Pulmonary Manifestations in Children with Invasive Community-Acquired Staphylococcus aureus Infection

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(See the editorial commentary by Etienne on pages 591–3)

Background. Primary pneumonia and metastatic pulmonary infection have become more common in patients with invasive community-acquired Staphylococcus aureus disease at Texas Children’s Hospital (TCH; Houston).

Methods. In this study, we sought to describe pulmonary involvement in children with community-acquired S. aureus invasive infection and to determine whether the presence of genes encoding Panton-Valentine leukocidin (PVL) (luk-S-PV and luk-F-PV) and collagen adhesin (cna) is correlated with pulmonary manifestations. Patients with invasive staphylococcal infections admitted to TCH between 1 August 2001 and 30 June 2004 were studied. Chest imaging and postmortem examination reports were reviewed. Isolates were tested for the presence of genes encoding PVL and collagen adhesin by PCR.

Results. A total of 47 of 70 patients with community-acquired methicillin-resistant S. aureus (MRSA) infection had abnormal pulmonary imaging findings, compared with 12 of 43 patients with community-acquired methicillin-susceptible S. aureus (MSSA) infection (P < .001). Pneumonia and/or empyema, in addition to septic emboli, were the most common findings. Metastatic pulmonary disease occurred more frequently among patients with osteomyelitis. Severe necrotizing pneumonia was present in 3 children coinfected with influenza and parainfluenza virus. The presence of genes encoding PVL was investigated in 67 MRSA and 36 MSSA isolates. Abnormal chest imaging findings were observed for 51 of 80 patients with PVL-positive isolates, compared with 2 of 23 patients with PVL-negative isolates (P < .001). Only 2 isolates (both of which were MSSA) from patients with abnormal chest radiograph findings carried cna. PVL remained independently associated with abnormal chest imaging findings in patients with secondary pneumonia in a multivariate analysis (P = .03).

Conclusions. Pulmonary involvement is commonly observed in patients with invasive community-acquired S. aureus infections. Community-acquired MRSA may cause primary community-acquired pneumonia, as well as metastatic pulmonary disease. The presence of genes encoding PVL is highly associated with pulmonary involvement by S. aureus.

Staphylococcus aureus infections have increased significantly at Texas Children’s Hospital (TCH; Houston) since 2001. Currently, 76% of community-acquired (CA) staphylococcal infections at TCH are caused by methicillin-resistant S. aureus (MRSA) [1]. Skin and soft-tissue infections account for 95% of CA MRSA infections. More than 90% of the CA MRSA isolates represent 1 predominant clone, USA300 [2]. However, since USA300 has become the dominant clone and since the introduction of the conjugate pneumococcal vaccine, CA MRSA has replaced Streptococcus pneumoniae as the most common pathogen isolated from patients with complicated pneumonia at TCH [3]. Metastatic pulmonary infections also have become increasingly apparent in patients with invasive Staphylococcus disease at TCH, particularly those with bone and joint infections [4].

Several determinants of virulence have been described in staphylococcal isolates, and associations with certain disease processes have been postulated [5–7]. For example, Panton-Valentine leukocidin (PVL) has been associated with severe necrotizing pneumonia [8–11] and complications of osteomyelitis [12], and collagen adhesin (CNA), which plays a role in the adher-
ence of the bacteria to collagen [13], has been associated with bone and joint infections and with endocarditis [13–15]. More recently, an in vitro study performed on human airway tissue specimens suggested that S. aureus strains carrying genes encoding CNA (cna) and PVL (luk-S-PV and luk-F-PV) showed increased binding capacity to collagen, compared with strains lacking these genes, implicating a role for CNA and PVL in the pathogenesis of S. aureus necrotizing pneumonia [16].

S. aureus can invade the lung directly through the tracheobronchial tree (primary disease) or via hematogenous seeding (secondary disease) [17]. The objectives of this study were to describe primary and secondary pulmonary involvement in children with CA S. aureus invasive infection (either CA MRSA or CA methicillin-susceptible S. aureus [MSSA]) and to determine whether the presence of the genes encoding PVL and CNA in recovered S. aureus isolates correlates with pulmonary manifestations.

