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Occupational acquisition of methicillin-resistant Staphylococcus aureus in humans – A description of MRSA carrier and infected cases from the Region of North Jutland in Denmark

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Abstract

Since 2006 in Denmark, there has been a statutory order on physicians' notification of methicillin-resistant Staphylococcus aureus (MRSA). Occupational cases notified in North Denmark Region in 2008 and 2009 were analysed. Overall, 109 cases (54 females and 55 males) were notified, of whom 56 were infected and 52 cases were carriers, whereas in one case the status was unknown. The most prevalent clonal complex (CC) was 398 (n=26; 23.9%), followed by CC5 (n=17; 15.6%), CC30 (n=14; 12.8%), and CC8 (n=12; 11%). Eighteen cases were occupational with a predominance of CC398 (n= 16; 88.8%); CC8 and CC22 accounted for one case each. There was a significantly higher proportion of occupational cases for CC398 compared with other clonal complexes (p<0.001). All CC398 occupational cases were either farmers or farm workers occupied in swine confinement buildings. The two other cases were nurses working in the region's public hospitals. Most occupational cases were carriers (n=15; 83%). Three were infected, two with impetigo and one with tonsillitis; CC398 was the causative agent in all three cases. CC398 has a porcine reservoir which is huge in Denmark with a total annual production of 27,700,000 pigs. The presented population-based retrospective study shows an infectious potential of CC398 in humans. Close monitoring of future trends in prevalence, occupational distribution and pathogenicity is still warranted.

Key words

MRSACC398, swine production, occupation

INTRODUCTION

Methicillin-resistant Staphylococcus aureus (MRSA) was first isolated in 1961 [1] and distinguished itself by the modified penicillin-binding protein PB2a which is encoded by the *mecA* gene. *MecA* is located on one of the to-date known 18 types of staphylococcal chromosomal cassettes that vary greatly in size [2]. For several decades, MRSA was considered primarily as a hospital-associated pathogen, but during the last decade MRSA has become a prominent cause of community acquired infections [3, 4]. Despite this changing role, environmental or occupational risk factors have rarely been pinpointed. However, some recent studies have addressed an association between MRSA infection and occupation, such as personnel working in health care and nursing homes [5, 6], veterinary facilities [7], penitentiaries and military accommodations [8], pig confinement buildings [9], and horse stables [10].

Since 2006 in Denmark, there has been a statutory order on physicians' notification MRSA, and in the presented population-based study, occupational cases in the North Denmark Region were ascertained in 2008 and 2009.

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MATERIAL AND METHODS

In January 2009, the Region North Denmark had 580,515 inhabitants. All the residents of the region have access to universal tax-supported health care provided by general practitioners and public hospitals. Since 1 November 2006, all Danish physicians have been legally bound to notify any MRSA carriage and infection in humans. For all incident cases, a paper form is sent to the physician in charge of the patient; the form has to be returned to the National Centre for Antimicrobial and Infectious Control, Statens Serum Institute. Diagnostic microbiology is provided by the Department of Clinical Microbiology at Aalborg Hospital. Isolates of S. aureus were screened for methicillin resistance with a cefoxitin disc diffusion assay (NeoSensitabs, Rosco, Denmark) on Mueller-Hinton agar. All resistant isolates were referred to the National Reference Laboratory at the Statens Serum Institute for confirmation and *spa* typing [11]. Clonal relationships were routinely inferred on the basis of *spa* types.

Data analysis. All incident cases of MRSA carriage and infection reported in the period January 2008 – December 2009 to the National Centre for Antimicrobial and Infectious Control, Statens Serum Institut, Copenhagen, from North Denmark Region were analysed.

Information was obtained on age, gender, status (carrier vs. infection), clonal relationship of MRSA, occupations defined as relevant for transmission of MRSA, and relation to work. Risk occupations are listed in Table 1.

