-lactams, and can also shield group A b-haemolytic streptococci from penicillins by producing b-lactamase.²² Sugita²³ recovered

MRSA in one hospitalised and 14 out-patient individuals. Of these isolates, five were from tonsillitis cases, four from patients with cancer and two from chronic otitis media cases.

Abscesses and wound infections of the head and neck

Ossowski *et al.*,²⁴ did the comparison on the proportion of community-acquired MRSA infections in paediatric head and neck abscesses in 1999–2001 versus 2002–2004. In the first period, 6 (40%) of 15 abscesses yielded *S. aureus*, compared with 17 (58.6 %) of 29 abscesses in the second period. The proportion of abscesses yielding MRSA increased from 0% (zero of six) in the first period to 64.7% (11/17) in the second (*p*, 0.01).

Bothwell *et al.*,²⁵ investigated 36 community-acquired MRSA isolates from head and neck infections, between 2003 and 2004. The MRSA infection rate increased from 21% to 64% over that period. The distribution of community-acquired MRSA infections was: Twelve from face, 7 from ear, 9 from nose, 6 from neck and 2 from other areas. All community-acquired MRSA isolates were resistant to penicillin and cefazolin, but most were sensitive to clindamycin.

Inman *et al.*,²⁶ studied 288 paediatric neck infections between 1999 and 2007. *Staphylococcus aureus* was isolated from 48% of abscesses out of which 29% of these isolates were community-acquired MRSA. Inman *et al.*, could find no clinical risk factors which differentiated those patients at higher risk of MRSA.

Johnigan *et al.*,²⁷ identified 7 patients with CA-MRSA in 4 months. The most common cause was superficial abscesses (3patients

[43%]) and suppurative lymphadenitis (3 patients [43%]). An erythromycin resistant and clindamycin sensitive (inducible clindamycin resistance) case was found in 6 (86%) out of seven cases.

Lemierre's syndrome

Three cases of Lemierre's syndrome associated with community-acquired MRSA, have been reported. Out of which one patient had orbital cellulitis, and another had splenic vein thrombosis.²⁸

Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections among young people without healthcare-associated risk factors have emerged during the past decade. Reported prevalence rates of CA-MRSA vary widely among studies. This could be largely due to the different definitions employed and different settings in which the studies have been performed. Although the majority of CA-MRSA infections are skin and soft tissue infections, severe life-threatening cases have been reported. CA-MRSA infections have mostly been associated with staphylococcal strains bearing the staphylococcal cassette chromosome mec type IV element and Panton-Valentine leukocidin genes. These strains are more frequently susceptible to a variety of non-beta-lactam antibiotics. Continued emergence of MRSA in the community is a public health problem, and therefore warrants prompt and vigilant diagnosis and management of suspected and confirmed staphylococcal infections.²⁹ The above data illustrate a significant increase in the incidence of MRSA in head and neck infections. This is in concordance with an overall increased incidence of MRSA in various other respiratory and non-respiratory infections.² Treatment of MRSA head and neck infections is challenging. Drainage and debridement are of major importance and

should be done whenever possible. This includes drainage of abscesses and of infected sinuses or ears.

Although topical therapy of some infections may be possible, it is important to administer systemic antimicrobials that cover these organisms as well as other potential aerobic and anaerobic pathogens that may be present in polymicrobial infections. Although vancomycin represents the 'gold standard' of MRSA therapy, reports of increasing in vitro resistance and of clinical failures⁵⁵ underscore the need for alternative therapies. Older agents with favourable activity, available in both oral and intravenous forms, include trimethoprim plus sulphamethoxazole and clindamycin. At present, there is only limited clinical data to support their routine use as initial therapy of MRSA infections. However, these and other agents are being re-explored as potential treatments for community-acquired MRSA. Newer treatment options include linezolid, quinupristin-dalfopristin, daptomycin and tigecycline.³¹ Moreover, unlike HA-MRSA, most CA-MRSA isolates are susceptible to several antimicrobial agents. In cases of CA-MRSA infection not requiring hospitalization but for which antibiotics are deemed necessary, oral antibiotics such as TMP-SMX, doxycycline, and clindamycin may be appropriate (32).

Prevention and control

CA-MRSA outbreaks have been controlled with proper wound care and containment, enhanced hygiene, and regular cleaning of frequently touched environmental surfaces. Persons with active infections should refrain from certain activities such as contact sports and day care if their wound drainage cannot be contained. Local health authorities should be informed of suspected outbreaks, and additional related cases should also receive

adequate treatment. Patient education regarding the nature of the disease, its spread, and the possibility of recurrence is important. Providing antibiotic prophylaxis to family members is currently not recommended, and administering decolonization regimens to whole families has not been studied, but may need to be used in specific circumstances.³³

In conclusion, CA-MRSA from head and neck space region has emerged as an important infection in the community. The rate of CA-MRSA infection is rapidly increasing and has become a threat to the community and to persons with unknown risk factors. Appropriate adjustment of treatment regimens and enforcement of better hygiene practices should prevent further evolution and spread of these highly adapted infectious agents.

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