Community-Associated Methicillin-Resistant *Staphylococcus aureus* Infections in Israel*

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ABSTRACT: **Background:** Community-associated methicillin-resistant *Staphylococcus aureus* infections are increasingly being documented worldwide. In Israel, however, CA-MRSA infections have not yet been reported, so awareness among physicians may be low.

Objective: To alert physicians to the possibility of CA-MRSA infection, which necessitates a distinct therapeutic approach.

Methods: We present three children with soft tissue infections caused by CA-MRSA who were treated in our medical center from January to March 2009.

Results: In all three cases CA-MRSA was identified as the causative pathogen after surgical or spontaneous drainage. On susceptibility testing, the organisms were resistant to beta-lactam antibiotics but susceptible to clindamycin, rifampicin and trimethoprim-sulfamethoxazole.

Conclusions: Physicians should maintain an index of suspicion for CA-MRSA infections. The antibiotic-resistance profile of *S. aureus* should be watched carefully, and in particular, cultures should be obtained whenever soft tissue infections fail to respond to conventional treatment.

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KEY WORDS: *Staphylococcus aureus*, soft tissue infection, antibiotic resistance, vancomycin, clindamycin

Methicillin-resistant *Staphylococcus aureus* is a well-established nosocomially acquired pathogen [1]. The more recent community-associated MRSA infection, first reported in the United States in 1981 [2], has shown an alarming worldwide spread. Its high virulence and complication rates, together with the wide spread, have led to changes in the therapeutic approach to presumed staphylococcal infections acquired in the community [3].

We are not aware of previous published reports of CA-MRSA infections in Israel. However, nasal carriage of MRSA in the community [4] and MRSA bacteremia in a neonatal intensive care unit with antibiotic susceptibility pattern similar to CA-MRSA have been described in Israel [5]. In this work, we present three children with soft tissue infections caused by CA-MRSA. Our aim was to prompt physicians to be more alert to the possibility of infection with CA-MRSA, which has a distinct antibiotic susceptibility profile and necessitates a distinct approach regarding empiric therapy.

PATIENT DESCRIPTIONS

Three patients with MRSA infections acquired in the community were treated in our medical center from January to March 2009 [Table 1]. All presented with soft tissue infections and were initially treated empirically with a first-generation cephalosporin, which is inappropriate for CA-MRSA. CA-MRSA was identified as the causative pathogen only after surgical or spontaneous drainage. Laboratory analysis showed that the organisms were resistant to beta-lactam agents but susceptible to clindamycin, rifampicin, and trimethoprim-sulfamethoxazole.

PATIENT 1

A 2 year old girl presented to the emergency department with fever and left inguinal swelling and redness. Physical examination revealed an inguinal abscess with spontaneous excretion of pus. The white blood cell count was 16,490 x 10^3/μl with 75.1% neutrophils, and the C-reactive protein level was 7.4 mg/dl. After obtaining pus for culture, we admitted the patient to the pediatric ward where she was treated intravenously with a first-generation cephalosporin (cefazolin). The fever resolved but the local findings persisted. The treatment was therefore empirically changed to intravenous amoxicillin-clavulanate and clindamycin. On the third day of hospitalization we received the laboratory report of a positive culture for MRSA. The child was later transferred to the surgical ward to drain the abscess; she was later discharged and prescribed oral trimethoprim-sulfamethoxazole for one week.

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CA-MRSA = community-associated methicillin-resistant *Staphylococcus aureus*

Table 1. Background, clinical and laboratory characteristics of three patients with CA-MRSA infection

Patient #	Age	Gender	Site of infection	Initial treatment	Surgical drainage	Time to diagnosis of MRSA	Antibiotic susceptibilities	Outcome
1	2 yrs 3 mos	F	Left groin	Cefazolin	Yes	3 days after admission	Clindamycin Rifampicin Trimethoprim-sulfamethoxazole Vancomycin Chloramphenicol Gentamicin Minocycline	Recovery
2	4 yrs 2 mos	M	Left temporal region	Cefazolin	Yes	13 days after admission		Recovery
3	14 yrs 5 mos	M	Left buccal region	Cephalexin	Yes	5 days after presentation		Recovery

PATIENT 2

A 4 year old boy presented to the emergency department with fever, left facial swelling and trismus of 3 days duration. Two weeks previously he had presented at the emergency department because of pneumonia and was discharged with oral amoxicillin. Physical examination at the latest admission revealed left facial swelling and tenderness and a left reactive submandibular lymph node. The WBC count was 16,070 x 10^3/µl with 38.6% neutrophils, and the CRP level was 1.29 mg/dl. The child was admitted to the pediatric ward and treated with intravenous cefazolin. Minor systemic and local improvements were noted, but significant swelling and tenderness remained. Magnetic resonance imaging was subsequently performed, demonstrating an abscess within the temporalis muscle, probably due to an infected congenital cyst. The abscess was surgically drained and culture of the aspirate yielded MRSA. After susceptibility testing, the antibiotic treatment was changed to IV vancomycin and oral trimethoprim-sulfamethoxazole. The clinical signs and symptoms resolved, and the child was discharged with a recommendation for ambulatory follow-up, including MRI.

