Background: Central nervous system (CNS) infections caused by Staphylococcus aureus are uncommon in pediatric patients. We review the epidemiology, clinical features and treatment in 68 patients with a S. aureus CNS infection evaluated at Texas Children's Hospital.

Methods: Cases of CNS infection in children with positive cerebrospinal fluid cultures or spinal epidural abscess (SEA) for S. aureus at Texas Children's Hospital from 2001 to 2013 were reviewed.

Results: Seventy cases of S. aureus CNS infection occurred in 68 patients. Forty-nine cases (70%) were secondary to a CNS device, 5 (7.1%) were postoperative meningitis, 9 (12.8%) were hematogenous meningitis and 7 (10%) were SEAs. Forty-seven (67.2%) were caused by methicillin-sensitive S. aureus (MSSA) and 23 (32.8%) by methicillin-resistant S. aureus (MRSA). Community-acquired infections were more often caused by MRSA that was clone USA300/pvl. Most patients were treated with nafcillin (MSSA) or vancomycin (MRSA) with or without rifampin. Among patients with MRSA infection, 50% had a serum vancomycin trough obtained with the median level being 10.6 µg/mL (range: 5.4–15.7 µg/mL). Only 1 death was associated with S. aureus infection.

Conclusions: The epidemiology of invasive S. aureus infections continues to evolve with MSSA accounting for most of the infections in this series. The majority of cases were associated with neurosurgical procedures; however, hematogenous S. aureus meningitis and SEA occurred as community-acquired infections in patients without predisposing factors. Patients with MRSA CNS infections had a favorable response to vancomycin, but the beneficial effect of combination therapy or targeting vancomycin trough concentrations of 15–20 µg/mL remains unclear.

Key Words: Staphylococcus aureus, Methicillin-resistant S. aureus, central nervous system, meningitis, vancomycin

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Central nervous system (CNS) infections caused by Staphylococcus aureus are uncommon in both adult and pediatric patients. Typically, these infections occur as a complication of invasive neurosurgical procedures (ie, shunt insertion or CNS tumor resection) or as a complication of bacteremia. Several studies have documented that S. aureus causes 1%–9% of bacterial meningitis cases in adults. The incidence in children in the United States has been reported to be <1%; however, a study in Brazilian children reported an incidence of 1.3% over a 16-year period. In a large study of 104 adult patients with S. aureus meningitis, 61 (59%) had undergone a neurosurgical procedure and 43 (41%) had hematogenous meningitis. In the group that had undergone surgery, only 7 (11%) did not have a CNS device in place at the time of infection.

In recent years, the number of CNS infections in adults caused by methicillin-resistant S. aureus (MRSA) strains has increased in the United States. In a series (1999–2008) of 33 patients with S. aureus meningitis, Aguilar et al reported an increase in the number of cases because of MRSA especially after 2003. Among the 33 cases, 16 (48.5%) were caused by MRSA with 6 infections occurring after a neurosurgical procedure and 10 as a complication of bacteremia. Two small studies have reported a trend toward higher morbidity and mortality in adult patients with MRSA meningitis compared with that caused by methicillin-sensitive S. aureus (MSSA). Although the Infectious Diseases Society of America has made recommendations for the treatment of S. aureus CNS infection, the optimal management of these infections had not been established.

To date, no large series of S. aureus CNS infections in children has been reported. In the study presented here, we review the epidemiology, clinical features and response to treatment in 70 cases (68 patients) of S. aureus CNS infection.

METHODS

Patients and Isolates

Isolates and patients were identified through a prospective S. aureus surveillance study. The database was searched for all isolates from August 1, 2001, to June 30, 2013, from children with the diagnoses of ventriculitis/ventriculoperitoneal shunt (VPS) infection, postoperative meningitis, hematogenous meningitis and spinal epidural abscess (SEA).

The medical records for all patients were reviewed, and clinical and laboratory information was recorded on a standard data collection form. This study was approved by the institutional review board at Baylor College of Medicine.

