Hospital acquired outbreak of methicillin-resistant *Staphylococcus aureus* infection initiated by a health care worker

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Infection nosocomiale par le *Staphylococcus auréus* méticilline résistant induite par le personel paramédical

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RÉSUMÉ

Pré-requis: Les infections nosocomiales à *S. aureus* résistant à la méticilline (SARM) constituent partout dans le monde un problème majeur de santé publique.
But : Devant le pic épidémique qui s'est déclaré entre 22 avril et le 11 juin 2002 dans le service de dermatologie de l'hôpital Charles Nicolle, une enquête épidémiologique a été menée.
Méthodes : Le typage des souches a été effectué par des méthodes phénotypiques et moléculaires afin de confirmer la présence d'une éventuelle épidémie hospitalière.
Résultats : L'enquête épidémiologique a permis de mettre en évidence un portage nasal de SARM chez l'une des infirmières responsables des soins des malades par typage moléculaire. Cette dernière a été immédiatement traitée par mupirocine, et l'épidémie a été ainsi jugulée.
Conclusion : Les épidémies nosocomiales à SARM constituent un problème alarmant. L'attitude à adopter est multidisciplinaire et repose sur le respect des mesures d'hygiène et la sensibilisation du personnel soignant.

Mots-clés

Staphylococcus aureus résistant à la méticilline (SARM) - Potage nasal - Epidémie - Electrophorèse en champ pulsé (ECP).

SUMMARY

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) has become an increasingly important pathogen leading to hospital acquired infections.
Aim: This study was done to confirm an outbreak of MRSA suspected at Charles Nicolle Hospital.
Methods : From 26 April to 11 June 2002, six patients hospitalized in the dermatologic ward at Charles Nicolle hospital of Tunisia have developed infections caused by MRSA. An investigation of the outbreak has been detected a nasal carriage nurse. This carrier received topical mupirocin treatment to decolonize the anterior nares and the outbreak was stopped without further incident.
Results Typing of the MRSA strains by pulsed field gel electrophoresis demonstrated the same pulsotype shared by all isolates showing that MRSA isolates belonged to a single clonal type responsible of outbreak. Colonized nurse was the source of MRSA dissemination.
Conclusion: This report illustrates the risk of nosocomial outbreak linked to cares delivered by the staff personnel. More sensibilisation and the respect of strict hygienic measures should be emphasized.

Key-words

Methicillin-resistant Staphylococcus aureus (MRSA), nasal carrier - Outbreak - Pulsed field gel electrophoresis (PFGE)

Methicillin resistant *Staphylococcus aureus* (MRSA) has become an important hospital acquired pathogen, with an increasing number of outbreaks reported worldwide (1, 2, 3). It is a major cause of morbidity and mortality (4). Humans are a natural reservoir for S. aureus and the anterior nares and skin are the usual sites of MRSA colonization. In health care facilities, patient to patient is the most common MRSA route of transmission and the contaminated hands or clothing of health care workers usually serve as intermediate transmission vectors (5) An increasingly rate of MRSA in the dermatologic ward of Charles Nicolle hospital have lead to more investigation to establish the possible presence of an outbreak.

MATERIALS AND METHODS

Outbreak investigation

From 26 April to 11 June 2002, a total of six patients had developed MRSA infections, all exhibited skin infection and one patient exhibited bacteremia. An epidemiologic investigation was conducted. Swab specimens were taken from anterior nares for culture.

Antimicrobial Susceptibly

The isolates were identified by conventional methods (Gram-positive cocci, catalase positive, mannitol fermenting and DNase-positive) and were confirmed as S. aureus by their ability to coagulate rabbit plasma (bioMérieux, Marcy l'Etoile, France) and produce clumping factor (Staphyslide test, bioMérieux). The biotype was determined by Api 20 Staph (bioMérieux, Marcy l'Etoile, France).

