A nosocomial outbreak of community-associated methicillin-resistant *Staphylococcus aureus* among healthy newborns and postpartum mothers

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BACKGROUND: Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) has increasingly been isolated from individuals with no predisposing risk factors; however, such strains have rarely been linked to outbreaks in the hospital setting. The present study describes the investigation of an outbreak of CA-MRSA that occurred in the maternal-newborn unit of a large community teaching hospital in Toronto, Ontario.

METHODS: Screening and clinical specimens collected from mothers and newborns delivered during the outbreak period, as well as from staff on the affected unit, were submitted for microbiological testing. Computerized delivery logs and nursing notes were reviewed, and a case control study was conducted.

RESULTS: Analysis by pulsed-field gel electrophoresis revealed 38 babies and seven mothers with MRSA colonization and/or infection by the same unique strain (Canadian MRSA-10-related) from September to December 2004. Isolates were characterized as having the staphylococcal chromosome cassette *mec* type IVa and were positive for the Pantone-Valentine leukocidin gene. No one health care worker was associated with all cases; however, mothers and newborns exposed to one particular nurse (Nurse A) were almost 23 times (odds ratio 22.7, 95% CI 3.3 to 195.9) more likely to acquire MRSA than those with no such contact. MRSA was successfully isolated from Nurse A and from an environmental swab of a telephone recently used by Nurse A; both isolates matched the pulsed-field gel electrophoresis pattern of the outbreak strain.

CONCLUSION: The first nosocomial outbreak of CA-MRSA among healthy newborns and postpartum mothers in Canada is described. Effective control of sustained MRSA transmission within an institution may require prompt identification, treatment and monitoring of colonized and/or infected staff.

Key Words: Community-acquired MRSA; Pantone-Valentine leukocidin; SCCmec type IV

Éclosion nosocomiale de staphylocoque doré méthicillinorésistant associé à la communauté chez des nouveau-nés et des nouvelles accouchées en bonne santé

HISTORIQUE : Un staphylocoque doré méthicillinorésistant associé à la communauté (ou CA-MRSA pour community-associated methicillin-resistant *Staphylococcus aureus*) est isolé de plus en plus souvent chez des individus ne présentant aucun facteur de risque prédisposant. Toutefois, ce type de souches a rarement été associé à une éclosion en milieu hospitalier. La présente étude décrit l'enquête entourant une éclosion de CA MRSA survenue dans une unité d'obstétrique/néonatalogie d'un grand hôpital universitaire communautaire de Toronto, Ontario.

MÉTHODES : Les spécimens de dépistage et cliniques recueillis chez des mères ayant accouché durant la période de l'éclosion et leur nouveau-né, de même que chez le personnel de l'unité affecté ont été soumis à des analyses microbiologiques. Les compte rendus informatisés des accouchements et les notes des infirmières ont été passés en revue et une étude cas-témoins a été réalisée.

RÉSULTATS : L'analyse par électrophorèse sur gel en champ pulsé a révélé que 38 bébés et sept mères ont présenté une colonisation et/ou une infection à la même souche de MRSA (liée au MRSA-10 canadien) entre septembre et décembre 2004. Les isolats se sont révélés dotés d'une cassette chromosomique *mec* du staphylocoque de type IVa et ils étaient positifs à l'endroit du gène de la leucocidine de Pantone-Valentine. Aucun travailleur de la santé n'a été associé à lui seul à tous ces cas; par contre, les mères et les nouveau-nés exposés à une infirmière en particulier (infirmière A) étaient près de 23 fois (rapport des cotes 22,7, IC à 95 %, 3,3 à 195,9) plus susceptibles de contracter le MRSA que ceux qui n'avaient pas été en contact avec elle. Le MRSA a été isolé avec succès chez l'infirmière A et dans un prélèvement provenant de la surface d'un téléphone récemment utilisé par l'infirmière A. Les deux isolats correspondaient à l'isolat de la souche associée à l'éclosion identifiée par l'électrophorèse sur gel en champ pulsé.

CONCLUSION : La première éclosion nosocomiale de CA-MRSA chez des nouveau-nés et des nouvelles accouchées en bonne santé au Canada est décrite ici. La lutte efficace contre la transmission soutenue du MRSA dans un établissement peut nécessiter une identification, un traitement et une surveillance rapides du personnel colonisé et/ou infecté.