Table 1. Occupations defined as relevant for transmission of bacteria

Social care workers
Daycare mother
Employed in nursery
Employed in kindergarten
Employed in school
Employed in recreation centre
Employed in refugee camps, detention centres, etc.
Employed in prisons
Employed in other social institutions
Service (+home help)
Health care workers (humans and animals)
Surgeon
Doctor (excluding surgeons)
Nurse employed in hospital or medical clinic
Nurse employed in nursing homes or in a home
Midwife
Laboratory technician
Dentist, dental technician, dental assistant
Health worker also employed in a hospital or medical clinic
Health worker also employed in nursing homes or home care
Pet and animal care
Other public servants
Uniformed Corps and the like (police, customs, emergency services, military, etc.)
Sewage and refuse collector
Transport workers
Railway worker
Sailor
Food industry workers
Slaughterhouse worker
Employed in other food industry
Farmer

Categorical variables were analysed by means of Chi square test and Fisher exact test. A level of 5% was taken as statistically significant.

RESULTS

The findings are summarised in Table 2. In total, 109 cases were notified, with a mean age of 37.1 years (range 0.3-91 years) with the highest mean age among cases affected by CC22 and lowest among ST 152/377. 54 cases (49.5%) were females and 55 were males (50.5%). In 56 cases (51.4%), infection was notified, while in 52 cases (47.7%) carrier status was described. In one of the reported cases (0.9%) there was no information of status.

Table 2. The distribution of reported cases according to clonal complexes, age, gender, occupation and clinical status.

Bacteria type	N	Mean age in years (min. – max.	Gender M/F	Occupational/ Non- occupational	Infection/ carrier
CC398	26	29 (2-59)	16/10	16/10	8/18
CC22	7	49 (8-69)	3/4	1/6	5/2
CC30	14	35 (16-66)	7/7	0/14	9/5
CC8	12	46 (15-91)	5/7	1/11	7/5
CC1	3	46 (17-66)	1/2	0/3	1/2
CC12	3	29 (21-45)	1/2	0/3	1/2
CC45	1	44	1/0	0/1	1/0
CC5	17	39 (0.3-66)	8/10	0/17	9/8
CC72	6	33 (3-72)	4/2	0/6	4/2
CC80	8	39 (1-67)	4/4	0/8	5/3
CC88	9	26 (0.4-66)	3/6	0/9	4/4*
CC97	1	52	1/0	0/1	1/0
ST 152/377	2	26 (19-33)	1/1	0/2	1/1
Total	109	37.1 (0.3-91)	55/54	18/91	56/52

*One case not categorised.

18 cases were reported as occupational, and CC398 accounted for 16 of these cases (88.8%), 1 was CC8 (5.60%), and 1 was CC22 (5.6%). When analysing for the distribution of occupational cases across the different clonal complexes, there was a significantly higher proportion of occupational cases among the CC398, compared with all the others ($p<0.001$).

There were no significant differences between the prevalence of clonal complexes and infection/carrier status. CC398 was the most prevalent type (n=26; 23.9%), followed by CC5 (n=17; 15.6%), CC30 (n=14; 12.8%), and CC8 (n=12; 11%).

Details for 18 reported occupational cases of MRSA are listed in Table 3. All 16 CC398 cases were farmers or farm workers occupied in swine confinement buildings, while the other 2 cases (CC22 and CC2) were nurses working in hospitals. 15 (83.3%) of the cases were carriers and 3 (16.7%) were infected. The infected cases were all associated to MRSA CC398, in 2 to impetigo and in 1 with tonsillitis. No difference in age or gender distribution was observed among the different occupational cases.

Table 3. Distribution of reported occupational cases according to clonal complexes, age, gender and clinical status

Bacteria type	N	Mean age in years (min. – max.)	Gender M/F	Job or Occupation	Infection/ carrier
CC398	16	32.5 (19-58)	11/5	Farmers	3/13
CC22	1	48	1/0	Nurse	0/1
CC8	1	52	0/1	Nurse	0/1
Total	18	34.4 (19 – 58)	12/6		3/15

DISCUSSION

Of the 109 cases of MRSA notified in North Denmark Region in 2008-2009, 18 (16.5%) were reported as occupational. CC398 accounted for 16 of these, all of whom were farmers, whereas 1 case each of CC22 and CC8 afflicted hospital nurses.

