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Multiple Cases of Familial Transmission of Community-Acquired Methicillin-Resistant *Staphylococcus aureus*

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The worldwide emergence of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) can have severe public health implications. Familial transmissions of CA-MRSA in The Netherlands were investigated. Among the families studied, two clusters of CA-MRSA could be identified. This report demonstrates that family members can serve as reservoirs of CA-MRSA which may become a serious problem in containing the spread of MRSA.

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major pathogen causing nosocomial infections worldwide. MRSA strains have largely been confined to hospitals and long-term care facilities but are also emerging in the community (22). The differentiation between community-acquired MRSA (CA-MRSA) and hospital-associated MRSA is becoming difficult since CA-MRSA could spread into hospitals (25). CA-MRSA causes primary skin infections, mainly furunculosis and abscesses, but can also cause necrotizing tissue infections and fulminant pneumonia in young and previously healthy individuals (4, 11, 18, 23). Most CA-MRSA isolates contain the virulence factor Panton-Valentine leucocidin (PVL) and carry staphylococcal cassette chromosome *mec* (SCC*mec*) type IV or V. The combination of the PVL loci, the *mecA* gene, and the spread of CA-MRSA makes this MRSA a well-adapted pathogen. It is of interest to see to what extent PVL-MRSA transmission within families occurs, especially in families with young children. Transmission of MRSA between patients receiving health care and family members (1, 6, 24) and case reports of intrafamilial spread of CA-MRSA have been described (3, 9, 16, 19). However, typing data from these familial MRSA transmissions is limited or even unknown.

The aim of this study was to determine the intrafamilial transmission of CA-MRSA in The Netherlands during a 2-year period (2003 and 2004). Approximately 10% of all Dutch MRSA isolates carry the genes for PVL (25). The MRSA strains associated with familial transmission were characterized by pulsed-field gel electrophoresis (PFGE) (13), protein A (*spa*) typing (5), multilocus sequence typing (2), SCC*mec* multiplex PCR (7, 15), and accessory gene regulator (AGR) typing (10). A toxin profile PCR was also determined (12). For the detection of exfoliative toxin D, oligonucleotides were developed on the basis of the nucleotide sequence deposited in the GenBank database under accession no. AB057421. The sequences of the exfoliative toxin D forward and reverse primers were 5′-ACTATCATGTATCAAGGATGGC-3′ and 5′-CAA ATCAGTTCCTTGTCCAT-3′, respectively. Both primers were used at a concentration of 0.8 μM. Family transmission was defined as two or more members within a family, living at the same postal address, who were colonized with an MRSA strain having the same PFGE type. In 2003 and 2004, 10 PVL-MRSA familial transmissions were found. In 7 out of the 10 families, skin infections were reported, and in 6 families a link with a foreign country was noted. The transmissions involved at least two family members, up to four members within a family of six. A total of 27 MRSA isolates were studied. The results (Table 1) showed that all MRSA strains within a family had the same typing characteristics, indicating the transmission of CA-MRSA within families. In 7 of the 10 families, it involved transmission from parent to child or vice versa. In two cases of parent-child transmission, it involved two affected siblings (families 3 and 6), and in one case three siblings were affected (family 10). In two cases (families 6 and 10), some family members were colonized with a PVL-negative MRSA (data not shown). Interestingly, in family 10 the PVL-negative MRSA of the mother (age 36) and one sibling (male, age 3) had the same PFGE type as the PVL-positive strains of the father and three siblings. No further typing of the PVL-negative strains was performed. Presumably, the MRSA strains of the father and siblings obtained PVL bacteriophages (14). This hypothesis was strengthened by the fact that the upper band in the PFGE pattern of the PVL-negative MRSA strains was about 41 kb smaller, approximately the size of a PVL phage genome.

Remarkably, twice the MRSA strains of two families (families 1 and 6 and families 4 and 8) had identical typing characteristics. MRSA strains with PFGE type 50A (according to the Dutch PFGE nomenclature classification) are rare in our national MRSA database. Further investigation revealed that families 1 and 6 lived in the same neighborhood. This indicates a possible spread of an MRSA strain not only within a family but also between families. Whether there is any relationship between the two families is unknown. Families 4 and 8 lived in different areas of The Netherlands.