PATIENTS, MATERIALS, AND METHODS

Since 1 August 2001, we have prospectively identified Houston children at TCH with infection caused by CA S. aureus. S. aureus isolates recovered from these patients are obtained from the microbiology laboratory and then coded and frozen at −80°C in horse blood in the TCH infectious diseases research laboratory. Antibiotic susceptibilities to various agents (clindamycin, erythromycin, gentamicin, oxacillin, penicillin, trimethoprim-sulfamethoxazole, and vancomycin) are determined by the disk diffusion method and are categorized according to Clinical and Laboratory Standards Institute (CLSI) guidelines [18]. Clinical and demographic data for the patients are collected from the medical records and are recorded on a standardized form by a research nurse. The study protocol is approved by the institutional review board of Baylor College of Medicine (Houston).

Patients with invasive staphylococcal infection (i.e., osteomyelitis, pneumonia, septic arthritis, and lymphadenitis) admitted to TCH between 1 August 2001 and 30 June 2004 were selected from the database. Chest radiographs and available CT scans, as well as radiology reports, were reviewed. Abnormal findings by the radiologists were recorded. Postmortem examination reports and slides performed by the TCH pathology department were reviewed.

Isolates recovered from these patients were grown on tryptic soy agar plates containing 5% sheep blood (BBL; Beckton Dickinson), and DNA was isolated using the UltraClean Microbial DNA Kit (MO Bio Laboratories) as recommended by the manufacturer.

Detection of luk-S-PV, luk-F-PV, and cna by PCR was performed as described elsewhere [2]. Statistical analysis was performed using True Epistat, fifth edition (Epistat Services). For univariate analysis, dichotomous variables were analyzed by the χ² test or by Fisher’s exact test; continuous variables were analyzed by Student’s t test. Multiple logistic regression analysis was used to assess independent associations. A P value of <.05 was considered to be statistically significant.

RESULTS

Ninety-two patients with invasive CA MRSA infection and 68 patients with invasive CA MSSA infection during the study period were identified from our database. Seventy patients (76%) with CA MRSA infections underwent pulmonary imaging (chest radiography or CT) during hospitalization. Forty-three patients (63%) in the CA MSSA group underwent pulmonary imaging. Demographic characteristics and primary diagnoses are shown in table 1.

Forty-seven (67%) of 70 patients with CA MRSA infection who underwent pulmonary imaging had abnormal findings, whereas only 12 (28%) of 43 patients with CA MSSA infection who underwent pulmonary imaging had abnormal findings (P < .001).

Two patients in the CA MSSA group had findings consistent with reactive airway disease. Both patients had rhinovirus isolated from the respiratory tract. Although these patients were bacteremic with S. aureus, radiographic findings revealed interstitial markings consistent with reactive airway disease that were considered to be most likely due to viral disease. Both patients were excluded from further analysis.

Table 1. Characteristics of children with invasive community-acquired (CA) Staphylococcus aureus infection who underwent pulmonary imaging studies.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CA MRSA (n = 70)</th>
<th>CA MSSA (n = 43)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, median (range)</td>
<td>8.1 (0.07–18)</td>
<td>6.8 (0.01–15.2)</td>
<td>.23</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td>.31</td>
</tr>
<tr>
<td>Black</td>
<td>23</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>30</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>16</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td>.84</td>
</tr>
<tr>
<td>Female</td>
<td>23</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>47</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Primary diagnosis</td>
<td></td>
<td></td>
<td>.009</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>38</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Pneumonia and/or empyema</td>
<td>21</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Septic arthritis</td>
<td>3</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>8</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

NOTE. Data are no. of patients, unless otherwise indicated. MRSA, methicillin-resistant S. aureus; MSSA, methicillin-susceptible S. aureus.

* Pyomyositis and/or myositis, epidural abscess, paraspinal abscess, renal abscess, cervical lymphadenitis, and sepsis.

