An outbreak of non-typeable MRSA within a residential care facility

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In a household setting within a residential care facility for visually and intellectually disabled people, a resident (index case) was diagnosed with dermal abscesses caused by a methicillin-resistant *Staphylococcus aureus* (MRSA) which was non-typeable by standard pulsed-field gel electrophoresis. In the process of 'search and destroy', all residents and staff in contact with the index case (a total of 200 people) were screened for MRSA. Five people (three personnel and two residents) carried non-typeable MRSA and were treated with antibiotics to eradicate the infection. The 'search and destroy' efforts did not result in the identification of a source. Goats and rabbits which were kept on the premises tested negative for MRSA. The condition of the index case is improving. Further restrictive measures were implemented within the facility to prevent wider spread of the MRSA. This discovery and spread within a residential care facility of a non-typeable MRSA which is often associated with livestock, is remarkable.

Introduction

A new methicillin-resistant *Staphylococcus aureus* (MRSA) isolate belonging to multi-locus sequence type ST398 was first described in a French study in 1998 [1]. No further reports concerning ST398 MRSA strains were mentioned until 2004, when a MRSA isolate belonging to ST398 was detected in the Netherlands [2]. This isolate could not be typed with *Sma*I pulsed-field gel electophoresis (PFGE) and was termed non-typeable MRSA (NT-MRSA). All NT-MRSA isolated so far belong to ST398.

Voss and colleagues were the first to report the isolation of NT-MRSA strains from people taking care of pigs [2]. Since then, NT-MRSA has become increasingly common among Dutch MRSA isolates. In 2007, 29% of the MRSA isolates forwarded to the Dutch National Institute of Public Health and the Environment (Rijksinstituut voor Volksgezondheid en Milieu, RIVM) belonged to this group of MRSA. Publications about a connection between NT-MRSA in various animal species and NT-MRSA in humans soon followed. A French study reported increased NT-MRSA carriage rate in pig farmers caused by transmission of the strain ST398 [1]. A later retrospective case-control study showed a strong association between human NT-MRSA carriage and contact with pigs or calves [3]. New data revealed that family members living on pig farms can also be NT-MRSA carriers, even when they have not been in direct contact with animals [4]. In reaction, screening of various animal species was performed. A survey of pigs in Dutch slaughterhouses showed that nearly 40% of the pigs were colonised with NT-MRSA ST398 [5]. NT-MRSA has also been isolated from horses and poultry [6,7].

On the basis of these results, it can be concluded that an NT-MRSA reservoir is established within a variety of animal species and could spread to humans. The emergence of NT-MRSA outside hospitals threatens the MRSA 'search and destroy' policy in Dutch healthcare facilities. It was considered only a matter of time before NT-MRSA would be transmitted from animals via farmers into healthcare settings. Indeed, both NT-MRSA colonisation of personnel and patients, and outbreaks within Dutch hospitals have recently been described [8-10]. It has been suggested that MRSA ST398 isolates are less virulent than other MRSA strains and have limited capacity to spread between humans, but recent reports have shown clinical manifestations of NT-MRSA such as wound infections [4] and endocarditis [11].

Here we describe an outbreak of NT-MRSA in a residential care facility for visually and intellectually disabled people.

One of the residents (index case) was diagnosed with abscessing acne and chronic hydradenitis in his armpits, loins, scrotum and between the buttocks. The index case was fully blind, had a severe intellectual disability and had been suffering from this skin condition since 2004. *S. aureus* isolated from wound swabs in the period between 2004 and 2007 were methicillin-sensitive. The patient was treated with several antibiotics (tetracycline, erythromycin, flucloxacillin, trimethoprim/sulfamethoxazole, clindamycin, minocycline, rifampicin), but this did not result in a significant clinical improvement. In October 2007, the abscesses where surgically treated, in combination with vitamin A therapy, but without success. All swabs taken at that time were suddenly positive for MRSA. Additional screening showed that nose, throat and perineum were colonised with MRSA.

The risk of MRSA transmission within the residential care facility to other residents and personnel was considered high because the index patient had already suffered from staphylococcal disease for

a long period. In the Netherlands, active 'search and destroy' efforts are taken to stop further transmission of MRSA within healthcare settings. The residential care facility therefore contacted the department of infectious diseases of the local municipal health service for advice. A multidisciplinary outbreak team was set up to asses all possible routes of MRSA transmission within the facility, and to identify all at-risk contacts of the index case.