Definitions

For the purposes of this study, patients with CNS infections were those with hematogenous meningitis, ventriculitis secondary to a CNS device, meningitis secondary to recent neurologic surgery not involving a CNS device or SEA. CNS devices included VP shunts, McComb reservoirs, lumbar-peritoneal shunts, cysotoperitoneal shunts or extraventricular devices. A definitive diagnosis of S. aureus CNS infection was confirmed by isolation of S. aureus from a cerebrospinal fluid (CSF) culture and the presence of CSF pleocytosis [CSF white blood cell (WBC) count >6 WBC/µL in children older than 3 months of age, >9 WBC/µL for infants 29–90 days of age and >19 WBC/µL for infants <28 days of age]. Fever was defined as an axillary temperature ≥100.4°F.

Infections were classified as previously described: community-acquired (CA) if a S. aureus infection was diagnosed within 48 hours of admission to the hospital in an otherwise normal child; community-onset healthcare-associated (CO-HCA) if a S. aureus infection was diagnosed within 48 hours of admission to the hospital and it occurred within 1 year of a previous hospitalization or if it occurred in a patient with an underlying condition predisposing to
frequent encounters with the healthcare system; or hospital-acquired (HA) if a \textit{S. aureus} infection developed at \(\geq 72\) hours after admission.

### Molecular Analysis

\textit{S. aureus} isolates were typed by pulsed field gel electrophoresis (PFGE) as previously described.\textsuperscript{6} Relationships between strains were determined based on previously published criteria; isolates differing by \(< 4\) bands were grouped into 1 pulsotype (PFGE type).\textsuperscript{11} Available strains were tested for the presence of the \textit{ lukSF-PV (pvl)} genes using a previously described polymerase chain reaction quantitative PCR method.\textsuperscript{14}

### Statistical Analysis

Statistical analyses were performed using STATA11 (StataCorp, College Station, TX) and included the Fisher exact and Wilcoxon rank sum tests. A \(P\) value <0.05 was considered statistically significant.

### RESULTS

#### Demographic and Epidemiologic Data

From August 2001 to June 2013, 70 cases of \textit{S. aureus} CNS infection occurred in 68 patients. This constituted approximately 5% of all invasive \textit{S. aureus} infections at Texas Children’s Hospital during the study period. Forty-two patients (61.8%) were male. The median age at the time of any CNS infection was 2.6 years (range: 0.03–18.1 years). Fifty-six (82.3%) of 68 had 1 or more underlying comorbidities. Twenty-three (32%) had a congenital CNS malformation, 19 (25%) had a history of intracranial tumor or cyst removal, 4 (5.5%) had chromosomal abnormalities, 1 (1.3%) had pseudotumor cerebi and 6 (8.3%) had an immunodeficiency syndrome.

Among the 70 cases of \textit{S. aureus} CNS infections, 49 (70%) were ventriculitis secondary to a CNS device, 5 (7.1%) were postoperative meningitis complicating recent neurologic surgery and not involving a CNS shunt, 9 (12.8%) were hematogenous meningitis and 7 (10%) were SEAs. A recurrent \textit{S. aureus} CNS infection was documented in 2 patients with a VP shunt infection. Table 1 compares demographic and epidemiologic information among all cases of \textit{S. aureus} CNS infections.

Of the 70 CNS infections, 47 (67.2%) were caused by MSSA and 23 (32.8%) by MRSA. Forty-nine cases (62.9%) were CO-HCA infections, 12 (17.1%) were CA infections and 14 (20%) were HA infections per epidemiologic definitions. CA infections were more likely to be caused by MRSA isolates that were USA300 and \textit{pvl}\textsuperscript{+} when compared with CO-HCA and HA infections (Table 1).

#### Clinical Presentation, Laboratory and Molecular Analysis

**Ventriculitis**

Forty-nine cases of CNS device–associated ventriculitis occurred in 47 patients. Forty-one (83.7%) of the 49 cases involved a VP shunt, 4 (8.2%) involved a McComb reservoir, 2 (4.1%) involved a cystoperitoneal shunt, 1 (2%) involved a lumbo-peritoneal shunt and 1 (2%) involved an extraventricular device. Two patients with VP shunts had 2 infections during the study period. The most common indication for placement of a CNS device was obstructive hydrocephalus (HCP). Eighteen (38.4%) of 47 patients had posthemorrhagic HCP, 10 (21.2%) had congenital HCP, 9 (19.1%) had HCP secondary to myelomeningocele repair, 9 (19.1%) had HCP secondary to an intracranial tumor or cyst and 1 (2.2%) had pseudotumor cerebi. The median age of patients with ventriculitis was 2.3 years (range: 0.04–18.1 years). The median time between device insertion and infection was 26.5 days (range: 1–3138 days). Fever was present in 77% of cases, seizures at admission were present in 9.6% of cases and abdominal pain was reported in 13.5%. Wound infection was present in 21% of cases (8 scalp, 2 scalp/ abdomen and 1 abdomen).