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Patients with invasive CA MRSA infection and abnormal chest radiograph and/or CT findings. Twenty-one (45%) of 47 patients with abnormal chest radiograph and/or CT findings received a primary diagnosis of pneumonia (table 2). Bacteremia occurred in 4 patients. Fourteen of these patients had empyema requiring video-assisted thoracoscopic surgery or chest tube placement. Three patients had uncomplicated pneumonia with bacteremia, and 4 patients had lung abscess (single or multiple). Two of the 4 patients with lung abscess and pneumonia had influenza A virus and *S. aureus* isolated from tracheal aspirates. One of these 4 patients died, and autopsy revealed necrotizing pneumonia and necrotizing tracheobronchitis (figure 1A).

Twenty patients (43%) received a primary diagnosis of osteomyelitis. The majority of these patients were bacteremic (85%). Atelectasis was revealed in 4 patients by chest radiography performed within 3 days after admission; 3 underwent chest imaging because of cardiorespiratory symptoms. Eight patients had pneumonia, of whom 3 also had effusions, and 4 had pneumatoceles. Six patients had septic emboli, and the remaining had multifocal air space disease or interstitial disease.

One patient who died was admitted to TCH with septic arthritis of the right knee, and a chest radiograph revealed numerous nodular lesions suggestive of septic emboli and an area of consolidation. Pathologic findings are shown in figure 1B. This patient had coinfection with parainfluenza virus 1. The radiographic features of all patients admitted with invasive disease are summarized in table 3.

Patients admitted to TCH with a primary diagnosis of pneumonia were significantly younger (mean age, 3.5 years) than patients admitted with other invasive CA MRSA disease and pulmonary manifestations (mean age, 9.9 years; *P* = .001) (table 2). Nine (45%) of the 20 patients with primary CA MRSA pneumonia were <1 year old.

None of the 7 patients with CA MRSA invasive infection and septic emboli revealed by chest radiography or CT had cardiac vegetations noted by transthoracic echocardiography, although 2 of these patients had deep thoracic echocardiography, involving the popliteal, femoral, and saphenous veins in lower extremities.

Patients with invasive CA MSSA infection and abnormal chest radiograph and/or CT findings. Only 2 of the 10 patients in this group received a primary diagnosis of pneumonia; both were complicated pneumonias with loculated empyema requiring chest tubes or video-assisted thoracoscopic surgery (tables 2 and 3).

Six patients with CA MSSA disease and abnormal radiograph findings had bone and/or joint infections. Three had radiographic changes consistent with septic emboli, 2 had multifocal airspace disease, and 1 had a lobar pneumonia. One of these patients died, and pathologic findings are shown in figure 1C and 1D.

Two patients with invasive CA MSSA had endocarditis. One patient had tricuspid valve endocarditis, and initial radiographic and CT findings were consistent with septic emboli. The other patient had aortic valve endocarditis, and diffuse interstitial edema was detected by radiography. The latter patient had a bicuspid aortic valve.

As in the CA MRSA group, patients admitted to TCH with a primary diagnosis of pneumonia were younger (mean age, 0.7 years) than patients with other invasive diseases (mean age, 12.1 years), although the small number of patients did not permit statistical analysis. When patients with CA *S. aureus* infection and abnormal pulmonary findings were grouped, patients with secondary pulmonary involvement caused by CA *S. aureus* were older (mean age, 9.82 vs. 3.36 years; *P* < .001) and more likely to be bacteremic (29 of 35 patients vs. 3 of 22 patients; *P* < .001) than were patients with primary pneumonia.

Findings of pathologic analysis. Postmortem examinations were performed on 3 patients who died from infection. One patient, an 18-month-old boy, had CA MRSA pneumonia com-

<table>
<thead>
<tr>
<th>Primary diagnosis</th>
<th>CA MRSA (n = 47)</th>
<th>CA MSSA (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of cases</td>
<td>No. of patients</td>
</tr>
<tr>
<td></td>
<td>diagnosed</td>
<td>with bacteremia</td>
</tr>
<tr>
<td>Pneumonia and/or empyema</td>
<td>21</td>
<td>4</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Epidural abscess</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Septic arthritis</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Othera</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