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The transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) in the health care setting has been frequently documented among high-risk populations. In pediatric patients, risk factors for MRSA colonization or infection include prior hospitalization, premature birth or low birth weight, chronic underlying diseases, prolonged or recurrent exposure to antibiotics, and invasive or surgical procedures (1,2). Newborns, especially those born prematurely and those requiring specialized care, are thus highly susceptible to infection with this organism; for this reason, outbreaks of MRSA have routinely been reported in neonatal intensive care units (NICUs) (3-6).

In recent years, however, MRSA has emerged as a source of skin and soft tissue infections in the community, and has increasingly been isolated from children and adults with no predisposing risk factors. Evidence suggests that these community-associated strains of MRSA (CA-MRSA) are genetically distinct from those associated with the health care setting and demonstrate different antibiotic susceptibilities (7-9). Transmission of CA-MRSA has been described in several community settings, such as child care centres (10), military bases (11), prisons (12,13) and school sports teams (14). Adding complexity to the epidemiology of MRSA, several reports have now documented the transmission of CA-MRSA in the hospital setting among patients with and without traditional risk factors for MRSA acquisition (15-22). However, nosocomial outbreaks of CA-MRSA have rarely involved healthy newborns and postpartum women (23-25).

In October 2004, an outbreak of CA-MRSA was identified among healthy discharged neonates and their mothers at a large community teaching hospital in Toronto, Ontario. Those affected had no known predisposing risk factors, and most were hospitalized for less than 24 h. The present article describes the investigation to determine the scope and source of this outbreak.

METHODS

Setting

Integrating four services on one floor, the maternal-newborn unit includes fetal assessment, labour and delivery, and postpartum and neonatal intensive care (24-bed level II NICU). Over 5000 deliveries are performed annually by family physicians, obstetricians and midwives, with assistance from the labour and delivery unit nursing staff. Following delivery, mothers are admitted to the postpartum unit; newborns are also admitted unless they require care in the NICU. Barring complications, both may be discharged home within 24 h to 72 h, depending on the method of delivery (eg, vaginal or caesarean).

Case finding

Mothers and babies: On October 13, 2004, the Infection Prevention and Control program (North York General Hospital, Toronto, Ontario) became aware of six babies with laboratory-confirmed MRSA infection who had been born at the hospital between September 30 and October 7, 2004, and were routinely discharged. All mothers who delivered during this time were contacted and advised to bring their newborns into the hospital to be screened for MRSA colonization or infection. Each infant was assessed by a physician and had screening specimens collected from three sites (eg, nasal, rectal and umbilical). When three additional infants and two mothers who had delivered after October 7 were identified as having been infected or colonized with MRSA, the screening clinics were expanded to include all mothers and

babies delivered at the hospital between September 29 and October 22, 2004.

As a result of ongoing media reports of the outbreak, several mothers and babies who had delivered before September 29 self-reported to the hospital. All mothers who gave birth between September 1 and September 28, 2004, were subsequently sent a letter advising them to seek medical attention if they had reason to suspect staphylococcal infection in themselves or their newborns.

Additional case finding efforts included enhanced surveillance for skin and soft tissue infections in neonates admitted to the inpatient pediatric unit and weekly screening of babies admitted to the NICU. Infection control professionals and physicians at other local hospitals, as well as pediatricians in the community, were alerted to monitor for infants with symptoms consistent with staphylococcal infections, and to report such cases to the hospital.

Because the source of the outbreak was not definitively established at the end of October 2004, a sentinel surveillance system was implemented. Selected obstetricians and pediatricians affiliated with the hospital were asked to obtain screening specimens from all the newborns seen in their offices (usually three to four days postdischarge). This enhanced surveillance by sentinel physicians was discontinued on November 15, 2004, in favour of routine laboratory-based surveillance.

Cases were defined initially as any mother or baby with delivery between September 29 and October 22, 2004, with a positive MRSA culture matching the outbreak strain (as determined by pulsed-field gel electrophoresis [PFGE]) isolated from either a screening specimen (colonized case) or a clinical specimen (infected case). This definition was later expanded to encompass both phases of the outbreak from September 1 to December 31, 2004. Secondary cases were defined as any mother or baby who either shared a room with an infected or colonized case or was admitted into a room previously occupied by a case within the previous 12 h.

