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## ORIGINAL ARTICLE

# Skin Infections Caused by Community-Acquired Methicillin-Resistant *Staphylococcus aureus*: Clinical and Microbiological Characteristics of 11 Cases<sup>☆</sup>

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### KEYWORDS

Methicillin-resistant  
*Staphylococcus aureus*;  
Community;  
Abscess;  
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Cotrimoxazole

### Abstract

**Introduction:** Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is an emerging pathogen that causes skin and soft-tissue infections.

**Objective:** To describe the clinical characteristics of skin infections caused by CA-MRSA and correlations with the available demographic and microbiological data.

**Material and methods:** This was a descriptive study of patients with a microbiologically confirmed diagnosis of CA-MRSA infection treated in a dermatology department between June 2009 and December 2011. We recorded demographic details, the clinical characteristics of lesions, and the treatments used.

**Results:** We studied 11 patients (5 men and 6 women); 91% were under 40 years of age and had no relevant past medical history. The most common presentation was a skin abscess (with or without cellulitis). In all such cases, marked tissue necrosis and little or no purulent exudate was observed when the abscess was drained. Fifty percent of these abscesses had been treated previously with  $\beta$ -lactam antibiotics, and in all cases the lesions resolved after surgical drainage, which was combined in 63% of cases with quinolones or cotrimoxazole.

**Conclusions:** Today, skin infections due to CA-MRSA affect healthy young athletes who have no contact with healthcare settings. The most common presentation is a skin abscess characterized by marked tissue necrosis and little or no purulent exudate. In cases with these characteristics in susceptible patients, the involvement of CA-MRSA as the causative agent should be suspected. The abscesses should be drained whenever possible and, if necessary, antibiotic treatment should be prescribed; empirical use of  $\beta$ -lactam antibiotics should be avoided.

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**PALABRAS CLAVE**

*Staphylococcus aureus* resistente a metilina;  
Comunidad;  
Absceso;  
Necrosis;  
Cotrimoxazol

## Infecciones cutáneas causadas por *Staphylococcus aureus* resistente a metilina de adquisición comunitaria: características clínico-microbiológicas en 11 pacientes

**Resumen**

**Introducción:** *Staphylococcus aureus* resistente a metilina de adquisición comunitaria (SARM-CO) constituye un patógeno emergente como agente productor de infecciones de piel y partes blandas.

**Objetivo:** Describir las características clínicas de las infecciones cutáneas causadas por SARM-CO, así como su correlación con los datos demográficos y microbiológicos disponibles.

**Material y métodos:** Se realizó un estudio descriptivo de los pacientes con diagnóstico de infección microbiológicamente confirmada por SARM-CO en el Servicio de Dermatología desde junio de 2009 a diciembre de 2011. Se recogieron los datos demográficos de los pacientes, las características clínicas de las lesiones y los tratamientos realizados.

**Resultados:** Se reclutaron 11 pacientes, 5 hombres y 6 mujeres. El 91% tenía menos de 40 años y no presentaba antecedentes médicos de interés. El absceso cutáneo (asociado o no a celulitis) fue la forma más frecuente de presentación. Tras su drenaje se observó una cantidad escasa o nula de exudado purulento junto a un componente de necrosis tisular marcado en todas estas lesiones. El 50% de los abscesos había recibido tratamiento previo con antibióticos betalactámicos y el drenaje quirúrgico, asociado en el 63% a quinolonas o cotrimoxazol, aseguró la resolución de los mismos.

**Conclusiones:** Actualmente las infecciones cutáneas causadas por SARM-CO se presentan en individuos jóvenes, sanos, deportistas, sin contacto con el ámbito sanitario. Los abscesos cutáneos, su forma más frecuente de presentación, se caracterizan por una marcada necrosis tisular, con escaso o nulo exudado purulento. Ante estos hallazgos en pacientes susceptibles debe sospecharse la implicación de SARM-CO como agente causal. El drenaje de los abscesos se realizará siempre que sea posible, y cuando resulte necesario añadir tratamiento antibiótico deberá evitarse el uso de betalactámicos de forma empírica.

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**Introduction**

The increase in infections caused by microorganisms resistant to conventional antimicrobials represents a major therapeutic limitation in the hospital setting.