**NOTE.** MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*; NA, not applicable.

*a* Renal abscess, paraspinal abscess, and cervical lymphadenitis.
Figure 1. Histopathologic findings revealed by hematoxylin-eosin staining of specimens obtained from 3 patients with invasive *Staphylococcus aureus* infection. A, Necrotizing tracheobronchitis in the first patient, with extensive sloughing of the bronchial mucosa microscopically and scattered small bacterial colonies and individual cocci on the surface. The subepithelial connective tissue shows extensive necrosis with inflammatory and necrotic debris. These changes may be secondary to viral infection with influenza A in this patient. B, Lung tissue with patchy areas of hemorrhagic necrotizing pneumonia in the second patient, consisting of extensive intra-alveolar hemorrhage admixed with neutrophil infiltrates, karyorrhectic debris, and large bacterial colonies of cocci consistent with *S. aureus*. C, A well-formed thromboembolus in the third patient distends a degenerating vessel wall and is surrounded by hemorrhagic necrosis with bacterial colonies. Many vessels are distended by bacterial colonies admixed with blood, which is evidence of hematogenous dissemination (D). The surrounding lung parenchyma shows hemorrhagic pneumonia with frequent karyorrhectic material and loss of integrity of the alveolar walls.

Complicating influenza A virus respiratory infection. At autopsy, the lungs showed areas of hemorrhagic necrotizing pneumonia with abundant intra-alveolar bacterial colonies but no septic emboli. The presence of necrotizing tracheobronchitis was consistent with the concurrent influenza A virus infection (figure 1A).

A 15-year-old boy with history of right knee arthritis and right anterior tibial skin ulcers received a diagnosis of CA MRSA sepsis. An autopsy revealed microabscesses in the brain and kidneys, and in the lungs, there was widespread severe necrotizing pneumonia with abscess formation and abundant intra-alveolar bacterial cocci (figure 1B). There was also evidence of hematogenous dissemination, with sheets of intraluminal bacterial colonies admixed with blood within vessel lumens, which, in one area, were associated with thrombus formation. Other findings included hemorrhagic pulmonary edema, diffuse alveolar damage, and fibrinous pleuritis. This patient was coinfected with parainfluenza virus 1.

A third patient with secondary (hematogenous) infection was a 13-year-old boy with a history of left knee septic arthritis caused by CA MSSA. Autopsy revealed extensive multifocal hemorrhagic necrotizing pneumonia with abscess formation, diffuse alveolar damage, and septic emboli. Areas with organizing emboli showed degeneration of the vessel wall with abundant karyorrhectic debris and surrounding zones of bland infarction and necrotizing pneumonia (figure 1C). Multiple other vessels showed bacterial cocci distending the vessel lumens (figure 1D). The *S. aureus* isolates from all 3 patients carried the genes encoding PVL.

**Presence of luk-S-PV and luk-F-PV.** Figure 2 summarizes the pulmonary manifestations and primary sites of infection...
Table 3. Radiographic findings for patients with invasive community-acquired (CA) *Staphylococcus aureus* infection.

<table>
<thead>
<tr>
<th>Radiograph findings</th>
<th>No. (%) of patients with CA MRSA (n = 47)</th>
<th>No. (%) of patients with CA MSSA (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septic emboli</td>
<td>7 (14.8)</td>
<td>4 (40)</td>
</tr>
<tr>
<td>Pneumonia/effusion</td>
<td>10 (21.2)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Empyema</td>
<td>14 (29.7)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Lung abscess</td>
<td>4 (8.5)</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonia with pneumatoceles</td>
<td>4 (8.5)</td>
<td>0</td>
</tr>
<tr>
<td>Diffuse air space disease and/or increased interstitial markings</td>
<td>4 (8.5)</td>
<td>3 (30)</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>4 (8.5)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

**NOTE.** MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*.

In the CA MSSA group with normal chest radiograph findings, only 7 isolates (26%) carried the genes encoding PVL. The primary diagnoses for these patients were septic arthritis (2 patients), pyomyositis (2), cervical lymphadenitis (2), and epidural abscess (1). Isolates from 7 (78%) of 9 patients with abnormal chest radiograph findings carried the genes encoding PVL. The 2 isolates lacking PVL were from patients with either endocarditis or osteomyelitis.

