STERNAL WOUND INFECTION AFTER HEART OPERATIONS IN PEDIATRIC PATIENTS ASSOCIATED WITH NASAL CARRIAGE OF *STAPHYLOCOCCUS AUREUS*

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A cluster of six pediatric cases of deep-seated *Staphylococcus aureus* infection after heart operations prompted us to perform molecular typing of the *S. aureus* isolates by pulsed-field gel electrophoresis. This revealed the presence of genotypically distinct isolates in four of the six patients. Isolates of two patients were genotypically identical. All patients carried *S. aureus* in the anterior nares. In each patient, the banding pattern of deoxyribonucleic acid in these isolates was indistinguishable from that in strains isolated from blood or wound cultures. Molecular typing with pulsed-field gel electrophoresis ruled out nosocomial transmission of *S. aureus* between four patients; at the same time, it provided evidence for an association between nasal colonization and postoperative wound infection. Epidemiologic investigation of potential links between two patients with identical isolates did not provide any evidence for nosocomial transmission of *S. aureus* between these patients. Because nasal colonization with *S. aureus* may be a risk factor for surgical wound infection in pediatric patients undergoing heart operations, preoperative decolonization appears to be warranted. (J Thorac Cardiovasc Surg 1996;112:681-6)

The spectrum of sternal wound infections after heart operations ranges from superficial infections to severe, deep-seated infections.¹ The latter usually necessitate both surgical intervention and prolonged parenteral antibiotic therapy. Because of the potential seriousness of this complication, measures to reduce the risk of sternal wound infection are important. These include preoperative antibiotic prophylaxis, sterile surgical technique, and skin disinfection at the surgical site.

A cluster of six pediatric cases of deep-seated *Staphylococcus aureus* infection after heart operations prompted us to perform molecular typing of the *S. aureus* isolates cultured from blood and from

swabs from the sternal wound, various skin folds, throat, and nares. Surprisingly, our investigations (which were carried out for hospital infection control reasons) revealed nasal carriage of *S. aureus* with genotypes identical to those of the respective isolates from blood and sternal wound in all patients. These results and the recently documented association of *S. aureus* nasal carriage with an increased risk of sternal wound infection² raise a question regarding whether preoperative nasal decolonization is warranted as a prophylactic measure for all patients undergoing sternotomy.

Patients and methods

Patients. Patients with clinical evidence of *S. aureus* sternal wound infection after heart operations at the University Hospital of Zurich between January and May 1995 were included in this report. On suspicion of sternal wound infection, swabs or specimens of clinically relevant body sites or body fluids, as well as swab samples from nares, throat, axilla, and inguinal folds, were obtained for bacterial culture.

Microbiologic analysis. *S. aureus* was isolated and susceptibility testing was performed with standard microbiologic procedures.

Molecular typing. Pulsed-field gel electrophoresis (PFGE) was performed essentially as described by Back and coworkers,³ with some minor modifications as follows: After overnight growth of *S. aureus* isolates in laked blood broth, the bacteria were centrifuged to form pellets,

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Table I. Synopsis of six children with congenital heart disease and sternum osteomyelitis after cardiac operations

Patient	Sex	Age	Underlying disease	Surgical procedure	Bypass time (min)	Postoperative course	Signs of sternal wound infection
1	Boy	16 mo	Transposition of great arteries, pulmonary atresia, mitral atresia, atrial septal defect, Blalock-Taussig shunt	Hemi-Fontan, ligation of Blalock-Taussig shunt	140	Low-output syndrome, supraventricular arrhythmias, thrombosis of femoral artery	Day 24 after operation: fever, tachypnea and tachycardia, local swelling, hyperemia, and tenderness
2	Girl	14 mo	Tetralogy of Fallot, Down syndrome	Complete surgical repair	181	Low-output syndrome	Day 20 after operation: fever; local swelling, hyperemia, and tenderness
3	Boy	9 yr	Congenital aortic valve stenosis, aortic insufficiency (surgical valvuloplasty at 6 months)	Ross procedure with pulmonary homograft	89	Rethoracotomy for major bleeding on day 1; sternum closure on day 2; surgical removal of wound drainage on day 5; recurrent atelectasis of left lung	Day 4 after operation: fever, purulent discharge from sternal wound
4	Girl	5 mo	Tricuspid atresia, ASD, PDA; Blalock-Taussig shunt at 1 day	Blalock-Taussig shunt	0	Recurrent atelectasis, pleural effusion; cardiac failure	Day 24 after operation: fever, drainage from sternal wound
5	Boy	4 yr	VSD repair at 3 months; pulmonary stenosis	Resection of pulmonary stenosis, reconstruction of pulmonary outflow tract	53	Uneventful	Day 21 after operation: fever, local swelling, hyperemia, tenderness
6	Boy	1 mo	Interrupted aortic arch, VSD, PDA	Resection of coarctation, end-to-side anastomosis, VSD patch closure, PDA ligation	100	Low cardiac output, seizures, renal failure	Day 18 after operation: fever, local swelling, hyperemia