Soon after the introduction of penicillin in 1941 the first strains of penicillin-resistant *Staphylococcus aureus* were isolated. Hospital strains of methicillin (oxacillin)-resistant *S aureus* appeared 2 decades later, and subsequently became one of the main bacterial causes of nosocomial infections. However, since the 1980s *S aureus* has also been detected in non-hospital-acquired infections,<sup>1</sup> and its incidence has grown exponentially in many countries, including the United States, where it is the leading cause of community-acquired skin and soft tissue infections in several states.<sup>2</sup>

Community-acquired methicillin-resistant *S aureus* (CA-MRSA) differs from its nosocomial counterpart in its clinical, epidemiological, and microbiological characteristics (Table 1),<sup>3-7</sup> and thus requires radically different therapeutic management in most cases.

Given that CA-MRSA predominantly affects skin and soft tissue, we reviewed 11 cases diagnosed in our hospital in order to describe the main clinical features of the disease and the correlation with available demographic and microbiological data. Based on our findings, we propose several specific clinical criteria to improve the initial empirical treatment of skin and soft tissue infections in outpatients.

**Materials and Methods**

This is a descriptive, observational, retrospective study of adult patients with a microbiological diagnosis of skin and soft tissue infection caused by CA-MRSA. The data were collected between June 2009 and December 2011 from the skin infection database of the dermatology department at the Hospital General Universitario Gregorio Marañón in Madrid, Spain.

All cases had been microbiologically confirmed by culture followed by antibiogram and molecular analysis.

The clinical variables studied were age, sex, clinical presentation (lesion type, presence of pus, necrosis, and location), the course of the lesions, treatments received, and the response to treatment. We analyzed the origin of the patients, the presence of recurrent skin infections in the patient's family, risk practices (contact sports or activities, shared use of personal hygiene items, membership of recruiting groups or institutions), contact with the health sector (employment, previous hospital admissions), and contact with domestic or farm animals.

**Results**

Data for the patients studied are summarized in Table 2.

Of the patients studied, 91% (10/11) were younger than 40 years, and the male to female ratio was 1:1.2. The individuals were healthy, immunocompetent patients with no

**Table 1** Differential Characteristics of Nosocomial and Community-Acquired MRSA Strains.

	Community-Acquired MRSA	Nosocomial MRSA
Risk groups/factors	Children, athletes, membership of recruitment institutions, sexual promiscuity, IVDAs, HIV, <sup>4</sup> tattoos, <sup>5,6</sup> origin in endemic area (Pacific Islanders, Central/South Americans, indigenous Australians)	Prolonged hospitalization, intravascular catheters, diabetes mellitus, immunosuppression, admission to intensive care unit, hemodialysis, peritoneal dialysis
Mechanisms of resistance (SCCmec genes)	IV	I, II, III
Production of Panton-Valentine leukocidin	Frequent	Infrequent
Antimicrobial resistance pattern	Resistance to $\beta$ -lactam antibiotics	Multidrug resistance
Clinical symptoms	Infections of skin and soft tissue, necrotizing pneumonia	Bacteremia associated with endovascular devices, urinary tract infection, nosocomial pneumonia, endocarditis, surgical wound infection
Colonization	Genital, perineal (recurrent infections)	Nasal

Abbreviations: HIV, human immunodeficiency virus; IVDAs, intravenous drug addicts; MRSA, methicillin-resistant *Staphylococcus aureus*; SCCmec, staphylococcal cassette chromosome.

Source: Kowalski et al.<sup>3</sup>

<sup>a</sup>In Spain CA-MRSA isolates frequently exhibit resistance to tetracycline and doxycycline mediated by the *tet(M)* gene.<sup>7</sup>

prior hospital admissions and no contact with the healthcare sector through either employment or family.

Eight (73%) of the 11 patients presented with abscesses (Figs. 1-4); half of these cases (4/8) involved perilesional cellulitis, and 63% (5/8) presented abscesses on exposed areas of the limbs. Surgical drainage removed small amounts of purulent material in 37% (3/8) of cases, and none in the remainder (63%; 5/8). Tissue necrosis, forming a cavity within the subcutaneous tissue, was the main feature of all lesions.