There was no statistical association between the presence of *luk-S-PV* and *luk-F-PV* and the presence of pulmonary findings among patients with CA MRSA invasive disease. This finding is expected, because virtually all of the CA MRSA isolates recovered from children at TCH are of the same clone [2]. However, among patients infected with CA MSSA, which is not clonal to the same extent [2], those with abnormal chest radiograph findings were more likely to be infected with a strain carrying genes encoding PVL than were patients with no pulmonary manifestations (P = .02).

Overall, 51 of 80 patients with PVL-positive isolates had abnormal chest radiograph findings, compared with 2 of 23 patients with PVL-negative isolates (P < .001).

**Presence of cna.** The gene encoding CNA was not detected for 103 children whose isolates were available for testing and were separated according to PVL status and radiographic findings. Sixty-seven isolates were CA MRSA, and 36 were CA MSSA. The genes encoding PVL were present in all CA MRSA isolates but 1, which was obtained from a patient with pyomyositis and normal chest radiograph findings.

Figure 2. Pulmonary manifestations and primary sites of infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA) strains, according to the Panton-Valentine leukocidin (PVL) status. *Other findings included pyomyositis and/or myositis, epidural abscess, paraspinal abscess, renal abscess, cervical lymphadenitis, and endocarditis.*
in any of the CA MRSA strains isolated from patients with abnormal chest radiograph findings, which is consistent with results of previous analysis of the predominant clone [2]. In the CA MSSA group, 2 of 10 strains isolated from patients with abnormal chest radiograph findings carried cna: one was isolated from a patient with tricuspid valve endocarditis and septic pulmonary emboli, and the other was isolated from a patient with osteomyelitis and left lower lobe pneumonia. Both of these isolates carried luk-S-PV and luk-F-PV.

Univariate analysis revealed no differences between patients with normal chest radiograph findings and patients with abnormal chest radiograph findings (due to CA MRSA and CA MSSA infections) with respect to age, race, sex, and presence or absence of bacteremia. Multiple logistic regression analysis of age, race, sex, bacteremia, and the genes encoding CNA and PVL revealed that the presence of the genes encoding PVL remained independently associated with abnormal chest radiograph findings, after excluding patients who received a primary diagnosis of pneumonia (P = .03).

**DISCUSSION**

Pulmonary involvement caused by *S. aureus* infection has been well described [19–25]. In 1982, Chartrand and McCracken [22] described a series of 70 infants and children with *S. aureus* pneumonia in Dallas, Texas. We describe children with pulmonary manifestations of staphylococcal infection in the era of CA MRSA that appears to be associated with clones of *S. aureus* very different from the ones described previously [19–25]. In 1982, Chartrand and McCracken [22] reported a median age of 6 months for patients with primary staphylococcal pneumonia. Chartrand and McCracken [22] reported a median age of 6 months for patients with primary *S. aureus* pneumonia. Children in our study with primary CA *S. aureus* pneumonia were also younger than those with secondary pulmonary involvement. Although our patients were older (mean age, 3.5 years) than patients in the Dallas study, our observations suggest that primary *S. aureus* pneumonia remains predominantly a disease of early childhood.

Metastatic pulmonary disease was seen mainly in patients with bone and joint infections. Two of our patients with bone and joint infections caused by CA MRSA had deep venous thrombosis and had septic emboli detected by chest radiography. Several reports have previously described deep venous thrombosis in association with staphylococcal osteomyelitis resulting in septic pulmonary emboli [26–28]. Gorenstein et al. [26] described 3 children with acute disseminated staphylococcal infections and pulmonary findings who were found to have deep venous thrombosis. Felman and Shulman [19] described similar patients, but the presence of deep venous thrombosis was not investigated. Thus, deep venous thrombophlebitis should be considered in patients who present with musculoskeletal infections and septic pulmonary emboli.

