ISSN 0325-7541
Revista Argentina de Microbiología (2012) 44: 303-305

A case of familial transmission of community-acquired methicillin-resistant *Staphylococcus aureus* carrying the *lnu*(A) gene in Santa Fe city, Argentina

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ABSTRACT

Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is increasingly recognized as an important pathogen causing skin and soft tissue infections as well as necrotizing pneumonia. We describe a case of familial transmission of CA-MRSA between a 6-month-old boy and his mother in Santa Fe City, Argentina. Both isolates showed an identical antimicrobial susceptibility profile, carried type IV SCC*mec* and harboured the *pvl* and the *lnu*(A) genes. Isolates showed indistinguishable *Sma*I-PFGE patterns confirming their genetic relationship. These results corroborate the intrafamilial transmission of CA-MRSA and might associate this strain with the repetitive events of furunculosis within the family.

Key words: CA-MRSA, familial transmission, PVL, SCC*mec* IV

RESUMEN

Caso de transmisión familiar de *Staphylococcus aureus* resistente a la meticilina adquirido en la comunidad portador del gen *lnu*(A) en la ciudad de Santa Fe, Argentina. *Staphylococcus aureus* resistente a la meticilina adquirido en la comunidad (SARM-AC) es reconocido como un patógeno importante que causa infecciones de piel y partes blandas y neumonía necrotizante. Describimos un caso de transmisión familiar de SARM-AC entre un niño de 6 meses de edad y su madre en la ciudad de Santa Fe, Argentina. Ambos aislamientos mostraron idéntico perfil de sensibilidad a los antimicrobianos, tenían el SCC*mec* tipo IV, y contenían los genes *pvl* y *lnu*(A). Los aislamientos presentaron patrones de *Sma*I-PFGE indistinguibles entre sí, lo cual confirmó su relación genética. Estos resultados corroboran la transmisión intrafamiliar de SARM-AC; asimismo, este aislamiento podría asociarse con los eventos repetitivos de furunculosis en la familia.

Palabras clave: SARM-AC, transmisión familiar, LPV, SCC*mec* IV

Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is a common cause of primary skin infections, mainly furunculosis and abscesses, but can also cause necrotizing tissue infections and fulminant pneumonia in young and previously healthy people (5, 6). Several cases of intrafamilial CA-MRSA transmission have been described in the last decades, especially in families with young children (1, 8, 9, 10). Most CA-MRSA isolates harbour the virulence factor Panton-Valentine leukocidin (PVL) and the *mec*A gene which is carried in the staphylococcal cassette chromosome *mec* (SCC*mec*) type IV or V (5). Resistance to macrolides, lincosamides and streptogramins in *S. aureus* is mainly mediated by *erm* (MLS phenotype) and *msr*A (MS_B phenotype) genes. However, an unusual mechanism of lincosamide resistance mediated by *lnu*(A) gene (L phenotype) has been occasionally described in clinical isolates (7, 11). In this report we describe a case of familial transmission of PVL producing CA-MRSA carrying SCC*mec* IV and the unusual *lnu*(A) gene.

Case report. In October 2010, a previously healthy 6-month-old boy was admitted to a private hospital in Santa Fe City, presenting with fever, shortness of breath, dysphagia and productive cough that had started 6 days earlier. The patient had no risk

factors associated to hospital infection, such as immunosuppression, corticoid treatment, diabetes, recent influenza, presence of any permanent indwelling catheter or percutaneous device, residence in a long-term care facility or others (e.g., daycare center) or previous *S. aureus* colonization/ infection.

Laboratory data showed hemoglobin levels of 8.2 g/dl and a white blood cells count of 36,000/µl (86 % neutrophils, 2 % eosinophils, 10 % lymphocytes, 2 % monocytes). Arterial blood gas was: pH = 7.4, Pa CO_2 32.9 mmHg. Erythrocyte sedimentation rate was 30 mm/h and was positive for C-reactive protein. Chest X-ray and lung ecography showed a 10 mm pleural displacement and a pleural drainage tube insertion was required.