ASD, Atrial septal defect; PDA, patent ductus arteriosus; VSD, ventricular septal defect.

which were resuspended and mixed with 2% low-melt agarose and lysostaphin at 45°C. Agarose plugs were incubated with lysozyme, followed by digestion of bacterial deoxyribonucleic acid with *Sma*I.

PFGE was performed with a 1% agarose gel in 0.5× Tris-boric acid-ethylenediaminetetraacetic acid buffer at 12°C. Run conditions of the CHEF DR III system (Bio-Rad, Glatthbrugg, Switzerland) were 5 volts at an included angle of 120 degrees from an initial switch time of 5 seconds to a final switch time of 60 seconds. The run was terminated after 24 hours, and the gel was photographed after staining with ethidium bromide. Banding patterns were compared visually. According to criteria published by Tenover and associates,⁴ strains were considered genotypically indistinguishable if their restriction patterns had the same number of bands and the same apparent size.

Results

Clinical course. During the course of 5 months, we observed six pediatric patients with deep-seated sternal wound infections. A synopsis of the underlying diseases, surgical procedures, clinical presentation, microbiologic assessment, antibiotic regimens, and outcomes is given in Table I. The patients received 25 mg/kg intravenous cefazolin 30 to 60 minutes before operation. Although most patients had uneventful surgical courses, patient 3 had major venous bleeding at the surgical site and required packing of the wound and secondary closure of the sternum. The sternum of patient 6 was closed on the first postoperative day because of low cardiac output.

Bacterial isolates	Treatment	Outcome
<i>S. aureus</i> cultured from blood and swabs from sternal wound, throat, and nares	Surgical drainage, intravenous vancomycin and gentamicin for 2 days, then switch to intravenous flucloxacillin for 4 weeks	Cured
<i>S. aureus</i> cultured from blood and swabs from sternal wound and nares	Surgical drainage, intravenous flucloxacillin for 4 weeks	Cured
<i>S. aureus</i> cultured from blood, sternal wound, axilla, throat, inguinal fold, and nares	Surgical drainage, gentamicin implants, intravenous flucloxacillin for 4 weeks	Cured
<i>S. aureus</i> cultured from sternal wound, inguinal fold, throat, and nares	Intravenous flucloxacillin for four weeks; intermittent amoxicillin-clavulanic acid	Died 2 weeks later of cardiac failure
<i>S. aureus</i> cultured from sternal wound and nares	Surgical drainage; intravenous flucloxacillin for 2 weeks	Cured
<i>S. aureus</i> cultured from sternal wound, venous catheter site, and nares	Surgical drainage; amoxicillin-clavulanic acid (4 weeks) and intravenous aminoglycoside (2 weeks), gentamicin implants	

Signs and symptoms suggesting sternal wound infection became apparent between 4 and 24 days after operation (Table I). All six patients were febrile up to a temperature of 41° C, had leukocytosis with leukocyte counts between 19,600 and 24,000 cells/ μ l, and had elevated levels of C-reactive protein ranging from 40 to 175 mg/l (normal < 5 mg/l). In all six cases, *S. aureus* was recovered from the sternal wound. Three patients had blood cultures positive for this organism. Surgical revision of the sternum and a 4-week course of intravenous flucloxacillin (100 mg $\cdot$ kg⁻¹ $\cdot$ day⁻¹) or amoxicillin-clavulanic acid in combination with an aminoglycoside resulted in complete recovery in five cases. One patient died of cardiac failure 2 weeks after cessation of antibiotic therapy, without evidence for recurrence or persistence of sternal wound infection. During the same 5-month period 60 surgical repairs

with bypass were performed in pediatric patients. There was no correlation between bypass time and occurrence of sternal wound infection (data not shown).