Thirty-five (71.4%) of the 49 cases of ventriculitis was caused by MSSA and 14 (28.6%) by MRSA. The majority of infections were classified as CO-HCA (n = 40, 81.6%). Thirty-nine of 40 patients (97.5%) with CO-HCA infections had been hospitalized in the 12 months before infection. Nine (18.4%) of 49 infections were classified as HA. PFGE was performed on 40 available isolates (13 MRSA and 27 MSSA) recovered from patients with VPS-associated ventriculitis (Table 2). Thirty-one of the 40 isolates (77.5%) were non-USA300 pulsotypes and 9 (22.5%) were USA300. MRSA isolates (7/13, 53.8%) were more often USA300 when compared with MSSA isolates (2/27, 7.4%; Table 2). MRSA isolates (7/13, 53.8%) were more often \textit{pvl}\textsuperscript{+} when compared with MSSA isolates (2/27, 7.4%). The 2 recurrent infections were caused by MSSA non-USA300 pulsotypes. A recurrence in 1 patient was diagnosed 3.3 months after the initial infection and in the second patient almost 4 years after the initial infection. In both cases, the isolates were indistinguishable by PFGE.

CSF samples were obtained from all 49 patients diagnosed with ventriculitis through aspiration of the device at the time of admission. No statistically significant differences were found in CSF WBC or CSF glucose when comparing cases of ventriculitis caused by MSSA or MRSA (Table 2). The CSF protein concentration was significantly higher in cases of MRSA ventriculitis (\(P < 0.05\)). A blood culture was collected at the time of admission in 31 of the 35 cases of MSSA ventriculitis with only 2 (5.7%) yielding MSSA. Nine (64.3%) of the 14 cases of MRSA ventriculitis had a blood culture collected with zero yielding MRSA.

#### TABLE 1. Demographics and Epidemiology of \textit{Staphylococcus aureus} CNS Infections at Texas Children's Hospital, 2001–2013

<table>
<thead>
<tr>
<th>Epidemiologic Characteristics</th>
<th>Ventriculitis, (N = 49)</th>
<th>Postoperative Meningitis, (N = 5)</th>
<th>Hematogenous Meningitis, (N = 9)</th>
<th>SEA, (N = 7)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr, median (range)</td>
<td>2.3 (0.04–18.1)</td>
<td>3.7 (0.2–12)</td>
<td>0.1 (0.03–9.4)</td>
<td>3.5 (0.18–12)</td>
<td>0.06</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>28 (57.1)</td>
<td>3 (60)</td>
<td>5 (55.6)</td>
<td>6 (85.7)</td>
<td>0.6</td>
</tr>
<tr>
<td>MRSA (%)</td>
<td>14 (28.5)</td>
<td>0 (0)</td>
<td>5 (55.5)</td>
<td>4 (57)</td>
<td>0.08</td>
</tr>
<tr>
<td>MSSA (%)</td>
<td>35 (71.5)</td>
<td>5 (100)</td>
<td>4 (45.5)</td>
<td>3 (43)</td>
<td>0.01</td>
</tr>
<tr>
<td>CA (%)</td>
<td>4 (8.2)</td>
<td>0 (0)</td>
<td>5 (55.6)</td>
<td>7 (100)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CO-HCA (%)</td>
<td>40 (81.6)</td>
<td>3 (60)</td>
<td>1 (11.1)</td>
<td>0 (0)</td>
<td>0.01</td>
</tr>
<tr>
<td>HA (%)</td>
<td>9 (18.4)</td>
<td>2 (40)</td>
<td>3 (33.3)</td>
<td>0 (0)</td>
<td>0.01</td>
</tr>
<tr>
<td>USA300 (%) (numbers tested)</td>
<td>9 (22.5) (40)</td>
<td>0 (4)</td>
<td>55.5 (9)</td>
<td>71.4 (7)</td>
<td>0.02</td>
</tr>
<tr>
<td>\textit{pvl}\textsuperscript{+} (%) (numbers tested)</td>
<td>9 (22.5) (40)</td>
<td>2 (50) (4)</td>
<td>45.5 (9)</td>
<td>5 (71.4) (7)</td>
<td>0.02</td>
</tr>
</tbody>
</table>
At presentation, all patients received empiric antibiotic therapy that included vancomycin (60 mg/kg/d in 4 divided doses). All components of the CNS device were removed at a median of 2 days (range: 1–12 days) after admission with placement of an extraventricular device for CSF drainage. Nafcillin alone was used as definitive therapy in 19 (54.2%) of 35 patients with MSSA ventriculitis. Eight patients (22.8%) were treated with nafcillin plus rifampin, 7 (20%) with nafcillin plus gentamicin and 1 (3%) with nafcillin plus gentamicin and rifampin. All 35 patients had follow-up CSF cultures with sterilization of CSF occurring at a median of 2 days (range: 1–9 days). The median duration of treatment was 14 days (range: 10–19 days). Among patients with MRSA ventriculitis, 8 (57%) were sterile at a median of 2 days (range: 1–9 days) after initiation of therapy. Definitive therapy consisted of the following regimens: nafcillin and rifampin for 5 days (n = 1). The median duration of therapy was 14 sterile days (range: 14–21 days). All 5 patients had follow-up CSF cultures obtained. CSF sterilization occurred at a median of 1 day (range: 1–3 days) after initiation of therapy. Blood cultures were obtained in all 5 patients and all were negative. No recurrences were documented and no patients died as a result of their infection.