Despite empirical treatment with ceftriaxone 100 mg/kg for 4 days and since the patient's condition continued to worsen, he was transferred to a high-complexity public hospital for further treatment.

At the hospital, he was diagnosed with severe community-acquired pneumonia presenting with septic shock and he was transferred to the Intensive Care Unit (ICU) where he was intubated and ventilated.

Staphylococcus aureus (MRSA-1) was recovered from pleural fluid culture but not from blood cultures. The isolate was identified by the Vitek System (bioMèrieux, Marcy l'Etoile, France) and the coagulase test. Susceptibility testing was performed by the disk diffusion method according to CLSI standards (3). MRSA-1 isolate was categorized as susceptible to erythromycin, ciprofloxacin, cotrimoxazole, rifampin, and linezolid, but resistant to β-lactam antibiotics and gentamicin. Although a susceptible inhibition zone was observed around the clindamycin disk, the lincomycin inhibition zone was of 9 mm, suggesting the presence of a mechanism of resistance to lincosamides. The minimal inhibitory concentration (MIC) of vancomycin was 0.75 µg/ml by Etest (bioMèrieux). Considering these results, the antibiotic therapy was switched to intravenous vancomycin (40 mg/kg bid) plus rifampin (10mg/kg bid).

The patient remained ventilator-dependent for 4 days. He showed clinical improvement and intravenous antibiotic therapy was continued for 20 days. On day 24th of hospitalization he was discharged on oral cotrimoxazole treatment (10 mg/ kg/day for 15 days).

In an attempt to detect the infection source, household contact information was evaluated, revealing a history of repetitive furunculosis affecting the mother and all siblings. The mother was screened by taking a sample from an abdominal furuncle, obtaining a methicillin-resistant *S. aureus* (MRSA-2). MRSA-2 showed identical antibiotic susceptibility profile than MRSA-1, and the same MIC value to vancomycin**.** Detection of *mec*A and *pvl* genes was positive in both MRSA-1 and MRSA-2 isolates by polymerase chain reaction (PCR) as previously described (6, 13)*.* Both isolates, MRSA-1 and MRSA-2, harbored the SCC*mec* type IV characterized by the multiplex PCR assay described by Oliveira (12). Interestingly, the *lnu*(A) gene was also detected in both isolates using lnuA-F: 5´- GGC GTA GAT GTA TTA ACT GG-3´, and lnuA-R2: 5´-GAA AAA GAA GTT GAG CTT C-3´, specific primers and confirmed by DNA sequencing. The presence of the unusual *lnu*(A) gene has been sporadically described in others countries, while only an MRSA-outbreak in a neonatal ward has been reported in Argentina (4, 7, 11).

The clonal relationship determined by pulsed field gel electrophoresis (PFGE) using *Sma*I enzyme for genomic DNA digestion showed that both isolates displayed indistinguishable electrophoretic patterns (2). These results confirm the genetic relationship between both isolates and the familial transmission of CA-MRSA harbouring SCC*mec* type IV and positive *pvl* gene.

The patient and household contact had no history of surgical procedures or of antimicrobial therapies. A repetitive history of furunculosis affecting the mother and all the siblings was registered; however no additional MRSA-positive samples were recovered.

The fact that both CA-MRSA isolates harbored the *lnu*(A) gene, limits the use of clindamycin as an option for the treatment of primary skin infections. However, it is important to note that none of the family had previously received clindamycin treatment.

In the present work, we confirm the familial transmission of CA-MRSA between a child and his mother, highlighting the importance of the search of contact carriage in community-onset MRSA infections.

Acknowledgment: this work was partly supported by research grants from the Universidad Nacional del Litoral, Santa Fe, Argentina (CAI+D 2009).

