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Surveillance report

EMERGENCE OF A NEW COMMUNITY ACQUIRED MRSA STRAIN IN GERMANY

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Analysis of community-acquired methicillin-resistant Staphylococcu aureus (c-MRSA) from Germany producing the Panton-Valentir leukocidin revealed a unique SmaI-macrorestriction pattern, differe from epidemic nosocomial strains. This molecular pattern correspon to those shown in c-MRSA strains from other countries in the Europea Union. All isolates exhibited resistance to fusidic acid, which is code by the far-1 gene. From data on geographical dissemination and time occurrence, this strain appears to have emerged in Germany in th second half of 2002, and so an already wider dissemination is likel The emergence of MRSA with resistance to fusidic acid is a first sign the emergence of a PVL-positive MRSA clone.

Introduction

The majority of Staphylococcus aureus isolates from deep skin infections, particularly furunculosis, and also from community-acquired necrotising pneumonia, possess the determinant for Panton-Valentine Leukocidin (lukS-lukF; 1, 2). True community-acquired methicillin-resistant S. aureus (c-MRSA) described up to now has often been isolated from skin infections and possess lukS-lukF (3, 4, 5) c-MRSA. Since the first reports (6), c-MRSA has spread further in North America, and has caused outbreaks of skin infections in the community and in prison inmates (7, 8). The North American c-MRSA exhibits characteristic patterns of molecular typing, and possesses a SCC-mec element of type IV and the lukS-lukF-determinant (9).
Community-acquired MRSA has been also reported from Australia (10). As indicated by MLST typing, c-MRSA from Australia is different from the North American strain although it also possesses SCC-mec IV and lukS-lukF (9).

The first data on true c-MRSA in Europe came from Finland where three different strains were recorded (11). Later in 2002, a French study described 1 cases of c-MRSA infection, including several cases of furunculosis and two fata cases of pneumonia (4). Six of the patients lived in Lyon, two in Algeria, and the rest in other French cities. The 14 isolates exhibited a unique pattern of characteristics with regard to SmaI-macrorestriction analysis, possessed lukS-lukF, and were resistant to oxacillin, kanamycin, tetracycline and fusidic acid (4).
A Panton-Valentine Leukocidin (PVL)-positive MRSA exhibiting the same SmaI-macrorestriction pattern has been observed among MRSA from sporadic nosocomial infections in the Netherlands (12). c-MRSA with comparable SmaI-patterns have also been detected in Norway (13) and Scotland, with demonstration of lukS-lukF (14).
In this paper, we report the emergence of lukS-lukF-positive MRSA in hospitals and in the community in Germany.

Methodology

Origin of strains

The German reference centre for Staphylococci operates a typing service for clinical microbiological laboratories located all over Germany. These laboratorie serve 221 hospitals and the general practitioners in the corresponding geographical areas. The reporting laboratory completes a form describing the type of infection, the affected unit in cases of nosocomial infection (clinical

discipline), and history with regard to previous stay in hospitals or long-term care facilities, and sends this to the reference centre with the staphylococcal isolate. The reference centre then performs typing on the isolate (phage typing for a first grouping followed by SmaI-macrorestriction patterns (for details see [15])). All isolates are also subjected to susceptibility testing by microbroth MI (16). MRSA exhibiting SmaI-macrorestriction patterns which are different from those of the known epidemic MRSA in central Europe (15) are furthermore characterised by spa sequence typing (www.ridom.de) and MLST-typing (www.saureus.mlst.net). They are also subjected to PCR detection of resistanc genes ([17] and for far1 [18]) as well as of pathogenicity associated determinants as tst, eta, etb, etc (19) and lukS-lukF. For detection of the lukS lukF determinant (coding for Panton-Valentine Leukocidin), primers according reference 1 were used. The specificity of this PCR was confirmed by sequencin (correspondence with sequence in gene bank accession no. X72700, methodology for sequencing as described previously [20]).

Results

Strain characteristics

MRSA possessing lukS-lukF isolates exhibited a unique SmaI-macrorestriction pattern that corresponds to patterns shown for the French, Scottish and Norwegian c-MRSA. They exhibit MLST-type 80 and a unique sequence of the X region of spa (r07, r23, r12, r34, r34, r33, r34). The pattern is strikingly different from those of epidemic MRSA prevalent in central European hospitals (Figure 1). Geographical regions and times of occurrence are shown in Figure 2

The isolates exhibited resistance to oxacillin (mecA), ciprofloxacin, oxytetracycline (tetM), and to fusidic acid (far1) with MIC ³ 4 mg/l (PCR demonstrated resistance genes in brackets).