### Hematogenous Meningitis

Nine patients (13.2%) of 68 were diagnosed with *S. aureus* hematogenous meningitis. The median age of presentation was 0.1 years (range: 0.03–9.4 years). Five (55.5%) of 9 patients had no predisposing condition identified. The remaining 4 patients had underlying conditions that included the following: prematurity (n = 4), cerebral cysts (n = 2), congenital brain abnormalities (n = 1) and intraventricular hemorrhage (n = 1). None of the 9 patients with hematogenous meningitis had eczema or a skin/soft tissue infection at the time of presentation. Four cases were caused by MSSA and 5 by MRSA. All MRSA cases were classified as CA infections (Table 1). All 5 MRSA isolates were USA300 and *pvl*+. Among the 4 cases due to MSSA, 2 were classified as CO-HCA and 2 as HA infections. The 4 MSSA isolates were of non-USA300 pulsotypes and *pvl*+. Bacteremia was present in 3 of 5 patients (60%) with MRSA meningitis and in 1 of 4 (25%) with MSSA meningitis. Two patients (1 MRSA and 1 MSSA) presented in septic shock. In the case due to MRSA (USA300 and *pvl*+), the patient was a neonate and died within 72 hours of admission.

Six (66.7%) of the 9 patients with *S. aureus* meningitis received vancomycin (60 mg/kg/d) as part of their empiric antibiotic therapy. The 3 patients not treated initially with vancomycin had a mean age of 22 days and were empirically treated with ampicillin plus gentamicin or cefotaxime. Definitive therapy for the 4 patients with MSSA meningitis consisted of the following regimens: nafcillin alone (n = 2), nafcillin plus rifampin (n = 1) and nafcillin plus rifampin and gentamicin (n = 1). The median duration of therapy for MSSA meningitis was 14 days (range: 10–14 days). Three of 4 patients with MSSA meningitis had follow-up CSF cultures obtained. In 2 patients, CSF sterilization occurred within 48 hours of initiation of therapy and within 5 days in the third patient.

### Postoperative Meningitis

Postoperative meningitis (in the absence of a CNS device) was the diagnosis in 5 (7.1%) of the 70 cases of *S. aureus* CNS infection. The median age for these children was 3.7 years (range: 0.2–12 years). Recent neurosurgery (n = 5) and CSF leakage (n = 4) were the most common conditions associated with postoperative meningitis. Postoperative meningitis occurred at a median of 16 days (range: 3–25 days) after surgery. All 5 cases were caused by MSSA: 3 were classified as CO-HCA and 2 as HA infections. All isolates were available for molecular analyses: all were of non-USA300 pulsotypes and 2 of 4 were *pvl*+. All 5 patients with postoperative meningitis received vancomycin (60 mg/kg/d) as part of their empiric antibiotic therapy. Four patients had an external ventricular drain placed and 1 a lumbar drain as part of the management of their postoperative meningitis. Definitive therapy consisted of the following regimens: nafcillin alone (n = 4) and nafcillin plus rifampin for 5 days (n = 1). The median duration of therapy was 14 sterile days (range: 14–21 days). All 5 patients had follow-up CSF cultures obtained. CSF sterilization occurred at a median of 1 day (range: 1–3 days) after initiation of therapy. Blood cultures were obtained in all 5 patients and all were negative. No recurrences were documented and no patients died as a result of their infection.