PATIENT 3

A 14 year old boy presented to the emergency department with a 1 day history of fever and left facial swelling following a local acne lesion. He was discharged with an oral first-generation cephalosporin (cephalexin). Two days later he returned because the fever persisted and the swelling worsened. Physical examination revealed local warmth, redness, swelling and tenderness of the left cheek. The WBC count was 14,820 x 10^3/µl with 64% neutrophils and the CRP level was 9.12 mg/dl. The patient was admitted to the pediatric ward and treated intravenously with a first-generation cephalosporin (cefazolin). Pus was drained from the swelling and sent for culture. The patient recovered and was discharged home with instructions for another 5 days treatment with cephalexin. The culture grew MRSA, but since the patient had recovered there was no clinical need for further antimicrobial treatment.

WBC = white blood cell
CRP = C-reactive protein

DISCUSSION

Soon after the introduction of penicillin in 1941, resistant strains of *S. aureus* emerged, first in hospital settings and then disseminated in the community [6]. Today, most *S. aureus* strains are resistant to penicillin. *S. aureus* resistance to other penicillins and cephalosporins has been undergoing a similar process as more and more strains have acquired the *mecA* gene that encodes penicillin-binding protein 2A [7]. Initially, for a relatively long period, MRSA infections were limited to hospitals, mainly intensive care units [8]. In recent years, however, they have been increasingly reported in the community in many locations worldwide [9]. In certain areas, the majority of community-associated *S. aureus* infections are now methicillin resistant [10]. Infections caused by CA-MRSA are severe and often complicated and have the potential for a high mortality rate [11,12].

The optimal antimicrobial management of the rapidly emerging CA-MRCA has not been completely elucidated [11-13]. It is obvious that appropriate surgical drainage is of prime importance and in mild cases may be sufficient, as our third case exemplified. Most isolates of CA-MRSA are susceptible to clindamycin, in contrast to nosocomial MRSA. Clindamycin can therefore be used, although clindamycin-resistant CA-MRSA was recently reported [14]. CA-MRSA is usually susceptible to trimethoprim-sulfamethoxazole, which can be used in mild cases, although it has not been approved by the U.S. Food and Drug Administration to treat staphylococcal infections [15]. These strains are always susceptible to vancomycin.

Practice guidelines for the diagnosis and management of skin and soft tissue infections still recommend the empiric use of semisynthetic penicillin, first- or second-generation cephalosporins, macrolides, or trimethoprim-sulfamethoxazole, with reevaluation within 48 hours pending culture results [13]. Our first patient received amoxicillin-clavulanate and clindamycin, to which the isolated CA-MRSA was susceptible, and was discharged on oral trimethoprim-sulfamethoxazole. In the second patient, vancomycin was started as we had been notified ahead on the growth of MRSA.

Several studies have attempted to elucidate the risk of

CA-MRSA in Israel. Schlesinger et al. [16], in an investigation of the prevalence of MRSA carriage in children in Jerusalem, found that MRSA colonized the nares of 0.6% of healthy children, whereas among chronically institutionalized children the carrier rate was 7.6%. In 2002, an outbreak of MRSA infection was reported in a chronic care institution for mentally retarded adults in Israel [17].

To the best of our knowledge, the present work is the first published description of MRSA infection acquired in the community in Israel, although nasal carriage of MRSA in the community [4,16] and MRSA bacteremia in neonatal intensive care units with antibiotic susceptibility pattern similar to CA-MRSA were described previously in Israel [5]. It is noteworthy that patient 2 had been treated with amoxicillin in the emergency department 2 weeks before he presented with the abscess, probably an infected cyst, caused by MRSA. Given the course of the infection, and considering that he was not treated with anti-staphylococcal penicillin or a cephalosporin, we assumed the soft tissue MRSA infection was acquired in the community. Patient 3 recovered from the infection after surgical drainage without the need for an additional antimicrobial agent, highlighting the major role of surgical drainage in CA-MRSA infections. The antimicrobial susceptibility profile of the CA-MRSA strains was similar in all three cases and was typical of CA-MRSA as opposed to nosocomial MRSA. Molecular studies to look for clonality of these three strains were not performed.

In conclusion, physicians should be alert to the possibility of infection caused by CA-MRSA. The antibiotic susceptibility pattern of staphylococcal infections should be monitored carefully and cultures should be obtained, especially when soft tissue infections fail to respond to conventional antimicrobial treatment.

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"Perfectionism is the enemy of creation, as extreme self-solitude is the enemy of well-being"

John Updike (1932-2009), American novelist, poet, short story writer, art critic, and literary critic. A Pulitzer Prize winner, he is considered one of the great American writers of his time

"I believe in evidence. I believe in observation, measurement, and reasoning, confirmed by independent observers. I'll believe anything, no matter how wild and ridiculous, if there is evidence for it. The wilder and more ridiculous something is, however, the firmer and more solid the evidence will have to be"

Isaac Asimov (1920-1992), Soviet-born American author and professor of biochemistry at Boston University, best known for his works of science fiction and for his popular science books