Staff: After the initial cases were identified, the medical charts of the MRSA-positive newborns and their mothers were reviewed for staff contacts. Occupational Health was notified, and health care workers who had direct contact with the infected patients were screened. As additional cases were discovered, screening was recommended for all staff on the maternal-newborn unit and included the collection of both nasal and rectal swabs. Any employee with symptoms consistent with staphylococcal infection was assessed by Occupational Health, tested for culture, prescribed antibiotic treatment, and advised to remain off work until the infection resolved.

Laboratory testing

All screening and clinical specimens collected from mothers, newborn infants and hospital staff were submitted for microbiological testing to the Shared Hospital Laboratory in Scarborough, Ontario. All specimens were processed according to standard microbiological methodology. MRSA isolates were forwarded to a tertiary care hospital laboratory for fingerprinting using *Sma*-I digested PFGE. Representative isolates were tested for the Panton-Valentine leukocidin (PVL) and staphylococcal protein A (*spa*) genes, as well as for staphylococcal chromosome cassette *mec* (SCC*mec*) typing.

Environmental investigation

On October 14, 2004, the Infection Prevention and Control team's medical director and nurse manager conducted a thorough inspection of the hospital's maternal-newborn unit. No environmental

samples were collected because all units had undergone enhanced environmental cleaning the previous day.

Risk factor assessment

Computerized delivery logs, which were obtained for all births recorded during the study period, provided information on the mother's gestational age, date and time of birth, the infant's sex and birth weight, type of delivery, method of membrane rupture, use and type of anaesthesia, and the names of all health care workers in attendance at delivery. Computerized nursing notes for each of the mothers documented details on all nursing and/or medical interventions (eg, positioning, administration of fluids, medications, etc) experienced during their stay in the labour and delivery unit. Finally, paper-based medical charts were retrieved from the postpartum unit for all confirmed MRSA cases, and inpatient medical records were obtained for the mothers of all infected or colonized babies.

An epidemic curve was generated for mothers and babies with MRSA colonization and infection by date of delivery. A spot map was also plotted with the patients' postpartum room assignments. Statistical tests of significance were performed for all risk factor variables (eg, χ^2 test for categorical variables and Student's *t* test for continuous variables).

Case control study

A case-control study was conducted to identify potential risk factors associated with the acquisition of MRSA infection or colonization. All of the mother and baby pairs who went through delivery between September 29 and October 11, 2004, and were screened for MRSA were considered eligible. Cases were defined as any mother and baby pairs in which at least one person met the case definition for MRSA infection or colonization. Individuals meeting the definition of a secondary case were excluded from the analysis, as were those whose PFGE pattern results were either unavailable or not related to the outbreak strain. All of the non-cases (eg, both the mother and baby were screened as negative for MRSA) were included as controls.

The main exposure of interest was hypothesized to be direct contact with an infected or colonized health care worker. For each of the cases and controls, computerized delivery logs and nursing notes were reviewed, and the names of all health care workers with documented contact with the patient were extracted. Odds ratios (ORs) and 95% CIs were calculated for each health care worker based on three levels of exposure: presence at delivery only, documented contact in the nursing notes only (eg, provided nursing care in the labour and delivery unit), and both the presence at delivery and documentation in the nursing notes. Additional variables of interest included mother's gestational age, date and time of birth, the infant's sex and birth weight, type of delivery, method of membrane rupture, and the use and type of anaesthesia. Statistical tests of significance were performed for all risk factor variables (eg, χ^2 test for categorical variables, Student's *t* test for continuous variables and 95% CIs).

RESULTS

Case finding

Mothers and babies: Of the 356 babies delivered at the hospital between September 29 and October 21, 2004, a total of 336 (94.4%) were screened for MRSA; of these, 27 (8.0%) were confirmed to be positive.

Three additional newborns who were delivered before September 29, 2004, were brought to the hospital by their

mothers following media reports of the outbreak. Sentinel physicians reported no new cases, but laboratory-based surveillance led to the identification of a second cluster of 11 babies with confirmed MRSA who had been delivered between December 15 and December 31, 2004. Therefore, a total of 41 babies were confirmed to have MRSA between September 1 and December 31, 2004, of which 15 (36.6%) were infected and 26 (63.4%) were colonized.

Only 225 mothers (63.2%) who delivered at the hospital between September 29 and October 21, 2004, underwent screening for MRSA. In total, nine mothers were identified as having acquired MRSA (eight infected and one colonized), and seven of their babies (77.8%) were also infected or colonized. Despite repeated screening during the outbreak period, none of the infants admitted to the NICU tested positive for MRSA.