### TABLE 2. Comparison of VP Shunt Infections Caused by MSSA and MRSA at Texas Children’s Hospital, 2001–2013

<table>
<thead>
<tr>
<th>Clinical Characteristics</th>
<th>MSSA (n = 35)</th>
<th>MRSA (n = 14)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr, median (range)</td>
<td>3.9 (0.042–18.1)</td>
<td>2 (0.40–13)</td>
<td>0.7</td>
</tr>
<tr>
<td>CSF WBC × 10³/mm³, median (range)</td>
<td>0.047 (0.001–3.55)</td>
<td>0.106 (0.002–3.98)</td>
<td>0.4</td>
</tr>
<tr>
<td>CSF glucose (mg/dL), median (range)</td>
<td>43 (10–94)</td>
<td>38 (20–86)</td>
<td>0.9</td>
</tr>
<tr>
<td>CSF protein (mg/dL), median (range)</td>
<td>91 (10–807)</td>
<td>345 (40–4267)</td>
<td>0.045</td>
</tr>
<tr>
<td>+ CSF days, median (range)</td>
<td>2 (1–9)</td>
<td>2 (1–9)</td>
<td>0.5</td>
</tr>
<tr>
<td>USA300 (%) (numbers tested)</td>
<td>2 (7.4) (27)</td>
<td>7 (60) (13)</td>
<td>0.002</td>
</tr>
<tr>
<td><em>pvl</em>+ (%) (numbers tested)</td>
<td>2 (7.4) (27)</td>
<td>7 (60) (13)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

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Seven patients (10.3%) of 68 were diagnosed with a SEA. The median age at presentation was 3.5 years (range: 0.5–12 years). The presenting symptoms included fever (100%), back pain (42.8%) and upper or lower extremity weakness (28.6%). The diagnosis was made in all patients using magnetic resonance imaging. The median length of the abscess was 8 vertebral bodies (range: 2–14 vertebral bodies). Four cases were caused by MRSA and 3 by MSSA. All 7 cases were classified as CA infections in patients without predisposing factors. The 4 MRSA isolates were USA300 and pvl\(^+\); 1 of 3 MSSA isolates was USA300 and pvl\(^+\). Four (2 MSSA and 2 MRSA, 57%) of the 7 patients had a positive blood culture at the time of diagnosis.

All 7 patients with epidural abscesses received vancomycin (60 mg/kg/d) as part of their empiric antibiotic therapy. Six (85.7%) of 7 patients underwent surgical drainage at a median of 1 day (range: 1–4 days) after diagnosis. One patient (MRSA) was treated conservatively with antibiotics alone. Definitive therapy for the 3 patients with MSSA SEA consisted of the following regimens: nafcillin (21 days) followed by cefazolin (21 days) and 2 with nafcillin (28 days) plus rifampin (14 days). Patients with MRSA SEA were treated with vancomycin alone (n = 2) or vancomycin plus rifampin (n = 2). The median duration of therapy was 42 days (range: 21–42 days). No recurrent infections were documented.

**DISCUSSION**

In the present study, *S. aureus* CNS infections accounted for approximately 5% of all invasive *S. aureus* infections at Texas Children’s Hospital between 2001 and 2013. Aguilar et al\(^3\) reported that from 1998 to 2008, MRSA was the causative agent in 50% of cases of postoperative meningitis and in 48% of cases of hematogenous meningitis in adult patients admitted to the Henry Ford Hospital. Molecular analysis of the MRSA isolates revealed that 56% belonged to the USA300 clone and that 33% carried the pvl gene. Pintado et al\(^5\) reported 86 cases of MRSA meningitis; 78 cases were postoperative meningitis and 8 were hematogenous meningitis with 93% being classified as nosocomial infections. Of the 70 *S. aureus* CNS infections reported in this study, 47 (67.2%) were caused by MSSA and 23 (32.8%) by MRSA with the majority of these infections (62.9%) being CO-HCA.