Recovery of *S. aureus*. The results of bacterial cultures done on suspicion of sternal wound infection are presented in Table II. *S. aureus* was recovered from the sternal wound and nares in all six patients. Furthermore, *S. aureus* was isolated from throat swabs in patients 1, 3, and 4 and also from the axilla or inguinal fold in patients 3 and 4 (Tables I and II). The susceptibility patterns of the isolates of five of the six patients were identical. The isolates from patient 6 were sensitive to all antibiotics tested, including ampicillin. All other isolates were resistant to ampicillin but uniformly sensitive to oxacillin, flucloxacillin, cefazoline, gentamicin, amikacin, vancomycin, teicoplanin, and mupirocin.

Genotype pattern. Molecular genotyping by PFGE revealed that the *S. aureus* isolates from sternal wound and nares were identical for each patient but differed among patients, except for isolates from patients 2 and 4, which showed indistinguishable banding patterns (Fig. 1). As shown in Fig. 1, *S. aureus* isolated from blood (patients 1 through 3), skin (patient 4), and entry site of a venous catheter (patient 6) were genotypically identical with the strains isolated from the sternal wounds and nares of individual patients. On the other hand, the throat isolate of patient 1 was genotypically distinct from the other isolates from that patient (not shown).

Epidemiologic investigation of possible modes of transmission between patients 2 and 4. Although the same two members of the surgical department performed the surgical procedures on both patients, there was an interval of more than 3 months between the two operations. No common source of the *S. aureus* strain isolated from both patients was apparent.

Discussion

We observed a cluster of deep-seated sternal wound infections after heart operations in pediatric patients. The infections were significant in all six patients, resulting in bacteremia in three patients and necessitating surgical drainage in all but one. Preoperative antibiotic prophylaxis was used in all cases. Despite the fact that the infections occurred over a period of less than 5 months, the results of molecular typing by PFGE ruled out nosocomial transmission of *S. aureus* between patients in four of

Table II. Recovery of *S. aureus* in patients with sternal wound infection after heart operations

Site	Bacterial cultures for <i>S. aureus</i>					
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Blood	Positive	Positive	Positive	Negative	Negative	Negative
Sternal wound	Positive	Positive	Positive	Positive	Positive	Positive
Nares	Positive	Positive	Positive	Positive	Positive	Positive
Throat	Positive*	Negative	Positive	Positive	Negative	ND
Axilla	Negative	Negative	Positive	Negative	Negative	Negative
Inguinal fold	Negative	Negative	Positive	Positive	Negative	Negative

Patient 6 had *S. aureus* isolated at insertion site of venous catheter. ND, Not done.

*Genotype distinct from genotype of the other isolates from the same patient.

the six cases. Each of these four patients was colonized and infected with a distinct isolate (Fig. 1).

Two patients had genotypically identical isolates, but nosocomial transmission between these two patients is unlikely because they had no contact and were hospitalized during two separate months. Transmission originating from a common source, such as a carrier of *S. aureus* is an obvious concern. Our epidemiologic investigation discovered that two members of the health care team were involved in surgery and perioperative care in both cases. Both persons perform surgical procedures regularly and have not been found to be nasal carriers of this particular genotype of *S. aureus*; however, transmission from ancillary staff cannot be completely ruled out because medical records list only professionals directly involved in anesthesia and surgery. So far no additional cases of wound infection caused by this genotype have been detected. Because nasal cultures were not routinely obtained from all patients undergoing heart operations, we cannot exclude the possibility that additional patients who did not acquire infectious complications were also colonized with one or more of these strains. Colonization of the two patients with this particular strain during the preoperative stay in the Children's Hospital must also be considered.

An intriguing aspect of this case series is the fact that nasal colonization by *S. aureus* with a genotype identical to the genotype of isolates recovered from the sternal wound, and in some cases also blood and other sites, was present in all cases. At this point, it remains speculative whether nasal colonization was present before onset of infection or whether nasal colonization was the result of secondary spread from an infected site. Nonetheless, the role of *S. aureus* nasal colonization as a risk factor for the development of sternal wound infection after heart operations has recently been reported.² During a 3-year

period, 1980 patients undergoing elective heart operations were screened for nasal carriage of *S. aureus* before operation. Nasal carriage of *S. aureus* was significantly associated with the development of wound infection (odds ratio 9.6, confidence interval 3.9 to 23.7) compared with a control population without surgical wound infection. The phage typings of the available preoperative and postoperative isolates were identical. The other relevant risk factor in this study was insulin-dependent diabetes mellitus.² A similar prospective study is currently planned to investigate whether preoperative screening and decolonization of pediatric patients would result in a reduced rate of postoperative infections by *S. aureus*. This study will also examine possible risk factors for nasal colonization, such as prolonged preoperative hospital stay, prolonged intubation, stay in intensive care unit, antibiotic use, and contact with colonized health care workers.