Six secondary cases were identified: two had shared a room with a confirmed MRSA case (within a range of 2 h to 20 h) and four were admitted into a room previously occupied by a confirmed case (within 3 h to 8 h after the case was discharged).

All the infected babies and mothers presented with skin and soft tissue infections, such as pustules, mastitis, breast abscesses and postcaesarean wound infections. No serious or invasive infections developed and no deaths were reported.

Staff: Of the 278 staff members identified as having direct contact with the maternal-newborn unit in the first phase of the outbreak, only 139 (50%) underwent screening for MRSA. This included 44.6% of the medical staff, and 63.8% of the nursing staff working in the labour and delivery unit and postpartum unit. The staff was informed of the outbreak and was simply asked to voluntarily undergo screening by occupational health and safety personnel, infection prevention and control personnel, or the unit administrator. None of the specimens collected from the 139 staff members tested positive for MRSA, including repeated screening of those identified by the case-control study.

Only one symptomatic health care worker (Nurse A) self-reported to Occupational Health during screening. Nurse A was experiencing a severe flare-up of eczema. In addition to nasal and rectal surveillance swabs, these skin lesions were superficially swabbed but were negative for MRSA. The assessing physician advised Nurse A to stay home from work for the next five days and prescribed a 10-day regimen of oral antibiotics. No mothers or babies delivered during this work absence were identified as having MRSA. Four babies delivered shortly after Nurse A's return to work subsequently acquired the organism. Simultaneously, a household contact of Nurse A was hospitalized with an MRSA-related skin infection. Clinical isolates from this household contact had the same unique PFGE pattern as the rest of the cases. Despite this circumstantial evidence and extra effort in the microbiology laboratory (eg, broth enrichment and prolonged incubation on several occasions), MRSA was not isolated from repeated screening samples from Nurse A during the first phase of the outbreak.

A retrospective review of the babies' delivery logs and nursing notes in the second phase of the outbreak discovered that Nurse A was linked to several cases. Finally, after repeated efforts in the laboratory, MRSA was isolated from Nurse A after broth enrichment. An environmental swab of a telephone recently used by Nurse A also tested positive for MRSA. Both isolates had the same PFGE pattern as the outbreak strain.

Laboratory testing

Molecular analysis revealed that 38 of the 41 babies (92.7%) and seven of the nine mothers (77.8%) with MRSA were infected or colonized with the same unique strain. The isolates were characterized as CMRSA-10-related, carried *spa* type 1 and the SCCmec type IVa, and were positive for the PVL gene (26). Antibigrams demonstrated resistance to beta-lactams, clindamycin, erythromycin and ciprofloxacin; the isolates were susceptible to vancomycin, gentamicin, rifampin, tetracycline, trimethoprim-sulfamethoxazole and mupirocin. Two newborns and one mother had PFGE patterns that were unrelated to the outbreak, and the isolates from one newborn and one mother were unavailable for molecular testing. Figure 1 presents the epidemic curve for the 45 cases (38 babies and seven mothers) with the same unique PFGE pattern.

Control measures

On October 13, 2004, after the first few cases were identified, enhanced environmental cleaning was initiated in the labour and delivery unit and the postpartum unit. Several commonly used items (eg, hand creams, ultrasound gels and petroleum jelly) were discarded, and dedicated supplies were provided to each room. Educational sessions were provided to staff to reinforce appropriate hand hygiene and cleaning of equipment.

On October 24, 2004, a baby who had been delivered on October 19 was admitted for treatment of MRSA infection. This indicated a possible failure of the aforementioned control measures and, therefore, blanket therapy for possible MRSA colonization was started (intranasal mupirocin ointment twice daily for five days). Regardless of screening status for MRSA, 238 (85.6%) of the staff on the maternal-newborn unit were provided with one course of the antibiotic. In total, 264 health care workers (95.0%) were either screened or received prophylaxis. Postpartum mothers and babies with delivery from October 24 to November 15, 2004, were also given prophylaxis.

