Severe Sepsis from Community-Associated Methicillin-Resistant *Staphylococcus aureus* Possibly due to Implantable Cardioverter Defibrillator

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First described in the United States in the mid-1990s [1], community-associated methicillin-resistant *Staphylococcus aureus* has now emerged all over the world [2]. CA-MRSA has distinctly different microbiological, epidemiological and molecular characteristics from those of nosocomial MRSA. CA-MRSA usually occurs in young healthy individuals in the community who have no risk factors typically linked with acquisition of nosocomial MRSA. CA-MRSA is primarily associated with skin and soft tissue infections (abscesses, cellulitis and furunculosis); however, there have been severe cases of CA-MRSA infection associated with septic shock, bacteremia, osteomyelitis, necrotizing pneumonia and necrotizing fasciitis [2].

MRSA (or oxacillin-resistant *Staphylococcus aureus*) is a relatively rare pathogen involved in cardiovascular implantable electronic device infections. It is responsible for 4% of the device infections, while 25% of infections are caused by oxacillin-sensitive *Staphylococcus aureus*, and 42% are due to coagulase-negative staphylococci, the most common pathogens [3].

We report yet another clinical presentation due to CA-MRSA, namely ICD-related sepsis. A thorough search in PubMed and Google did not disclose a similar publication in the literature.

PATIENT DESCRIPTION

A 55 year old man was admitted to the hospital because of shortness of breath and fever of one week duration and was unresponsive to amoxacillin-clavulanate that was prescribed for presumed pneumonia. His medical history included ischemic cardiomyopathy, hypertension, congestive heart failure (ejection fraction 30%), insulin-dependent diabetes mellitus, implantation of cardioverter defibrillator 8 months prior to his admission, orthopedic surgery 2 years earlier, and obesity. Physical examination disclosed a tachypneic obese man. His body temperature was 39.0°C, respiratory rate 24/min, blood pressure 120/65 mm Hg, pulse rate 84/min, and pulse oximetry on room air indicated an oxygen saturation of 88%. On auscultation of the lungs rales were audible at the bases; no heart murmurs were noted. There was no skin rash, no evidence of skin infection and no signs of inflammation at the generator-pocket site. Laboratory tests on admission produced the following results: White blood cell count 15.8 x 10^3/µl, hemoglobin 13.6 g/dl, and platelet count 29.0 x 10^3/µl; blood glucose 234 mg/dl, creatinine 1.34 mg/dl, C-reactive protein 17.63 mg/dl, and minimally perturbated liver enzymes. Chest radiograph showed an enlarged heart silhouette and no lung infiltrates; chest computed tomography showed diffuse parenchimal infiltrates involving both lungs.

Due to pending respiratory failure the patient was transferred to the intensive care unit on the same day, where he was tracheally intubated. After blood samples were obtained for culture, empiric intravenous treatment with ertapenem 1.0 g/day and vancomycin 1.0 g/12 hours was initiated. *Staphylococcus aureus*, resistant to penicillin and oxacillin, but susceptible to all other antistaphylococcal agents tested including clindamycin, grew in several blood cultures. The antimicrobial susceptibility profile was determined with an automated system (Vitek 2, bioMérieux, France). Minimal inhibitory concentration of vancomycin was 0.7 µg/ml. Ertapenem was discontinued, and vancomycin dosage was guided by blood levels.

After an initial impression of improvement in his clinical condition, the patient deteriorated on the fifth hospital day, when vasopressor support was initiated. Concomitantly, acute renal failure developed with complete anuria. Blood culture continued to grow the same MRSA strain, creatinine was now 6.8 mg/dl, platelet count dropped to 20.0 x 10^3/µl, C-reactive protein increased to 19.59 mg/dl. Continuous renal replacement

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

ICD = implantable cardioverter defibrillator

therapy was initiated. Trans-esophageal echocardiogram did not reveal valvular structural abnormalities, and no vegetations were seen either on heart valves or on the pacemaker leads. Nevertheless, it was decided to remove the ICD immediately; no vegetations were seen on inspection of the removed leads. The device was removed completely. Culture of the hardware was negative. Following the procedure, the patient's condition improved: blood cultures became negative for *S. aureus* from the sixth hospital day, along with hemodynamic stabilization with decreasing doses of noradrenaline, renal replacement therapy was discontinued, and he was extubated on the 30th hospital day (extubation was delayed because of ICU myopathy). Other than two episodes of intercurrent bacteremia (by *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*) and an episode of ventilator-associated pneumonia, the remaining stay in the ICU was uneventful, and the patient was discharged from the ICU on the 40th day. On follow-up 3 months after discharge the patient is at home and doing well, although he is functionally incapacitated.