Primary follicular involvement (staphylococcal folliculitis and anthrax) was observed in 2 patients, and recurrent paronychia in another. Due to the nature of the lesions, it was not possible to clearly establish the amount of purulent exudate in these 3 patients.

Thirty-six percent (4/11) of the patients were Spanish, 45% (5/11) were Latin American, and 18% (2/11) were

Polish. Possible risk factors associated with the development of infection included sports (2 patients, 18%), dance (2 patients, 18%), and noninvasive cosmetic procedures (1 patient, 9%).

Two patients had a history of recurrent, uncomplicated skin infections.

All cases had been confirmed by culture followed by an antibiogram and molecular analysis. The bacterial strains isolated in 64% (7/11) of the cases studied were resistant to erythromycin. Levofloxacin resistance was also detected in 1 case (1/7) and inducible clindamycin resistance in another (1/7), both of which were confirmed by D-test. Genes encoding Panton-Valentine leukocidin (PVL) were expressed in all staphylococcal isolates analyzed (except 1 case in which no



**Figure 1** Abscess and perilesional cellulitis.



**Figure 2** Characteristic appearance of abscess after drainage: necrosis and absence or scarcity of purulent exudate.

**Table 2** Demographic, Clinical, and Microbiological Data for Patients Included in the Study.

Patient/Age/Sex	Origin	Lesion Type	Lesion Location	Purulent Exudate	Tissue Necrosis	Risk Factors	Prior Treatments	NBA Resistance	PVL Production	Treatment
1/38/M	Spain	Abscess + cellulitis	Leg	No	Yes	Sport (futsal)	Cloxacillin, amox-clav	Erythromycin	Yes	SD + oral ciprofloxacin
2/40/M	Ecuador	Abscess	Arm	No	Yes	Camping in rural Thailand, dance, tattoo		Erythromycin	Yes	SD
3/27/M	Spain	Abscess	Leg	No	Yes			No	Yes	SD + oral ciprofloxacin
4/26/F	Cuba	Abscess	Iliac fossa	Scarce	Yes			Cloxacillin, amox-clav, cefuroxime	Erythromycin, levofloxacin	Yes
5/43/M	Colombia	Abscess	Abdomen	Scarce	Yes		Amox-clav	Erythromycin	Yes	SD + IV vancomycin
6/37/F	Spain	Anthrax	Upper lip	Scarce	No		Amox-clav	No	Yes	SD + oral ciprofloxacin
7/35/M	Poland	Paronychia	Big toe	Scarce	No	Ingrown toenail	Amox-clav, cefuroxime	No	Yes	Oral cotrimoxazole + deferred SD of ingrown toenail
8/37/F	Poland	Abscess + cellulitis	Thigh	No	Yes	Sports (swimming, diving)		No	Yes	SD + oral cotrimoxazole
9/18/F	Ecuador	Abscess + cellulitis	Abdomen	No	Yes	Noninvasive cosmetic procedures		Erythromycin	Yes	SD + oral ciprofloxacin
10/18/F	Colombia	Folliculitis	Back	Yes	No	Recurrent skin infections		Erythromycin	Yes	Cotrimoxazole
11/24/F	Spain	Abscess + cellulitis	Leg	Scarce	Yes	Dance	Amox-clav, ery-thromycin	Erythromycin, clindamycin		SD + vancomycin

Abbreviations: Amox-clav, amoxicillin-clavulanate; F, female; IV, intravenous; M, male; NBA, non- $\beta$ -lactam antibiotics; PVL, Panton-Valentine leukocidin; SD, surgical drainage.



**Figure 3** Erythematous-violaceous border and fibrinous center after spontaneous drainage of an abscess on the leg.

analysis was performed as the patient came from another health care center).

Of the patients analyzed, 55% (6/11) had been previously treated with amoxicillin-clavulanate with no clinical response. Of these, 67% (4/6) experienced treatment failure after a second round of antibiotic therapy with  $\beta$ -lactam (cefuroxime/cloxacillin) or erythromycin.

