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Case Report

Intrafamilial spread of a Panton-Valentine leukocidin-positive community-acquired methicillin-resistant *Staphylococcus aureus* belonging to the paediatric clone ST5 SSC*mec*IV

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Introduction: Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is increasingly recognized as an important pathogen. Panton–Valentine leukocidin (PVL)-producing CA-MRSA constitutes a public health concern because it can be responsible for severe, progressive necrotizing skin, soft-tissue and pulmonary infections.

Case presentation: We describe a case of recurrent transmission of PVL-producing ST5, staphylococcal cassette chromosome *mec* type IV MRSA (paediatric clone) from an asymptomatic nasal carrier to his family causing severe skin and soft-tissue infections in the mother and children. Nasal application of mupirocin in the carrier was successful for prevention of new infections.

Conclusion: Recurrent skin infections are often not taken into account but may represent a serious threat if caused by a PVL-producing MRSA strain. Family members of MRSA carriers are in danger of transmission. Characteristics of currently circulating CA-MRSA strains require closer surveillance. Identification and decolonization of carriers is important to reduce the risk of spread into the community.

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Introduction

Originally isolated from hospitalized patients in the 1960s and still endemic in many hospitals worldwide, methicillin-resistant *Staphylococcus aureus* (MRSA) has been increasingly observed in community settings, predominantly affecting healthy individuals without connections to healthcare facilities (Prosperi *et al.*, 2013). Community-acquired (CA)-MRSA strains are distinguishable from hospital-acquired (HA)-MRSA strains by virtue of the carriage of certain staphylococcal cassette chromosome *mec* (SCC*mec*) types, which are usually types IV and V (Chambers & Deleo, 2009), the production of the bicomponent cytotoxin Panton–Valentine leukocidin (PLV) and by assignment to distinct *spa* types and clonal complexes (CCs) and sequence types (STs) (Cookson *et al.*, 2007). Previous studies have shown that, in contrast to the situation in the USA where epidemic CA-MRSA clones ST1-IV (USA400) and ST8-IV (USA300) prevail, a larger genetic diversity is observed in Europe (Rolo *et al.*, 2012), with ST80-IV being the most common CA-MRSA (Otter & French, 2010). Here, we describe the intrafamilial transmission of a PVL-positive CA-MRSA strain belonging to the so-called paediatric clone, which is a clone originating from the hospital environment and hitherto, in contrast to previous reports (Liassine *et al.*, 2004), not described as a clone typical for CA-MRSA in Switzerland. Community-acquired skin infections are rarely characterized, and hence the prevalence of CA-MRSA in Switzerland may be underestimated. A picture of the local epidemiology of CA-MRSA and the detection of carriers is necessary for successful transmission control.

Abbreviations: CA, community acquired; CC, clonal complex; HA, hospital acquired; MRSA, methicillin-resistant *Staphylococcus aureus*; PVL, Panton–Valentine leukocidin; SSC*mec*, staphylococcal cassette chromosome *mec*; ST, sequence type

Case report

A 41-year-old female presented to her general practitioner with a 4-day history of an enlarging painful lesion on her

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left arm that she attributed to a mosquito bite. Her personal history was unremarkable, but she reported her 4-year-old son as having had an untreated lesion located on his upper lip and her 1-year-old daughter as having received antibiotic therapy for an MRSA-related gluteal abscess, which had been diagnosed and treated at a children's hospital several weeks prior to consultation. The patient was diagnosed with a volar abscess including erysipelas extending from the wrist to the elbow. Incision and drainage was performed and a swab was taken for microbiological analysis. Culture of the pus yielded MRSA. Oral therapy with cotrimoxazole (800 mg sulfamethoxazole/160 mg trimethoprim, twice daily for 14 days) was initiated. Quarantine measures were recommended regarding exposure of the wound to immunosuppressed persons, persons with open wounds and pregnant women. Over the next 3 days, the wound was inspected and rinsed daily, and was disinfected with iodine tincture (11 mg ml^{-1}), while therapy with cotrimoxazole continued. Following an initial amelioration, the accumulation of pus necessitated renewed and extensive incision and drainage, to the extent of partial exposure of the flexor tendon. Four days after diagnosis, the patient's son presented to the same general practitioner with a painful lesion on his right thigh. Therapy with cotrimoxazole (200 mg sulfamethoxazole/40 mg trimethoprim, twice daily for 5 days) was initialized. Culture of pus taken from the lesion revealed MRSA. Over the next days, treatment was carried out as described above, and after 6 days, both mother and son presented with granulating wounds without further signs of irritation. Seven days later, the son presented again with two painful lesions on his right knee that he attributed to mosquito bites. Culture of the pus yielded MRSA. Treatment as described above was administered. To elucidate a possible reservoir within this family, nasal swabs were obtained from both nares of each family member. No pets were present in this family. Culture of the swabs revealed MRSA from both nares of the 44-year-old father who had never presented with MRSA infections, while the samples obtained from the mother, son and daughter yielded negative results. Decolonization therapy with nasal ointment containing 20 mg mupirocin g^{-1} was initiated and maintained for 5 days. Two days after termination of antibiotic treatment, nasal swabs yielded negative MRSA results.