Most cases of *S. aureus* meningitis occur in patients who have undergone previous neurosurgical procedures or trauma to the CNS.\(^4,5\) In our series, 70% of cases were associated with a CSF shunt device. *S. aureus* is the second most common cause of CSF shunt infections in children accounting for 19%–29% of infections.\(^1,16\) In a case series of 33 adult patients with *S. aureus* meningitis, 60% of cases of VP shunt–associated ventriculitis and postoperative meningitis were caused by MRSA with 33% of strains belonging to the USA300 clone.\(^1\) Among our patients, we found that the majority (71.4%) of VP shunt–associated ventriculitis and postoperative meningitis (100%) cases were caused by MSSA isolates that were primarily of non-USA300 clones and pvl\(^+\). Previous studies have suggested that invasive MRSA infections, especially strains carrying the pvl gene, are associated with a higher inflammatory host response and diseases severity.\(^19,20\) We did not observe significant differences between patients with pvl\(^+\) or pvl\(^−\) strains or between MSSA or MRSA isolates with regard to initial CSF WBC counts or CSF glucose concentration; however, the initial CSF protein concentration was higher in cases of MRSA versus MSSA infection. Bacteremia was uncommon in cases of VP shunt–associated ventriculitis or postoperative meningitis whether the infection was caused by MSSA (5.7%) or MRSA (0%). This finding is in agreement with previous series of postoperative *S. aureus* meningitis in which the rate of bacteremia ranged from 0% to 37%.\(^1,12\)

The Infectious Disease Society of America (IDSA) meningitis guidelines suggest that cure of infection is successfully achieved by immediate removal of all components of the infected shunt, external CSF drainage and antibiotic therapy specific for the infecting pathogen.\(^3\) In 1 pediatric study, removal of the VP shunt led to successful treatment in 90%–100% of cases while treatment without shunt removal led to a 30% cure.\(^21\) In our series, all components of the shunt were removed at a median of 2 days (range: 1–12 days), and vancomycin was part of the empiric antibiotic regimen in all patients. Nafcillin monotherapy or in combination with rifampin was the definitive treatment in the majority (77%) of infections caused by MSSA, with sterilization of CSF occurring at a median of 2 days (range: 1–9 days). The IDSA MRSA guidelines recommend vancomycin (15 mg/kg/dose every 6 hours) for children with invasive MRSA infections, such as meningitis, and suggest targeting trough concentrations of 15–20 μg/mL for optimal clinical outcomes in adults and considering this for children.\(^22\) Among adult patients, a vancomycin serum trough concentration of 15–20 μg/mL is associated with the goal ratio of the area under the curve/minimal inhibitory concentration >400, which predicts successful outcome when treating invasive MRSA infections.\(^21\) In our series, vancomycin (15 mg/kg/dose every 6 hours) as monotherapy (42.9%) or in combination with rifampin (57.1%) was used to treat all patients with MRSA VP shunt infections with CSF sterilization occurring at a median of 2 days (range: 1–9 days) after initiation of therapy. Among patients with MRSA infection, 50% had a serum vancomycin trough obtained with the median trough level being 10.6 μg/mL (range: 5.4–15.7 μg/mL). Pintado et al\(^5\) reported a mean vancomycin trough of 11.3 μg/mL (range: 4.28–28 μg/mL) in 10 of 86 adult patients with MRSA postoperative meningitis. However, because of the small number of patients, no conclusion on the effect of vancomycin troughs on outcomes such as mortality could be reached. Using pharmacokinetic modeling, Frymoyer et al\(^24\) demonstrated that a dose of 15 mg/kg/dose every 6 hours with a vancomycin trough of 7–10 μg/mL predicted an area under the curve/minimal inhibitory concentration >400 in over 90% of children. Recently, McNeil et al\(^25\) reported that in children with healthcare-associated *S. aureus* bacteremia, there was no clinical benefit to vancomycin trough concentrations >15 μg/mL. Moreover, higher vancomycin troughs (>15 μg/mL) were associated with increased nephrotoxicity.