Similar linkage of nasal carriage of *S. aureus* with postoperative wound infection was demonstrated by two studies published in 1959. Williams and coworkers,⁵ reporting on 722 patients, observed that the wound infection rate was 2% among patients without nasal carriage of *S. aureus* and 7.1% among carriers of *S. aureus*. Although this study did not specify the types of surgical procedures performed,⁵ Weinstein⁶ reported on 125 procedures, 101 of which involved the lung. Again, the wound infection rate was lower (1.2%) in the group with negative bacterial cultures of the nose than in the group with positive bacterial cultures (11.7%). Comparison of bacterial isolates by phage typing showed that the strains recovered from the infected wound and from the nares were identical.⁶ The rate of nasal carriage was 34% in Weinstein's study⁶ and 38% in the study published by Williams and coworkers,⁵ who in addition demonstrated that nasal carriage rate increased with prolongation of the preoperative hospital stay.

A more recent study in a surgical intensive care unit also demonstrated that nasal colonization by *S. aureus* was associated with a higher rate of infection caused by this organism.⁷ The observation that the systematic use of mupirocin nasal ointment in all patients admitted to the unit was temporarily associated with a significant reduction in the incidence of *S. aureus* infections lends further support to the postulate that nasal colonization precedes rather than follows colonization or infection at other body sites.⁷ The indiscriminate use of mupirocin in all patients admitted to intensive care units cannot be recommended, however, because such a practice might facilitate the development of resistance.⁸

Nasal colonization as a risk factor for infection at a distant site is not unique to surgery, however. Increased rates of infection in nasal carriers of *S. aureus* have been reported in patients infected with human immunodeficiency virus,⁹ users of illicit intravenous drugs,¹⁰ persons with diabetes,¹¹ and patients undergoing hemodialysis¹²⁻¹⁴ or peritoneal dialysis.¹⁵

In patients undergoing hemodialysis, attempts at nasal decolonization by topical decontamination with mupirocin have been successful.¹³ Mupirocin has been shown to effectively eradicate nasal carriage of methicillin-resistant *S. aureus* in most carriers.¹⁶ It is well tolerated and does not cause any significant side effects.¹⁷ The development of resistance in settings where this compound is used widely, however, may limit its usefulness in the future.¹⁸

To avoid the spread of mupirocin resistance as a result of wide use of this compound, the clinical indications for use should be clearly defined. A recent study by Kluytmans, Vandenberg, and Verbrugh¹⁹ indicates that mupirocin treatment may indeed result in a reduction of the rate of postoperative wound infections after heart operations. Conceivably, preoperative screening of patients followed by mupirocin treatment of nasal carriers of *S. aureus* could be a useful strategy to reduce surgical wound infections. Alternatively, certain risk groups could be targeted for screening, including patients with diabetes or renal insufficiency and pediatric patients with congenital heart disease. Patients in the last group typically have spent a relatively large amount of time in hospitals and other medical facilities, which may further increase the risk for nasal colonization.⁵

Finally, isolates from five of the six patients reported on here had identical susceptibility pat-

Fig. 1. Deoxyribonucleic acid fingerprints obtained for *Staphylococcus aureus* strains by PFGE of *Sma*I-digested bacterial deoxyribonucleic acid. Lowercase lambda (λ) indicates molecular size markers. Isolates from patients 1 through 6 are labeled according to source: nares, N; sternal wound, W; blood culture B; skin S; venous catheter site, C.

terns. They were all resistant to ampicillin but uniformly sensitive to all other antibiotics tested, including mupirocin. This fact also underlines the importance of molecular typing methods to distinguish among isolates and to determine whether further epidemiologic investigations focusing on nosocomial transmission are needed. This report shows that rapid investigation with molecular epidemiologic tools allows the clinician to rule out nosocomial transmission of *S. aureus* between patients. A time-consuming epidemiologic investigation of possible risk factors and modes of transmission was thus avoided in four cases, and efforts could be concentrated on the investigation of possible links between the other two patients. In addition, the discriminatory power of genetic fingerprinting clearly established the distinctness of isolates from individual patients, as well as the identity of various isolates recovered from single patients. This information formed the basis for the hypothesis that nasal colonization of pediatric patients undergoing heart operations may be a risk factor for the development of surgical site infection. On the basis of our observa-

tions, we suggest that the role of nasal colonization with *S. aureus* as a predisposing factor for postoperative infections in pediatric patients undergoing heart operations should be evaluated in a prospective study and that this study should include research into the effects of mupirocin on the rate of postoperative infections in colonized patients.

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