REFERENCES

1. Adam H, McGeer A, Simor A. Fatal case of post-influenza, community-associated MRSA pneumonia in an Ontario teenager with subsequent familial transmission. Can Commun Dis Rep 2007; 33: 45-8.
2. Chung M, de Lencastre H, Matthews P, Tomasz A, Adamsson I, Aires de Sousa M, Camou T, Cocuzza C, Corso A, Couto I, Dominguez A, Gniadkowski M, Goering R, Gomes A, Kikuchi K, Marchese A, Mato R, Melter O, Oliveira D, Palacio R, Sá-Leão R, Santos Sanches

I, Song JH, Tassios PT, Villari P. Molecular typing of methicillin-resistant *Staphylococcus aureus* by pulsed-field gel electrophoresis: comparison of results obtained in a multilaboratory effort using identical protocols and MRSA strains. Microb Drug Resist 2000; 6: 189-98.

3. Clinical and Laboratory Standards Institute. Disk diffusion. Performance Standards for Antimicrobial Susceptibility Testing. 22th Informational Supplement, 2012; M100-S22. Wayne, PA, EE.UU.
4. Corso A, Faccone D, Togneri AM, Podesta L, Perez M, Gagetti P. Methicillin-resistant *Staphylococcus aureus* (MRSA) outbreak in a neonatal unit carrying an unusual genotype of macrolide-lincosamide-resistance: *erm*C plus *lnu*A genes. 6th World Society for Pediatric Infectious Disease, 2009, PW01A, Ciudad Autónoma de Buenos Aires, Argentina.
5. 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.
6. Lina G, Piemont Y, Godall-Gamot F, Bes M, Peter MO, Gauduchon V, Vandenesch F, Etienne J. Involvement of Panton-Valentine leukocidin-producing *Staphylococcus aureus* in primary skin infections and pneumonia. Clin Infect Dis 1999; 29: 1128-32.
7. Lina G, Quaglia A, Reverdy ME, Leclercq R, Vandenesch F, Etienne J. Distribution of genes encoding resistance to macrolides, lincosamides, and streptogramins among staphylococci. Antimicrob Agents Chemother 1999; 43: 1062-6.
8. Hollis RJ, Barr JL, Doebbling BN, Pfaller MA, Wenzel RP. Familial carriage of methicillin-resistant *Staphylococcus aureus* and subsequent infection in a premature neonate. Clin Infect Dis 1995; 21: 328-32.
9. Ho PL, Cheung C, Mak GC, Tse CWS, Ng TK, Cheung CH, Que TL, Lam R, Lai RW, Yung RW, Yuen KY. Molecular epidemiology and household transmission of community-associated methicillin-resistant *Staphylococcus aureus* in Hong Kong. Diagn Microbiol Infect Dis 2008; 61: 135-42.
10. Huijsdens WX, van Santen-Verheuvel MG, Spalburg E, Heck MEOC, Pluister GN, Eijkelkamp BA, de Neeling AJ, Wannet WJ. Multiple cases of familial transmission of community-acquired methicillin-resistant *Staphylococcus aureus*. J Clin Microbiol 2006; 44: 2994-6.
11. Novotna G, Adamkova V, Janata J, Melter O, Spizek J. Prevalence of resistance mechanisms against macrolides and lincosamides in methicillin-resistant coagulase-negative staphylococci in the Czech Republic and occurrence of an undefined mechanism of resistance to lincosamides. Antimicrob Agents Chemother 2005; 49: 3586-9.
12. Oliveira DC, de Lencastre H. Multiplex PCR strategy for rapid identification of structural types and variants of the *mec* element in methicillin-resistant isolates of *Staphylococcus aureus*. Antimicrob Agents Chemother 2002; 46: 2155-61.
13. Soloaga R, Corso A, Gagetti P, Faccone D, Galas M, Grupo Colaborador MRSA. Detección de meticilino-resistencia en *Staphylococcus aureus*: Comparación de métodos convencionales y aglutinación con MRSA-Screen latex. Rev Argent Microbiol 2004; 36: 36-40.

Recibido: 29/5/2012- Aceptado: 8/11/2012