The antibiotic susceptibility of the isolates was performed using the disk diffusion method according to the NCCLS guidelines (6). The following antimicrobial disks were tested: penicillin (10UI), oxacillin (1μg), cefoxitin (30μg), amoxicillin + clavulanic acid (20/10μg), kanamycin (30μg), gentamicin (10μg), tobramycin (10μg), tetracyclines (30μg), chloramphenicol (30μg), ofloxacin (5μg), cotrimoxazole (1.25+23.75μg), erythromycin (15μg), clindamycin (2μg), vancomycin (10μg), rifampin (5μg) and fosfomycin (5μg). Methicillin resistance was confirmed by the MIC determination of oxacillin using E-test (AB biodisks). The detection of mecA gene was done by PCR as described previously (7).

Pulsed field gel electrophoresis (PFGE):

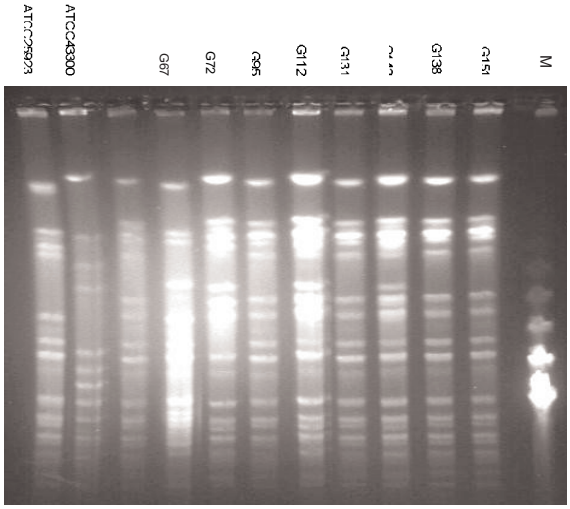
Genomic DNA was performed in a low-melting-point agarose plugs and digested with the SmaI restriction enzyme, as previously described by Murchan S et al (8). Electrophoresis was done with a contour clamped homogeneous electric field (CHEFDRII; Biorad, Ivry sur Seine, France). Run conditions were 180v during 23h, with switching from 7 to 37s at 14°C. For technique discrimination, 4 non epidemic strains were included: S. aureus ATCC 25923, S. aureus ATCC 43300, S. aureus G6 (an MRSA strain with the same phenotype isolated in the same ward far from the outbreak) and S. aureus G67 (an MRSA strain isolated during the outbreak with a different phenotype). PFGE patterns were analyzed as described by Tenover et al (9).

RESULTS

The demographic and clinical data of the six patients are described in Table I. Cultures of anterior nares from nursing staff and physicians working in this ward revealed an MRSA nurse carrier. Topical mupirocin was prescribed for the nurse and one week after, swab nares culture failed to find MRSA. No further cases of MRSA infections were detected by subsequent monitoring.

Microbial investigations showed the same biotype and antibiotype for all isolates that carried mecA gene and exhibited high MICs values (≥ 256μg/L). The PFGE patterns of the isolates from all patients and the nurse were indistinguishable (Table I and Figure1).

Figure1: PFGE of SmaI macrorestriction fragments of MRSA isolates. Lane 1: ATCC25923, lane 2: ATCC43300, lane 3: S. aureus G6, lane 4:S. aureus G67, lanes 5, 6, 7, 8, 9, 10 demonstrate identical banding patterns shared by MRSA strains from the six epidemic strains, lane11: isolate from the anterior nares of nurse, lane 12: molecular weight marker: Lambda DNA



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of outbreaks and has become endemic in many regions where it adds to the morbidity, mortality and cost of care associated with hospital acquired infection (13). Although MRSA outbreaks directly attributed to patient care equipment is rare, the hospital environment and inadequate cleaning have been identified as factors in several MRSA outbreaks (14, 15).