All abscesses (8/8) were surgically drained and antibiotics administered in 88% of cases. Ciprofloxacin and cotrimoxazole were the drugs of choice in 73% of patients (8/11). In 1 case treatment with oral clindamycin was discontinued due to gastrointestinal intolerance (diarrhea). Two patients with uncomplicated abscesses were treated with intravenous vancomycin as an alternative to  $\beta$ -lactam antibiotics. None of the patients presented systemic complications or myofascial involvement.



**Figure 4** Abscess next to a tattoo on a young woman.

## Discussion

CA-MRSA is emerging as a causative agent of skin and soft tissue infections. Its incidence remains low in Spain, in contrast to other industrialized countries, where it constitutes one of the main community-acquired bacterial pathogens.<sup>8,9</sup>

The epidemiological data presented here are similar to those reported in the scientific literature: those affected are young, healthy patients who engage in contact sports/activities or come from endemic areas such as Central or South America.<sup>9</sup>

Often, patients present single abscesses, located in areas of skin that are exposed or subject to contact during sports/activity.<sup>10</sup> Tissue necrosis is the main characteristic of these abscesses and very little pus is produced. A study evaluating the presence of eschar and perilesional cellulitis as clinical predictors in abscesses caused by CA-MRSA reported a sensitivity of 92% and a positive predictive value of 94%.<sup>11</sup> These findings may be explained by the cytotoxic effects that PVL is thought to exert on neutrophils and epidermal cells, and by the release of proinflammatory factors secondary to granulocyte lysis.<sup>12</sup> However, further studies are needed to confirm the role of this toxin in the pathogenesis of infections caused by CA-MRSA.

The differential diagnosis of these lesions should include pyoderma gangrenosum, spider bites,<sup>13</sup> loxoscelism,<sup>14</sup> and cutaneous leishmaniasis.

Other common cutaneous manifestations have been described, including folliculitis, carbuncles (recurrent infections), and impetigo (especially in children).<sup>15</sup>

CA-MRSA strains have microbiological characteristics that differentiate them from nosocomial strains; they are usually resistant only to  $\beta$ -lactam antibiotics and carry the genes that encode the PVL subunits LukF-PV and LukS-PV. However, depending on the source of the strain CA-MRSA may be also resistant to other antibiotics, as is the case with the predominant clone in the USA, USA300 (ST8-MRSA-IV), which is highly resistant to macrolides.<sup>7</sup> Therefore, where possible, samples should be taken in all cases for microbiological analysis of the lesions.

In this series 91% of patients received antimicrobial therapy, combined with surgical abscess drainage. However, some authors claim that lesion drainage and daily local treatment is sufficient in cases of extrafacial abscesses of less than 5 cm in diameter in nondiabetic, immunocompetent patients without myofascial involvement.<sup>16-18</sup> Table 3 summarizes the various relevant therapeutic modalities for the treatment of infections caused by CA-MRSA.

Since this bacterium mainly causes uncomplicated skin infections, treatment does not usually require hospitalization. However, cases of septic arthritis, pyomyositis, fasciitis,<sup>20</sup> and necrotizing pneumonia<sup>21</sup> have been described. Necrotizing pneumonia<sup>21</sup> should be considered in patients with uncomplicated skin infections and past or simultaneous symptoms of respiratory infection.<sup>22</sup> These cases always require antimicrobial treatment and close clinical observation.

The determination of carrier status by nasal swab is not recommended as a regular procedure.<sup>16</sup> Nasal colonization is often low in patients with lesions that are not associated with community-acquired MRSA outbreaks (the majority of cases in Spain), and the bacteria may be detected in other