Methodology and results

Assessment of the risk of MRSA transmission

The index patient lived in a household-like setting together with seven other residents and 15 staff members. Other contacts included staff members who also worked at various other units within the residential care facility, such as doctors and nurses, household, day care and facility personnel. The unit consisted of two groups living separately but sharing sanitation. The whole residential care facility has 35 units, situated in various buildings on the premises.

The outbreak team decided to screen all residents living and personnel working in the same unit as the index case, as well as doctors, nurses and family who had been in direct contact with the index case. A total of 43 people were identified as being at risk. Nose and throat cultures were collected from all those screened. In addition, perineum and/or wound cultures were set up from samples from residents.

Preventive measures

In order to reduce the risk of further MRSA transmission, hygienic measures were implemented around the index case. His private room as well as the sanitation area he was using were disinfected daily, and nurses wore gloves, aprons and surgical masks during direct contact with the index case. He started using a private shower and toilet within the sanitary room. No other residents were allowed in the sanitary room while the index case was there, and the room was cleaned with hypochlorite after he used it. The index case's social contacts with other residents who lived in other units were restricted to a minimum, organised group day care was changed into private day care, and the whole unit is considered contaminated until the cultures of all included individuals are MRSA negative.

Screening results

Two other residents and three staff members from the same unit as the index case tested positive for MRSA. Three of them had positive nose cultures only, one had positive nose, perineum and skin cultures, and one person was MRSA-positive in nose and

Table 1

Antibiogram of isolates from residents and staff, NT-MRSA outbreak, the Netherlands, 2007

	Resident A (index)	Resident A (index)	Resident B	Resident C	Staff A	Staff B	Staff C
Date of sample	**Nov 2005**	**Oct 2007**	**Oct 2007**	**Oct 2007**	**Oct 2007**	**Oct 2007**	**Oct 2007**
Penicillin		R	R	R	R	R	R
Flucloxacillin	S	R	R	R	R	R	R
Gentamicin	S	R	R	R	R	I	R
Trimethoprim/ Sulfamethoxazol	S	S	R	R	R	S	R
Doxycylin		R	R	R	R	R	R
Erythromycin	R	R	R	R	R	R	R
Clindamycin	R	R	R	R	R	R	R
Rifampicin		S	S	S	S	S	S
Fusidine acid		S					

S: sensitive; R: resistant; I: intermediate sensitive.

Table 2

Isolate typing, NT-MRSA outbreak, the Netherlands, 2007

	Resident A (index)	Resident A (index)	Resident B	Resident C	Staff A	Staff B	Staff C
Date of sample	**Nov 2005**	**Oct 2007**	**Oct 2007**	**Oct 2007**	**Oct 2007**	**Oct 2007**	**Oct 2007**
Spa-type	Not done	t2383	t011	t2383	t011	t2383	t2383
SSC*mec*	Not done	IV	IV	IV	IV	IV	IV*
PVL	Not done	Negative	Negative	Negative	Negative	Negative	Negative
MLST	Not done	ST398	ST398	ST398	ST398	ST398	ST398
PFGE *Sma*I	Not done	NT	NT	NT	NT	NT	NT
PFGE *Crf9I*	Not done	**	**	**	**	**	**

* SSC*mec* typing by multiplex PCR-typing according to the method of Kondo *et al.* [12] showed a PCR product for multiplex 1 and 3, but not for multiplex 2.
** PFGE *Crf*9I is shown in Figure 1.
PVL: Panton-Valentine leucocidin; MLST: multi-locus sequence typing; PFGE: pulsed-field gel electophoresis.

throat. These results indicated considerable MRSA transmission within the unit and prompted the expansion of the ring for MRSA screening to the relevant direct contacts of all six MRSA-positive individuals. This resulted in the screening of a further 160 people. In this group, no new MRSA infections were detected; the outbreak seemed to be restricted to the unit of the index case. Personnel who work at various units, such as cleaning personnel and medical doctors, did not test positive for MRSA.