Figure 1

***Sma*-I-macrorestriction patterns**

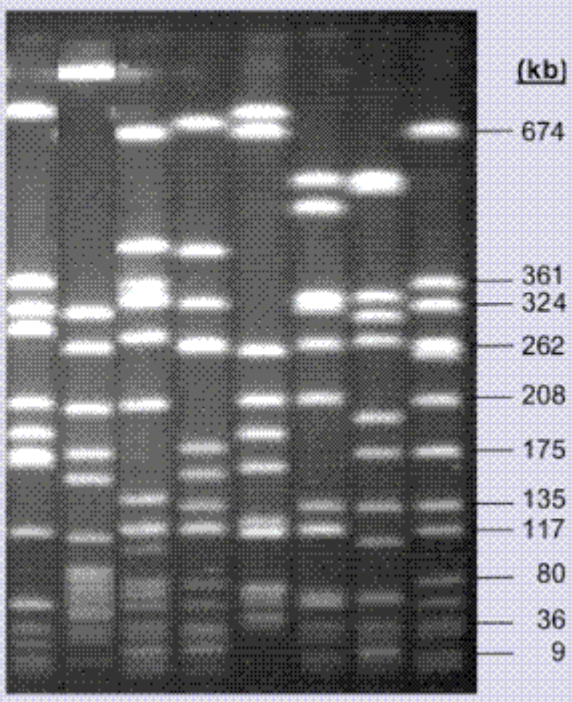

Figure 2

Geographical regions and times of occurrence of lukS-lukF positive MRSA in German hospitals (•) and in the community (*)

Emergence in hospitals and in the community
The strain obviously emerged in the second half of 2002, and was sent for typing from sporadic infections in nine German hospitals in different geographical regions. Of these isolates, five were from wound infections in surgery, medicine and dermatology, one from septicaemia, one from pneumonia and two from colonisation (one nose, one skin) in dermatological patients. None of these patients had had a previous stay in a hospital or a long -term care facility.
Between December 2002 and June 2003, four cases of skin infections with this strain in patients without previous hospitalisation have been recorded in different geographical areas of Germany. Patient 1 was a child in an Arab fami living in Germany. The child had a skin abscess, and varicella superinfection. Patient 2 was a woman who divided her time between Egypt and Germany wh had multiple skin abscesses. Patient 3 was a child in Greek family living in Germany. The child had impetigo, and skin abscesses had been seen in three other family members, although microbiological diagnostics had not been carried out on these three members. Patient 4 had a whitlow on one finger, which had obviously been acquired in Russia.

Discussion
As PVL-positive and fusidic acid-resistant MRSA had been isolated from patient in different, unrelated hospitals, we cannot exclude an already wider dissemination. As no PVL-negative MRSA exhibiting the same SmaI-macrorestriction pattern as the PVL-positive clone had previously been seen in S. aureus sent in for typing since 1994, and as this pattern is clearly different from patterns of methicillin-susceptible strains from cases of furunculosis (n = 26), acquisition of lukS-lukF by a pre-existing MRSA or of the mecA gene by a PVL-positive strain can be excluded. It is likely that the strain already known from France, Scotland, Finland, and probably Norway is widespread. No previous hospitalisation was known for the four outpatients affected. Whether the strain could have been acquired by family association with the Mediterranean area, as has been discussed for French community-acquired MRSA (4), needs to be established.
Of particular interest is resistance to fusidic acid encoded by the far1-gene in the MRSA strain described here. PCR for lukS-lukF is not generally performed i primary bacteriological diagnostics. As resistance to fusidic acid is quite rare in MRSA from central Europe (~3%; 22), the emergence of MRSA with fusidic aci resistance is a first signal for the emergence of the PVL-positive MRSA clone.
Another aspect is the therapeutic use of fusidic acid. Topical fusidic acid is use in dermatology for treatment of impetigo, atopical dermatitis and acne.
Although short-term treatment seems not to have an influence on fusidic acid resistance rates in *S. aureus* (23), the possibility that topical fusidic acid may l driving selection and dissemination of PVL-positive, fusidic acid resistant MRSA should be watched closely

In case of request the authors are prepared to carry out molecular typing of fusidic acid-resistant community-acquired MRSA from other countries.

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