In the current study, we report a local outbreak of MRSA infections occurred in dermatologic ward, where MRSA is an uncommon problem. The potential source of contamination was successfully identified by the current epidemiologic investigations (screening for nasal carriage) and comparison to the patients isolates by routine microbiologic methods (biotype,

Table I Characterization of MRSA strains included in the study

Strain	Date of isolation	Origin	Specimen	Antibiotics															Pulsotype
				Oxa	Fox	Amp	Amc	K	G	Tb	Te	C	Ofx	Sxt	E	Cl	Van	Rif	Fos	
G72	26/04/2002	Patient 1	Skin	R	R	R	R	R	S	R	R	S	S	S	S	S	S	R	S	P1
G95	28/05/2002	Patient 2	Skin	R	R	R	R	R	S	R	R	S	S	S	S	S	S	R	S	P1
G112	06/06/2002	Patient 3	Skin	R	R	R	R	R	S	R	R	S	S	S	S	S	S	R	S	P1
G131	07/06/2002	Patient 4	Skin	R	R	R	R	R	S	R	R	S	S	S	S	S	S	R	S	P1
G138	08/06/2002	Patient 5	Skin	R	R	R	R	R	S	R	R	S	S	S	S	S	S	R	S	P1
G143	11/06/2002	Patient 6	Blood	R	R	R	R	R	S	R	R	S	S	S	S	S	S	R	S	P1
G151	19/06/2002	nurse	Nasal carriage	R	R	R	R	R	S	R	R	S	S	S	S	S	S	R	S	P1
G6	22/01/2002	Patient	Skin	R	R	R	R	R	S	R	R	S	S	S	S	S	S	R	S	P1
G67	16/04/2002	Patient	Skin	R	R	R	R	R	S	S	R	S	S	S	R	S	S	R	S	P2

Oxa: oxacillin, Fox: cefoxitin, Amp: ampicillin, Amc: amoxicillin+clavulanic acid, K: kanamycin, G: gentamicin, Tb: tobramycin, Te: tetracyclines, C : chloramphenicol, Ofx: ofloxacin, Sxt : cotrimoxazole, E: erythromycin, Cl: clindamycin, Van: vancomycin, Rif: rifampin, Fos: fosfomycin

antibiotype). This emphasizes the importance of routine surveillance for antimicrobial resistant microorganisms. The molecular analysis using PFGE has confirmed the spread of a unique epidemic clone and the implication of a health care worker. This method considered as the gold standard for epidemiological typing on bacterial isolates, including MRSA, is characterized by high reproducibility and resolving power (2, 8, 9, 16, 17, 18)

The strain isolated on January (G6b), exhibiting the same pattern than the one of epidemic strains, seems to have been transmitted to the nurse four months before. This is probably due to a variable expression of the accessory gene regulatory locus (agr). In fact, during colonization cell surface adhesins are maximally expressed. However, during infection the agr is activated, inducing the synthesis of toxins and tissue degrading enzymes that promote symptoms of disease (19).

Colonization of the nose with S. aureus is documented in up to 50 % of hospital personnel (12). Patient to patient transmission is well established but previously linked to asymptomatic carriage by health care workers (20, 21, 22, 23, 24). For the present study, an MRSA nasal carrier nurse was identified. This carriage was eradicated by topical mupirocin treatment for one week. The follow-up cultures from her anterior nares all became negative for MRSA. Thus, we successfully control the outbreak and no more new cases were observed. In a previous report, the results of double-blind, placebo-controlled studies confirmed that S. aureus nasal carriage was eliminated from 91% of health care workers 48-96h after completing a five day course of mupirocin calcium treatment applied to the anterior nares twice daily, 74% continued to have negative cultures several weeks later (4).

Overcrowding, limited space, nurse mix and absence of frequent hand washing between handling different patients, as noted in the dermatologic unit of Charles Nicolle hospital, constitute a general risk situation for the spread of resistant bacteria. The battle against the dissemination of these strains depends upon a health policy that recognizes the value of preventive measures (25). The importance of a multidisciplinary approach to control MRSA transmission must be emphasized including identification and isolation of all patients with MRSA colonization or infection, use of mupirocin for nasal carriers among healthcare workers and patients, strict adherence to hand washing, protocols and monitoring of compliance to these precautionary measures (26).

CONCLUSION

The spread of MRSA in hospital settings is favored by absence of hygienic measures that can lead to outbreaks. An active surveillance by the laboratory can help the infection control team in determining where to focus its efforts. Genomic DNA macrorestriction analysis is a useful complement to phenotypic methods for delineating epidemic isolates of MRSA, for identifying their nosocomial reservoir and for tracing their hospital spread (27, 28).

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