Some authors recommend that echocardiography be performed routinely for adults with *S. aureus* bacteremia [29]. Four of 36 pediatric patients with *S. aureus* bacteremia had abnormal echocardiograph findings in one report from South Africa [30]. Clinical symptoms of endocarditis were absent in these children. Another prospective pediatric study demonstrated endocarditis in children with *S. aureus* bacteremia primarily in the presence of congenital heart disease as well as in indwelling catheters [31]. Two patients in our study had infective endocarditis. One patient had septic emboli and no structural heart defect, and the other had a bicuspid aortic valve. Routine performance of echocardiography for patients with *S. aureus* bacteremia is controversial [25, 32, 33]. However, it seems prudent to evaluate children for endocarditis when blood culture results are persistently positive (i.e., for >4 days) despite adequate antibiotic therapy or when findings consistent with pulmonary emboli are noted on chest radiograph images [31].

PVL, a pore-forming protein encoded by *luk-F-PV* and *luk-S-PV*, has been linked to severe necrotizing pneumonia (a condition with a high mortality rate) in France, Minnesota, and the Baltimore, Maryland, area [8–11]. The specific condition described in the aforementioned reports, consisting of a rapidly progressive necrotizing pneumonia with fever, leukopenia, and hemothysis that is preceded by viral symptoms, has rarely been observed at TCH, where the number of children with *S. aureus* pneumonia has increased during the past 5 years. Only 2 patients in our series presented with flulike symptoms and radiological findings indicating multiple sites of lung necrosis that were consistent with those described in France and Minnesota. Influenza A and PVL-positive CA MRSA strains were isolated from tracheal secretions obtained from these 2 patients, and both were leukopenic at the time of admission. Although no history of hemothysis was elicited from these patients, bloody secretions were noticed upon intubation. Autopsy of one of our patients revealed necrotizing pneumonia and necrotizing tracheobronchitis. Another patient who had necrotizing pneumonia revealed by pathologic analysis did not present with flulike symptoms, but parainfluenza virus 1 was isolated from cultures of tracheal aspirates obtained immediately after intubation. He was also leukopenic. Interestingly, chest radiography showed multiple nodular densities suggestive of septic emboli.

We found that the genes encoding PVL in *S. aureus* were highly associated with pulmonary manifestations in children with invasive staphylococcal infections, supporting the findings of other investigators that PVL may play a role in pulmonary tissue damage. However, most of the pulmonary manifestations in our patients were lobar pneumonia, pneumonia with pneumatoceles (nonsevere necrotizing pneumonia) [34], empyema, and septic pulmonary emboli; severe necrotizing pneumonia...
was observed in only 3 patients. In addition, all but 3 patients with invasive staphylococcal infection and pulmonary findings survived. As mentioned above, one of our patients had abnormal chest radiograph findings suggestive of septic emboli but had postmortem findings consistent with necrotizing pneumonia. This suggests that severe necrotizing pneumonia may not be suspected on the basis of clinical and radiographic findings alone, especially early in the course of the disease.

De Bentzmann et al. [16] recently showed that, once the airway epithelium is injured, PVL-positive S. aureus strains that also carry cna have an enhanced capacity to bind type I and IV collagen and laminin and that PVL does not directly cause the initial mucosal damage. A preceding viral infection is proposed as the initiating event in severe necrotizing pneumonia. The MW2 strain associated with pediatric deaths in Minnesota and North Dakota has been fully sequenced and contains both cna and the genes encoding PVL [35]. At TCH, a majority of the S. aureus isolates belong to 1 clone, which typically carries luk-S-PV and luk-F-PV but lacks cna. Investigation showed that all of the CA MRSA strains in this study lacked cna, which might, in part, explain the paucity of cases of severe necrotizing pneumonia at TCH. However, when severe necrotizing pneumonia is observed at our hospital, it is in the setting of coinfection with influenza or parainfluenza infection.

In summary, pulmonary abnormalities in children with invasive staphylococcal infections are common. Once CA MRSA isolates account for a large proportion of the CA S. aureus isolates in a community, then, depending on the particular clones in circulation, S. aureus is likely to be a more common cause of primary pneumonia, especially cases that are complicated by empyema or abscesses. At this point, initial empirical antibiotic treatment for children with suspected pleural empyema or other serious invasive infections for which S. aureus is a possible pathogen should include an agent that is active against the CA MRSA strains in the particular community. Although the presence of genes encoding PVL is highly associated with pulmonary involvement by S. aureus, the role of PVL in the pathogenesis of pulmonary manifestations of staphylococcal infections needs further clarification.

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