For MRSA detection, samples were subjected to a two-step enrichment procedure in Mueller–Hinton broth supplemented with 6.5 % NaCl (24 h at 37 °C) and brain–heart infusion broth with 75 mg aztreonam l^{-1} and 5 mg cefoxitin l^{-1} (24 h at 37 °C), and plated onto Brilliance MRSA Agar (Oxoid) and incubated for 24 h at 37 °C. Four selected isolates were further characterized by SCC*mec* typing (Boye *et al.*, 2007), determination of multilocus sequence typing (Enright *et al.*, 2000) and *spa* typing (Aires-de-Sousa *et al.*, 2006). An *S. aureus* Genotyping kit (Alere Technologies) was used to detect the presence or absence of 333 genes and their allelic variants including species markers and virulence genes, as well as genes conferring resistance to antimicrobial agents. Microarray results allowed the confirmation of strain assignment to CCs (Monecke *et al.*, 2008). Susceptibility to penicillin, cefoxitin, ciprofloxacin, clindamycin, erythromycin, gentamicin, rifampicin, sulfamethoxazole/trimethoprim, tetracycline and vancomycin was tested using antibiotic disks (Becton Dickinson) according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI, 2013). Susceptibility to daptomycin and linezolid was tested using Etest strips (bioMérieux).

All isolates were ascribed to CC5, SCC*mec* type IV, ST5 and spa type t002 (paediatric clone), produced PVL and exhibited resistance to penicillin, cefoxitin and erythromycin (Table 1). Based on their toxin gene profiles, the isolates were assigned to the first of the three major variants of the paediatric clone, which harbours *sea*-N315, *sed*, *sej* and *ser* (Supplementary Table S1, available in the online Supplementary Material), discerning them from the two other variants, which are positive for both *sea* and *edinA*, or *edin A* only, respectively (Monecke *et al.*, 2011). The complete microarray data is presented in Supplementary Table S1.

Discussion

The establishment of CA-MRSA as a cause of infections in healthy individuals is a matter of great concern. Because of their high virulence capability, skin infections with PVL-positive MRSA can rapidly progress to tissue necrosis and severe necrotizing pneumonia with a high mortality rate, and are additionally associated with increased risk of transmission (Boyle-Vavra & Daum, 2007).

Previous studies addressing the epidemiology of CA-MRSA in Europe indicate that most infections are caused by a limited number of specific clones with the European clone (ST80-IVc, t044, PVL^+) predominating (Chua *et al.*, 2011; Otter & French, 2010). In recent years, a changing trend in the epidemiology has been registered, which is characterized by a high level of genetic diversity and the predominance of clones USA300 (ST8-IVa and variants), the European clone and the Taiwan clone (ST59-IVa and variants) (Rolo *et al.*, 2012). By contrast, the clone described in this report is related to the international HA-MRSA 'classical' paediatric clone first reported in a paediatric hospital in Portugal in 1992 (Oliveira *et al.*, 2002). This finding is supportive of the notion of geospatial diversity of currently circulating CA-MRSA strains.

The prevalence and characteristics of PVL-positive CA-MRSA in Switzerland is unknown because CA skin infections are rarely characterized. Overall, the precise prevalence of CA-MRSA is likely to be higher than reported because primary manifestation of infection consisting of the spontaneous appearance of a raised tender red lesion often leads to the suspicion of a spider

Table 1. Molecular and phenotypical characteristics of CA-MRSA isolates from the patients (MN-10 as a representative) and from the carrier (MN-02)

Isolate no.	Patient (age)	Sample	Body location	SCC*mec* type	*spa*	ST/CC	PVL	Virulence-associated genes	Resistance profile
MN-10	Son (4 years)	Skin lesion	Knee	IV	t002	5	+	*egc, hl, hla, sak, scn, sea, sed, sei, sej*	P, FOX, E
MN-02	Father (44 years)	Nasal	Right nare	IV	t002	5	+	*egc, hl, hla, sak, scn, sea, sed, sei, sej*	P, FOX, E

P, penicillin; FOX, cefoxitin; E, erythromycin.

bite in regions where such occurrences are common, such as North America and Australia (David & Daum, 2010; Stryjewski & Chambers, 2008). Most reports of such lesions have come from the USA and have not been reported as frequently from other countries. In Switzerland and other countries where spider bites are rare, these lesions may be often mistaken by patients for mosquito bites, as described in this report.

As illustrated by this case, healthy asymptomatic individuals can serve as reservoirs for this clinically significant and virulent pathogen, causing repeated transmission among family members. Although PVL-positive MRSA is rarely found in asymptomatic carriers (Monecke *et al.*, 2009), this report suggests that the prevalence may be higher than hitherto understood and illustrates the need to test the social environment of an affected patient for MRSA colonization. The occurrence of PVL genes in MRSA with ST5 is of concern because of its high capacity to spread easily and hence its epidemic potential (Müller-Premru *et al.*, 2005; Sola *et al.*, 2012)

There is evidence that increased colonization in the community may be responsible for infiltration of CA-MRSA into hospital settings, blurring the boundaries between HA- and CA-MRSA (Stryjewski & Chambers, 2008; Wilson *et al.*, 2010), as exemplified by cases of transmission of a CA-MRSA from the community to a neonatal ward and a teaching hospital in Switzerland (Sax *et al.*, 2006; Valsesia *et al.*, 2010).

Consequently, community-based healthcare providers such as family doctors play a key role in transmission prevention. This case highlights the importance of increased awareness when dealing with recurrent skin infections affecting either individuals, or individuals closely associated with each other, as in a family setting.

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