MRSA with the same antibiogram was also isolated from the nares of the patient's wife. Because of the antibiotic susceptibility pattern, the *S. aureus* isolates from the patient and his wife were further investigated at the Government Central Laboratories. Polymerase chain reaction was performed for the detection of the Panton-Valentine leukocidin (*PVL*) gene mecA gene. The strains were analyzed by Staphylococcal Cassette Chromosome mec (SCCmec) typing, Staphylococcal Protein A (spa) typing, and pulsed-field gel electrophoresis. The wife's isolate showed a PFGE pattern identical to that of the patient. The patient's MRSA isolate and that of his wife were PVL-negative, SCCmec type IVa, and spa type t065 (which corresponds to MLST types ST45 and ST46).

ICU = intensive care unit
PFGE = pulsed-field gel electrophoresis

COMMENT

The isolate responsible for the severe ICD-related sepsis in our patient was defined as CA-MRSA on the basis of its antimicrobial susceptibility profile and molecular characteristics: it was susceptible to clindamycin and other non-beta lactam antistaphylococcal antibiotics (erythromycin, gentamicin, rifampin, minocycline, linezolid and trimethoprim-sulfamethoxazole), and the strain carried a SCCmec type IVa. The patient also fulfilled the epidemiological and clinical criteria for the definition of "community-associated MRSA." In 2000 the U.S. Centers for Disease Control and Prevention issued a set of criteria that define the likelihood of persons with MRSA infections to have CA-MRSA infections if they meet all of them: diagnosis of MRSA in an outpatient or within 48 hours of hospitalization; the patient lacks the following traditional risk factors for MRSA infection: hemodialysis, surgery, or residence in a long-term care facility; the presence of an indwelling catheter or a percutaneous device at the time culture samples were obtained; or previous isolation of MRSA [4]. Although our patient was hospitalized during the previous year, he stayed in the hospital for less than 24 hours [Table].

Unlike the large disease burden caused by CA-MRSA in the United States, CA-MRSA is uncommon in Israel. Colonization or infection was documented exclusively in the pediatric population. Most of the isolates are PVL negative [5]. This the first case of CA-MRSA infection in an adult patient described in Israel.

We believe that the bloodstream infection was a manifestation of ICD infection, based on the following clinical parameters: growth of *Staphylococcus aureus* in blood cultures, no other identified source for bacteremia, persistence of bacteremia for more than 24 hours, and the cardiovascular implantable electronic device was an implantable ICD [3]. The importance of device removal as part of the treatment has been stressed by several recent publications [3]. Indeed our patient deteriorated clinically despite prompt initiation of appropriate treatment, and only after the removal of the cardioverter defibrillator did he improve dramatically.

Criteria for Identification of CA-MRSA* and their presence in our patient

Criterion	Presence in our patient
48 hour	+
Clindamycin susceptible	+
Non-MDR	+
SCCmec IV	+
PVL	-
ST8	ND
SSTI	-
Lack of health care risk factors	+

* *J Infect Dis* 2008; 197: 1235-43
48 hour = diagnosis of MRSA in an outpatient or within 48 hours of hospitalization, MDR = multidrug resistant, ST = sequence type, ND = not done, *PVL* = Panton-Valentine leukocidin, SSTI = skin and soft tissue infection (mainly in children)

To conclude, our patient developed severe septic shock although the pathogen was of the *PVL*-negative strain. The severe presentation was probably due to the involvement of the implantable cardioverter defibrillator in the CA-MRSA sepsis, an association not previously reported.

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References

1. Moreno F, Crisp C, Jorgensen JH, Patterson JE. Methicillin-resistant *Staphylococcus aureus* as a community organism. *Clin Infect Dis* 1995; 21: 1308-12.
2. David MZ, Daum RS. Community-associated methicillin-resistant *Staphylococcus aureus*: epidemiology and clinical consequences of an emerging epidemic. *Clin Microbiol Rev* 2010; 23: 616-87.
3. Baddour LM, Epstein AE, Erickson CC, et al. Update on cardiovascular implantable electronic device infections and their management: a scientific statement from the American Heart Association. *Circulation* 2010; 121: 458-77.
4. Morrison MA, Hageman JC, Klevens RM. Case definition for community-associated methicillin-resistant *Staphylococcus aureus. J Hosp Infect* 2006; 62: 241.
5. Glikman D, Davidson S, Kudinsky R, Geffen Y, Sprecher H. First isolation of SCCmec IV- and Panton-Valentine leukocidin-positive, sequence type 8, community-associated methicillin-resistant *Staphylococcus aureus* in Israel. *J Clin Microbiol* 2010; 48: 3827-8.