Seven out of the 10 families could be grouped into two clusters: the well-known ST8 (USA300) clone and the ST59 CA-MRSA clone. Remarkably, all MRSA strains with ST8

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TABLE 1. Characteristics of family members colonized with PVL-positive MRSA[a]

Family and patient gender[b] (age [yr])	PFGE type	*spa* type	MLST[c]	SCC*mec* type	AGR type	Toxin profile[d]
1						
M (36)	50	t437	59	V	1	SEB
F (31)	50	t437	59	V	1	SEB
FS (0)	50	t437	59	V	1	SEB
2						
M (29)	46	t008	8	IV	1	LukED
MS (8)	46	t008	8	IV	1	LukED
3						
F (28)	297	t441	59	NT[e]	1	SEB
FS (5)	297	t441	59	NT	1	SEB
FS (2)	297	t441	59	NT	1	SEB
4						
M (57)	218	t008	8	IV	1	LukED
F (48)	218	t008	8	IV	1	LukED
5						
M (42)	206	t008	8	IV	1	LukED
F (41)	206	t008	8	IV	1	LukED
6						
M (40)	50	t437	59	V	1	SEB
MS (2)	50	t437	59	V	1	SEB
FS (0)	50	t437	59	V	1	SEB
7						
M (68)	28	t131	80	IV	3	ETD
F (68)	28	t131	80	IV	3	ETD
8						
M (39)	218	t008	8	IV	1	LukED
F (38)	218	t008	8	IV	1	LukED
FS (3)	218	t008	8	IV	1	LukED
9						
M (37)	373	t313	30	NT	3	—[f]
F (36)	373	t313	30	NT	3	—
FS (0)	373	t313	30	NT	3	—
10						
M (39)	289	t355	377	V	1	—
FS (8)	289	t355	377	V	1	—
FS (5)	289	t355	377	V	1	—
MS (0)	289	t355	377	V	1	—

[a] All MRSA strains contained the *mecA* gene, the *S. aureus* fragment, and PVL genes and were negative for LukM.
[b] M, male; F, female; S, sibling.
[c] MLST, multilocus sequence type.
[d] Only genes, encoding the different toxins, which were positive in the PCR are shown.
[e] Only a *mecA* band detected.
[f] —, no toxins detected.

were *spa* type t008, SCC*mec* type IV, AGR type 1, and LukED positive (families 2, 4, 5, and 8). The PFGE types of the ST8 MRSA strains were 46, 206, and 218. These PFGE types are closely related (≥80%), indicating a clonal relatedness. This PFGE cluster is identical to the well-known PFGE USA300 CA-MRSA clone, which has been found in several outbreaks in the United States. Our findings confirm the recently described transatlantic spread of the USA300 clone (20, 26). A second MRSA cluster was also detected; the MRSA strains of families 1, 3, and 6 seemed to be related to each other as well. The MRSA strains in this cluster were ST59, either *spa* type t437 or *spa* type t441 (two closely related *spa* types), SCC*mec* type V or nontypeable, AGR type 1, and SEB positive. MRSA ST59 is also a well-known CA-MRSA which has been found in different parts of the world (8, 17, 25). MRSA ST80 was only found in one family. The ST80-IV clone is a well-known CA-MRSA in Europe (25, 27) and was also found in familial transmissions in Denmark (21).

In conclusion, transmission of community-acquired MRSA outside the healthcare setting poses a threat to public health and may be a serious problem in containing the spread of MRSA. This report demonstrates that family members can serve as reservoirs of PVL-positive MRSA and that transmission can occur among family members. The prevalence of family transmission is probably much higher than that described in this study because family members of a patient are not routinely tested for MRSA colonization. In 7 of the 10 families, young children no more than 8 years old were involved. When a child gets pneumonia, possibly preceded by flu-like symptoms, it is important to consider MRSA infection especially when one of the family members is known to be MRSA positive.

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