The occupation as nurse and as hospital or nursing home staff has been associated with MRSA carrier status or infection. In a study from Iran among health care workers, the occupation as nurse was independently associated to MRSA carriage (odds ratio 3.6, 95% CI 1.3-9.7) [5], and a German study [6] identified 17 cases of occupational disease with MRSA infections predominantly among staff in hospitals and nursing homes. The most frequent infection sites were ears, nose, and throat, followed by skin infections.

Only MRSA CC398 (3 cases) were associated to infection; the other cases were notified with carrier status. It is essential for the interpretation of the notification data that the quality of the data is high. It is appreciated that the routinely collected data may be of inadequate quality for scientific purposes. The cases notified will have different sources from clinical samples, contact tracing, screening of risk groups, and clinical presentation (disease, colonisation). Therefore, the findings based of these data ought to be considered with care, especially epidemiological analysis, as clearly stated

in a recently published study from Sweden [12]. Despite this reservation and recognizing the limited number of observations in the presented study, it is surprising to observe both the dominance of the MRSA CC398 as an occupational transmitted bacteria and the clinical importance. It has been stated that the MRSA CC398 may cause more colonization than infection, than other *S. aureus* [13]. However, the data in the presented study does not support this assumption, since all cases of infection (2 cases of impetigo and 1 case of tonsillitis) were linked to the MRSA CC398. This subtype has been recognised in animals since 2004 and first described in Danish slaughter pigs in 2007 [14], and especially pigs may serve as a reservoir for a new type of MRSA in humans; MRSA CC) 398 [15]. The bacteria consists of 8 multilocus sequence typing (MLST) types, with (ST)398 type as the most prevalent, and the other closely related protein A (*spa*) gene types (i.e., t011, t034, t108, t567, t899, and t939) [16]. Although transmission may primarily appear to be between animals, data has been published describing colonization and infection with MRSA CC398 among subjects living and working on farms, especially pig farms [17]. An increased risk of colonization and infection of MRSA CC398 by occupation horizontal transmission occurs in families occupied with swine production [18]. It is not known whether MRSA CC398 has the same potential for colonizing or infecting humans as the hospital acquired (HA) MRSA, but localised infections, such as abscesses [19, 20], wound infections [21, 22], and conjunctivitis [23] have originated from MRSA CC398, as well as invasive infections, such as osteomyelitis [24] and postoperative infections [25].

There has been an increase in Denmark of notified cases of MRSA from a total of 727 cases and 9 MRSA CC 398 cases in 2006, to a total of 1,050 cases and 105 MRSA CC 398 cases in 2010 [26, 27]. The reason for the increase is not known but might be associated with increased awareness followed by contact tracing and screening of risk groups. In the same period, the use of antibiotics and ß-lactam stable antibiotics in swine production has increased from 3.2 ADD kg/kg and 6 ADD kg/kg (Animal Daily Dose/ kg animal/kg meat) in 2001 to 4.2 ADD kg/kg and 9.5 ADD kg/kg in 2009 [26]. This increase might explain the increase in MRSA CC 398 cases, e.g. the use of $ZnCl_2$. $ZnCl_2$ is used in the water and fodder for pigs to ensure high weight gain and low frequency of diarrhoea Aarestrup et al [28] found that 74% of the MRSA CC398 isolates had reduced susceptibility to $ZnCl_2$ involving the gene *czr*C. This gene is strongly associated with SCCmec type V, the most prevalent SCCmec-type in MRSA CC 398. The use of $ZnCl_2$ might therefore select for MRSA CC398.

Recent Danish data [26] have identified 13% positive nasal swab samples (101 of 789 pigs at slaughterhouse) from 100 Danish farms, and 81 of the isolates were spa-typed and 93% were CC398.

CONCLUSION

Recognising that the total production of swine in Denmark in 2009 was 27,700,000 [29], there is a huge bacterial reservoir with unpredictable infectious consequences. We therefore face an infectious occupational exposure of huge quantitative dimensions but of unknown clinical importance. Well-designed epidemiological studies that focus on MRSA CC398 infection and carrier status, as well as risk factors among subjects working in swine confinement buildings, ought to be encouraged in order to provide solid data on the health consequences due to this rural occupational exposure.

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