Case-control study

During the study period of September 29 to October 11, 2004, there were a total of 195 live births, including one set of twins (eg, 194 mothers). A total of 183 babies (93.8%) and only 81 mothers (41.5%) underwent screening for MRSA; of these, five mothers and 22 babies (including five mother and baby pairs, and 17 single babies) were identified as having MRSA. However, only 24 mothers and babies (four mother and baby pairs, and 16 single babies) had the same unique PFGE pattern and were thus eligible for inclusion. Of these, four mother and baby pairs ($n=8$) and one single baby were excluded because they were deemed to be secondary cases. Fifteen cases were therefore included in the study. All noncases born during the study period in which the mother and baby had both been screened as negative for MRSA were included as controls ($n=70$).

Three health care workers in the labour and delivery unit, including Nurse A, were found to be significantly associated with increased odds of acquiring MRSA colonization or infection. The odds of acquiring MRSA were almost 23 times higher for mothers and babies with exposure to Nurse A (OR 22.7, 95% CI 3.3 to 195.9) than for those with no such contact. Direct contact with a second nurse (Nurse B, OR 8.5, 95% CI 1.0 to 83.58) and a physician (OR 8.7, 95% CI 1.8 to 43.1) were also associated with acquisition, although the odds were much lower than for Nurse A.

Figure 1 Epidemic curve for babies and mothers ($n=45$) with nosocomial methicillin-resistant *Staphylococcus aureus* (CMRSA-10-related, SCCmec IVa) colonization or infection by delivery date (September to December 2004)

Despite repeated screening with broth enrichment, MRSA could not be isolated from any of these three health care workers in October 2004.

DISCUSSION

To our knowledge, this outbreak is the first evidence of transmission of a community-associated strain of MRSA among healthy newborns and postpartum mothers in the Canadian health care setting. Genetically and phenotypically distinct from health care-associated MRSA, CA-MRSA often demonstrates susceptibility to numerous antimicrobial agents, including clindamycin, rifampin, tetracyclines and trimethoprim-sulfamethoxazole (7-9). CA-MRSA strains carry an SCCmec type IV or V that is uncommon in health care-associated MRSA isolates and is rarely found in contemporary hospital settings (7-9,24-26). In fact, in a study characterizing 117 CA-MRSA isolates from three continents (9), only two genes were unique and shared by all isolates: a type IV SCCmec and the locus for PVL.

PVL is a cytotoxin that causes leukocyte destruction and tissue necrosis, and has been associated with severe necrotizing *S aureus* infections that have proven to be fatal in some cases (7-9,15,16,19,27). Despite the presence of the PVL virulence factor, most CA-MRSA infections – especially those among healthy children – have resulted in skin and soft tissue infections that resolve with appropriate antibiotic treatment (17-22). Our cases had similar outcomes, and these outcomes have also been reported in other documented outbreaks of CA-MRSA affecting healthy newborns and postpartum mothers (24-26).

No staff member had documented exposure to all of the cases; however, based on the results of the case-control study, the temporal coincidence of removal from work with the cessation of cases, the household contact diagnosed with the same strain of MRSA and the fact that eczema is known to predispose to MRSA carriage (28,29), Nurse A was hypothesized to be the most likely source and/or amplifier of the outbreak. This hypothesis was later confirmed when MRSA of the same PFGE pattern was successfully isolated and cultured from screening specimens obtained from Nurse A during the second phase of the outbreak in December 2004. However, it is impossible to discern whether Nurse A introduced the organism into the

labour and delivery unit or whether it was introduced by another individual (eg, a staff member or patient) and then further transmitted by Nurse A, aided in part by environmental contamination.

There were several factors limiting our investigation. Active and passive case finding activities was only extended back to September 1, 2004, making it difficult to ascertain exactly when the outbreak started. As soon as the outbreak was identified, enhanced environmental cleaning was carried out in all areas of the maternal-newborn unit. This action precluded the investigators from collecting any environmental samples, thereby limiting the ability to study the role of the environment in the transmission of MRSA. The blanket use of nasal mupirocin in the absence of a confirmed colonized health care worker early in the outbreak made it difficult to subsequently isolate the organism from potential carriers. Finally, because the first six cases were newborns, screening of postpartum mothers was initially felt to be unwarranted. This decision effectively limited the number of mother and baby pairs available for inclusion in the case-control study because of the

potential for misclassification of an unscreened mother as a noncolonized or noninfected case.

Nosocomial transmission of MRSA in the health care setting, particularly among children and neonates with high-risk conditions, has frequently been recognized. Although new strains of MRSA affecting healthy children and adults have emerged in community settings in recent years, their introduction into the health care setting presents new challenges for infection control.

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