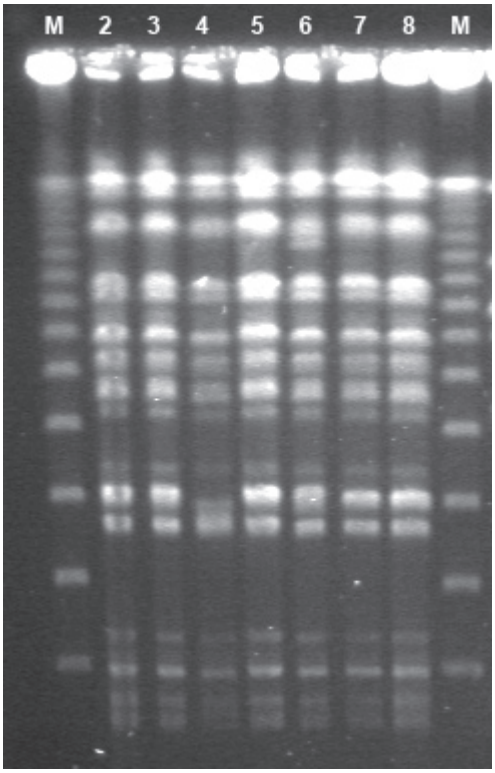
MRSA typing

In order to evaluate the transmission of MRSA strains, the bacterial isolates were typed. All six MRSA isolates had an almost identical antibiogram (see Table 1) and carried staphylococcal cassette chromosome *mec* (SSC*mec*) type IV* according to the method of Kondo *et al.* [12] (see Table 2).

All isolates were Panton-Valentine leucocidin (PVL)-negative and their genome did not contain the restriction site *Sma*I (Table 2). Therefore, they could not be typed by PFGE using *Sma*I and were considered NT-MRSA. In PFGE analyses using the restriction enzyme *Crf*9I (a neoschizomer of *Sma*I that is less sensitive to methylation), all isolates showed very similar banding patterns (Figure 1).

Figure 1

PFGE of *Crf*9I macro-restriction fragments of non-typeable (ST398) isolates, NT-MRSA outbreak, the Netherlands, 2007



Lane 2: resident A (index), lane 3: resident B, lane 4: resident B, lane 5: staff B, lane 6: staff A, lane 7: resident C, lane 8: staff C.
M: molecular length marker.
PFGE: pulsed field gel electophoresis.

Spa-typing revealed two *spa*-types t011 and t2383, both belonging to the ST398 family, which in the Netherlands are primarily found among livestock (cattle and pigs) and people working with livestock (see www.spaserver.ridom.de). Two patients carried *spa*-type t011. The remaining four isolates, including the strain obtained from the index patient, had an uncommon *spa*-type t2383. Multi-locus sequence typing (MLST) confirmed that all strains belonged to the ST398 family (www.mlst.net).

Outbreak source and transmission

The index patient's laesions continued producing pus. The index could thus have functioned as a reservoir and may have maintained the outbreak. It is unclear if the index was the source of the outbreak.

This outbreak in a residential care setting indicates that NT-MRSA is also a public health issue. NT-MRSA is most often associated with direct contact with pigs or calves [4,13], but none of the MRSA-positive individuals had any contact with livestock. However, rabbits, chickens and goats were living on a farm on the premises of the residential care facility. The outbreak team decided to screen the goats and rabbits because various animals have been described as a source of MRSA and there had been sporadic contact between the residents and these animals. All cultures of the animals' anterior nares (three goats and four rabbits) were MRSA-negative.

A definite source for the NT-MRSA could not be traced. The outbreak of NT-MRSA was most probably caused by direct human to human transmission facilitated by the intensive contact between the residents and staff living and working in the unit. The contact between staff and clients is randomly organised, frequent and intense. An exact route of NT-MRSA transmission within the unit is therefore indistinct. Furthermore, there was no significant difference between MRSA-positive and negative staff regarding the intensity of physical contact with MRSA-positive residents.

MRSA eradication

To eradicate the MRSA, all MRSA-positive residents and staff (except the index case) were given oral and topical therapy (mupirocin nose gel and washing with chlorhexidine for five days), followed by three successive control cultures taken from the nose and throat. MRSA-positive residents were temporarily banned from group activities and MRSA-positive staff had to stay at home during the period of eradication. The residents' sanitary room and sleeping rooms were cleaned daily. Also hand-touch sites, such as door handles were thoroughly cleaned on a daily basis. All control cultures taken after completion of the eradication therapy tested MRSA-negative.