**Table 3** Therapeutic Modalities in Infections Caused by CA-MRSA.

Treatment	Indications	Dose <sup>a</sup> /Route of Administration	Adverse Effects and Precautions	Comments
Surgical drainage	Should be performed for all abscesses			
Cotrimoxazole	1. Abscesses > 1 cm or < 1 cm in case of infants, patients over 65 y, facial location, diabetics, immunosuppression, perilesional cellulite 2. Impetigo, ecthyma, cellulitis, folliculitis, paronychia	Oral Adults and patients ≥ 12 y: 800/160 mg/12 h Children: 6-12 y, 400/80 mg/12 h 6 mo-5 y, 200/40 mg/12 h 6 wk-5 mo, 100/20 mg/12 h IV /IM Adults and patients > 12 y: 800/160 mg/12-24 h Children 6-12 y: 400/80 mg/12-24 h Mean dose: 80/16 mg /5 kg/12 h Children > 2 mo: 6-12 mg/kg/d trimethoprim	Toxicoderma, leukopenia, thrombocytopenia, hemolytic anemia, megaloblastic anemia, photosensitivity Not for use in case of pregnancy, lactation, infants < 2 mo, glucose-6-phosphate dehydrogenase deficiency, porphyrias, treatment with methotrexate, combination with azathioprine or metformin	High rate of resistance in infections caused by <i>Streptococcus pyogenes</i> : caution advised in the empirical treatment of abscesses with perilesional cellulitis
Clindamycin	1. Abscesses > 5 cm or < 5 cm in case of infants, patients over 65 y, facial location, diabetics, immunosuppression, perilesional cellulite 2. Impetigo, ecthyma, cellulitis, folliculitis, paronychia	Oral Adults: 150-450 mg/6 h Children > 1 mo: 8-25 mg/kg/d in 3-4 doses IV /IM Adults: 1.2-1.8 g/d in 3-4 doses Children > 1 mo: 20-40 mg/kg/d in 3-4 doses	Diarrhea, risk of pseudomembranous colitis, unpleasant metallic taste Should not be used in cases of pregnancy, lactation, or in combination with erythromycin or aminoglycosides	Can present resistance that is undetectable with standard antibiograms (confirm that D-test has been performed if conventional antibiogram indicates erythromycin resistance)
Quinolones (ciprofloxacin, levofloxacin)	1. Abscesses > 5 cm or < 5 cm in case of infants, patients over 65 y, facial location, diabetics, immunosuppression, perilesional cellulite 2. Impetigo, ecthyma, cellulitis, folliculitis, paronychia	Ciprofloxacin <sup>a</sup> Oral: Adults, 500 mg/12 h IV: Adults, 200-400 mg/12 h Levofloxacin <sup>a</sup> Adults: Oral, 250-500 mg/d IV, 500 mg/d	Risk of tendinopathy, arthropathy (greater in children, the elderly, and in patients receiving long-term corticosteroid therapy) Adjust dose in cases of renal impairment Avoid in cases of pregnancy, lactation. Should not be ingested with dairy products or calcium	Rates of resistance to these drugs are currently low <sup>19</sup>
Tetracyclines (Doxycycline, minocycline)	1. Abscesses > 5 cm or < 5 cm in case of infants, patients over 65 y, facial location, diabetics, immunosuppression, perilesional cellulite 2. Impetigo, ecthyma, cellulitis, folliculitis, paronychia	Doxycycline <sup>a</sup> Oral: Adults and children > 8 y (weight ≥ 45 kg), 100-200 mg/24 h in 1 or 2 doses Minocycline <sup>a</sup> Oral: Adults and children > 8 y (weight ≥ 45 kg), 100 mg/12 h	Photosensitivity, hepatotoxicity, benign intracranial hypertension (increased risk when administered in children or with retinoids), vestibular toxicity (minocycline), esophagitis Avoid in cases of pregnancy, lactation, children < 8 y (risk of tooth and bone metabolism disorders)	Not effective in monotherapy The ST80-MRSA-IV strains (present in Northern and Eastern Europe and in some countries of the Mediterranean basin) are resistant to tetracycline

Table 3 (Continued)