Hematogenous *S. aureus* meningitis occurred in 9 patients in our series. Four patients had underlying conditions that might have predisposed them to their infection (prematurity cerebral cyst, congenital brain abnormality and intraventricular hemorrhage). In the remaining 5 patients, extensive evaluations did not identify an occult CNS abnormality or an immune deficiency. The majority of cases (55.5%) were caused by MRSA (USA300/pvl\(^+\)) with all being CA. In a series of 30 pediatric cases with CA-MRSA meningitis,\(^4\) predisposing conditions such as an occult CNS abnormality or an immune deficiency were not identified. However, a probable focus as the source of CNS seeding was identified in 80% of patients with skin infections being the most commonly reported. In adult patients, *S. aureus* meningitis usually develops as a complication of bacteremia related to endocarditis, pneumonia, osteomyelitis or soft tissue infections.\(^1\) Aguilar et al\(^3\) also reported that bacteremia and extra-CNS infections were seen more frequently (71%) in hematogenous than postoperative *S. aureus* meningitis. Bacteremia was documented in 44% of our cases, which is slightly lower than the reported incidence of 64%–100%.\(^4,5,15\)

Empiric antimicrobial therapy that included vancomycin was administered to 6 of 9 patients (66.7%). Three patients with CA-MRSA meningitis did not receive vancomycin as part of initial therapy and 1 died within 72 hours of admission. These 3 patients
had a mean age of 22 days at the time of presentation. A similar finding was reported in adult patients with MRSA meningitis where initial therapy was considered appropriate more frequently (84%) in postoperative than in hematogenous meningitis (50%). The optimal treatment of MSSA or MRSA hematogenous meningitis has not been established, although the IDSA guidelines recommend the use of a 2-week course. In our patients, the median duration of therapy was 14 days. Only 5 patients (2 MRSA and 3 MSSA) had a repeat lumbar puncture to document CSF sterilization. In all cases, CSF sterilization occurred at a median of 2 days. Aguilar et al. reported that in adult patients with S. aureus meningitis, sterilization of the CSF occurred at a mean time of 7.7 days. In the current study, nafcillin was the treatment of choice for patients with MSSA meningitis and vancomycin for MRSA meningitis. In 33% of patients (2 MSSA and 1 MRSA), rifampin was used as adjunctive therapy. Mortality associated with S. aureus meningitis is high in adults, especially in cases of hematogenous meningitis (19%–71%). Rodrigues et al. reported a mortality rate of 3.3% in children with CA-MSSA hematogenous meningitis and CNS sequelae in 33.3% at discharge. In our series, 1 of 9 patients (11%) died, and 1 of 6 (16.7%) who underwent an audiologic evaluation had significant hearing loss. Thus, pediatric patients appear to have a better prognosis than adults.

SEAs are uncommon in children with a reported incidence of 0.6–1.5 cases/10,000 hospital admissions. Among our patients, SEA accounted for 10% of cases of S. aureus CNS infections. As reported in previous studies, our patients presented with fever (100%), back pain (43%) and/or upper or lower extremity weakness (28.5%). All cases were CA with 57% being caused by MRSA. The incidence of bacteremia was 57%, which is similar to the 37%–66% incidence reported in pediatric series.

The management of SEA typically requires surgical decompression and drainage plus intravenous antibiotics. In our series, 85.7% of patients underwent surgical drainage with a median duration of 42 days of intravenous antibiotics. Aulella and John reported that 75% of their pediatric patients with SEA underwent surgical drainage and 12.5% received antibiotic treatment alone. In a recent series of pediatric SEA, 2 of 9 patients (22.3%) underwent surgery plus antibiotic treatment, 3 of 9 (33.3%) underwent computed tomography-guided needle drainage plus antibiotic treatment and 4 of 9 (44.4%) were treated with antibiotics alone. None of the 9 patients had neurologic complications suggesting that SEA may be managed successfully without surgery.

Some limitations in our study need to be mentioned. This is a single-center, retrospective study that limits the generalizability of findings. The sample size of hematogenous meningitis and SAEs cases was small, thus not allowing us to make specific comments regarding management and outcomes. Finally, not all patients had a follow-up CSF culture obtained, and in cases of MRSA infection, not all patients had a vancomycin serum trough measured.

REFERENCES