The preventive measurements were restricted to the unit of the index case. To date, the index patient is being treated with a combination therapy with rifampicin and trimethoprim/sulfamethoxazole and surgical incision of the abscesses. The skin laesions are slowly diminishing, and recent cultures taken from wounds, nose and throat in late December were MRSA-negative. Once his skin laesions have healed, eradication therapy will be started.

Discussion and conclusions

This MRSA outbreak in a residential care setting highlighted particular challenges. Firstly, the healthcare setting described in this article is not a hospital, but a permanent care facility for people with visual and intellectual disabilities. The outbreak

caused commotion among the staff members, and they had a lot of practical questions as they were unfamiliar with MRSA and an MRSA-outbreak in particular. Furthermore, it turned out that the use of gloves, surgical masks and aprons during washing and clothing was perceived as threatening by the clients.

The restriction of the index case's social contacts was difficult implement. His wounds were resolving slowly, and hygiene measures were lifted to some extent after six months. In addition, follow-up samples of the wounds proved to be MRSA-negative under antibiotic treatment. It was therefore decided that after careful bandaging of the wounds, social contacts could be allowed within the unit.

To our surprise, two different *spa*-types were discovered by molecular typing. The rare *spa*-type t2383 only contains the first two repeats (08-16) of the seven repeats present in the t011 gene (08-16-02-25-34-24-25). Considering that the strains share the same antibiogram and have very similar PFGE patterns, it is tempting to speculate that the initial introduced strain had *spa*-type t011. It could very well be that one of the individuals carrying the t011 strain was the primary source for the other case. After a deletion of five repeats, this strain could then have colonised the cases infected with the t2383 strain. Alternatively, we can not exclude that both *spa*-types were introduced independently.

NT-MRSA is not only a Dutch problem, but has been discovered in a number of European countries, as well as in Canada, China and Singapore [14-16]. *Spa*-type t2383 (Figure 2) is a rare relative of t011 (Figure 3) (see https://mrsa.rivm.nl/flash/flash.aspx).

NT-MRSA transmission from human to human is relevant for the impact of NT-MRSA in public health care. Inter-human transmission of NT-MRSA has been described earlier within families of animal farmers [2] and on a larger scale in patients and personnel of a Dutch hospital [9]. This outbreak within a non-hospital healthcare setting adds proof for the potential of NT-MRSA for inter-human transmission. Therefore, NT-MRSA might be able to gain a foothold in the human population.

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An earlier report of this outbreak was published in Dutch [17].

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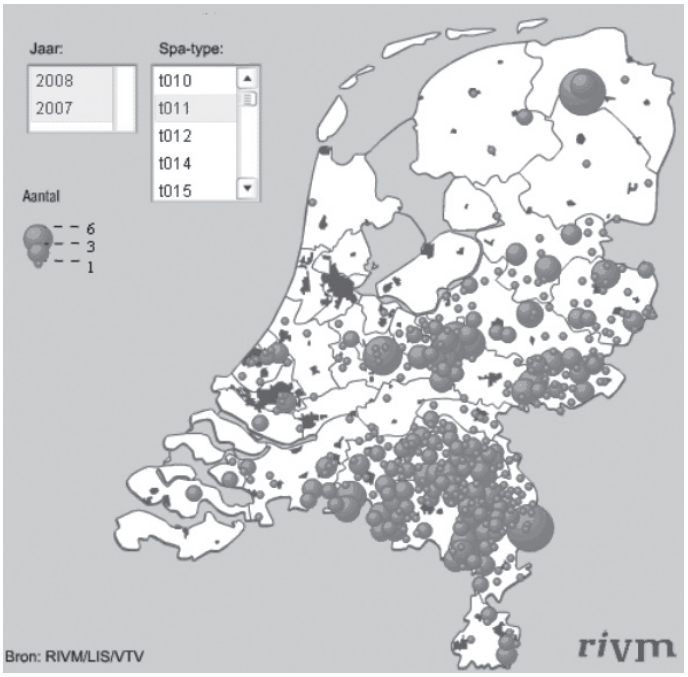
Figure 2

NT-MRSA *spa*-type t2383 isolated in the Netherlands in 2007-2008

Figure 3

NT-MRSA *spa*-type t011 isolated in the Netherlands in 2007-2008



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