Treatment	Indications	Dose <sup>a</sup> /Route of Administration	Adverse Effects and Precautions	Comments
Rifampicin	1. Abscesses > 5 cm or < 5 cm in case of infants, patients over 65 y, facial location, diabetics, immunosuppression, perilesional cellulite 2. Impetigo, ecthyma, cellulitis, folliculitis, paronychia	Oral Adults: 450-600 mg/d Children > 5 y: 10-20 mg/kg/d in 1-2 doses (maximum 600 mg/d)	Hepatotoxicity, changes in color of urine/bodily secretions, multiple drug interactions (cytochrome p450 inducer)	Synergistic effect with other antimicrobials. Do not use in monotherapy (frequent emergence of resistant strains)
Daptomycin <sup>b</sup>	Complicated skin and soft tissue infections	IV Adults: 4-6 mg /kg/d Safety and efficacy not established in patients < 18 y	Myotoxicity Dosage adjustment in case of renal disease Alterations in hemostatic parameters (INR/prothrombin time)	Do not use if there is a risk of necrotizing lung infection (action inhibited by pulmonary surfactant)
Vancomycin <sup>b</sup>	Complicated skin and soft tissue infections	IV Adults: initial dose, 30-50 mg /kg/d; typical dose, 1 g/12 h or 500 mg/6 h Children > 1 mo: 10 mg/kg/6 h	Nephrotoxicity. Red man syndrome: avoid rapid intravenous administration (minimum 1 h)	Monitor serum levels in patients with renal failure or in cases of coadministration with nephrotoxic drugs
Linezolid <sup>b</sup>	Complicated skin and soft tissue infections	Oral and IV Adults: 600 mg/12 h Not recommended in patients < 18 y	Myelosuppression, tyramine reaction, optic nerve neuropathy, hypertension, elevated transaminase levels	Given its high cost and adverse effects, its use must be strictly warranted.
Quinupristin-dalfopristin <sup>b</sup>	Complicated skin and soft tissue infections	Administered through central venous catheter in 5% glucose for 60 min: 7.5 mg/kg/8 h (not diluted in saline)	Increased QT interval, hepatotoxicity, increased plasma levels of drugs metabolized by CYP3A4	Should be used only in case of treatment failure with other available alternatives

Abbreviations: AHT, arterial hypertension; INR, international normalized ratio; IM, intramuscular; IV, intravenous.

<sup>a</sup> There is no consensus on the duration of administration regimens for the majority of these drugs. In general, it is recommended to re-evaluate after 7 days of treatment and extend treatment to 14 days if necessary (treatment with quinupristin-dalfopristin should not be extended for more than 7 days).

<sup>b</sup> Valid alternatives in cases of complicated infections, bacteremia, or in cases of treatment failure with other available options.

locations such as the inguinal/perineal area, the axillary folds, the rectum, or the pharynx.<sup>23</sup> There is no consensus on the measures necessary to achieve decolonization of this bacteria,<sup>24</sup> although some authors have proposed showering with antiseptic soap solutions (chlorhexidine or povidone iodine, although use of the latter is limited by its staining of the skin and the risk of local sensitization or irritation<sup>25</sup>), or using topical intranasal (mupirocin) and systemic (cotrimoxazole) antibiotics,<sup>26,27</sup> with varying results.

## Conclusions

Uncomplicated infections of the skin and soft tissue are one of the main reasons for visits to dermatological practices and emergency health services. The epidemiology

of these infections has changed in recent years, with the appearance of pathogens that were hitherto considered exclusively nosocomial. CA-MRSA represents a paradigm in dermatological practice, as its main pathogenic targets are the skin and skin adnexa. The collection of samples for culture and subsequent antibiogram remains the gold standard in diagnosis. However, while awaiting the results of microbiological tests, we believe it is essential to individualize the initial empirical antibiotic treatment and to include this pathogen in the bacterial spectrum covered.

Although the small number of cases analyzed and the retrospective nature of our study do not allow us to generalize based on the results obtained, we propose that the use of  $\beta$ -lactam antibiotics as an initial therapeutic measure should be avoided in young, healthy patients with cutaneous abscesses with a significant necrotic component and

scant purulent exudate, with or without cellulitis. Similarly, in cases of recurrent skin infections, family outbreaks of abscesses, folliculitis, and carbuncles, or treatment failure after 1 or more cycles of  $\beta$ -lactam antibiotics, CA-MRSA should be considered as a potential causative pathogen.

## Ethical Disclosures

**Protection of Human and Animal Subjects.** The authors declare that no experiments were performed on humans or animals during the course of this study.

**Confidentiality of Data.** The authors declare that they have followed the protocols of their place of work concerning the publication of patient data and that all patients included in the study were appropriately informed and gave their written informed consent.

**Right to Privacy and Informed Consent.** The authors declare that no private patient data are disclosed in this article.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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