

Purpura Fulminans Due to *Staphylococcus aureus*

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(See the article by Chambers on pages 948–50)

Background. Purpura fulminans is an acute illness commonly associated with meningococcemia or invasive streptococcal disease, and it is typically characterized by disseminated intravascular coagulation (DIC) and purpuric skin lesions. In this article, we report the first 5 cases (to our knowledge) of purpura fulminans directly associated with *Staphylococcus aureus* strains that produce high levels of the superantigens toxic shock syndrome toxin-1 (TSST-1), staphylococcal enterotoxin serotype B (SEB), or staphylococcal enterotoxin serotype C (SEC).

Methods. Cases were identified in the Minneapolis–St. Paul, Minnesota, metropolitan area during 2000–2004. *S. aureus* infection was diagnosed on the basis of culture results, and susceptibility to methicillin was determined. The ability of the isolated organisms to produce TSST-1, SEB, SEC, and Panton-Valentine leukocidin (PVL) was determined. TSST-1, SEB, and SEC levels were also quantified after in vitro growth of the organisms.

Results. In 3 of the 5 cases, the infecting *S. aureus* strain was isolated from the blood cultures. In 2 of the 5 cases, the infecting *S. aureus* strain was isolated only from the respiratory tract, indicating that purpura fulminans and toxic shock syndrome resulted from exotoxin and/or other host factors, rather than septicemia. One of these latter 2 patients also had necrotizing pneumonia, and the isolated *S. aureus* was a methicillin-resistant strain that produced both SEC and PVL. Only 2 of the 5 patients survived, and 1 of the survivors received activated protein C.

Conclusions. Staphylococcal purpura fulminans may be a newly emerging illness associated with superantigen production. Medical practitioners should be aware of this illness.

Staphylococcus aureus causes disease by invasion and elaboration of exotoxins. Among the exotoxins made by *S. aureus* is a family referred to as “superantigens” on the basis of their unusual non-antigen-specific activation of T cells [1]. Superantigens include toxic shock syndrome toxin-1 (TSST-1) and staphylococcal enterotoxin serotypes A–R. Superantigens bind major histocompatibility complex class II molecules and bridge certain variable regions of the β chain of the T cell receptor ($V\beta$ TCR) [2]. This triggers a massive release of cytokines by both macrophages (IL-1 β and TNF- α) and T cells (IL-2, IFN- γ , and TNF- β) manifesting as toxic shock syndrome [3]. For example, TSST-1 activates all T cells bearing $V\beta$ TCR 2 and expands these cells from the normal proportion of 10%–20% to 60%–70% of all T cells during toxic shock syndrome illness [4]. Not all superantigens are

equally associated with toxic shock syndrome. TSST-1 and staphylococcal enterotoxins serotypes B (SEB) and C (SEC) account for most cases, probably because these toxins are made in high concentrations relative to other superantigens [5–9].

Purpura fulminans is synonymous with severe meningococcemia to most physicians. This is because of the high percentage of cases (10%–20%) of acute meningococcemia that result in purpura fulminans [10]. However, meningococcal infections are relatively rare: only 2501 cases of meningococcal infection (bacteremia and/or meningitis) were reported in the United States in 1998 [11]. Thus, ~500 cases of purpura fulminans were due to meningococcemia in the United States that year. *S. aureus* bacteremia occurs much more frequently than does meningococcemia, but because it is not categorized by the Centers for Disease Control and Prevention as a notifiable disease, precise data on the incidence are not available. A study of all hospital discharges for metropolitan New York City, New York, in 1995 reported 4400 cases of *S. aureus* bacteremia among 1,351,312 nonobstetrical discharges [12]. Extrapolating these numbers to the 35 million estimated hospital discharges annually in the United States, we

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predict that there were a total of 100,000 cases of *S. aureus* bacteremia [13]. Thus, the frequency of *S. aureus* bacteremia may be 200 times greater than meningococemia.

Previously, *S. aureus* infections have only rarely been complicated by purpura fulminans [14–18]. In fact, purpura fulminans did not complicate *S. aureus* bacteremia in any of 122 cases reported in the preantibiotic era [19] or in 113 community-associated cases reported recently [20]. We recently observed 5 patients with purpura fulminans due to *S. aureus* bacteremia and/or pneumonia. Four of the cases occurred in otherwise healthy young adults, and 4 occurred in women. These cases all occurred in the Minneapolis–St. Paul, Minnesota, area within a 4-year span of time. The *S. aureus* strains from these cases produced TSST-1, SEB, or SEC. Purpura fulminans due to *S. aureus* may be an emerging clinical entity.

PATIENTS, MATERIALS, AND METHODS

The 5 patients studied were from the Minneapolis–St. Paul area, and the cases occurred during the years 2000–2004. Bacteriologic cultures and methicillin susceptibility tests were performed at the admitting hospital laboratories. Subcultures were sent to the Schlievert laboratory for superantigen Pantone-Valentine leukocidin (PVL) testing.

TSST-1, SEB, and SEC production were assessed by antibody tests [21, 22]. Strains were streaked in localized areas on Todd Hewitt agar (1%) plates (BD) and were cultured overnight at 37°C. Subsequently, monospecific rabbit antisera against TSST-1, SEB, or SEC were added to wells (diameter, 4 mm) placed 4 mm from the growing lawn. The plates were incubated for an additional 4 h and were examined for lines of precipitation indicating immunologic identity of toxins made by the strains, with purified control toxins added to other adjacent wells. The *S. aureus* strains were also cultured until the stationary phase at 37°C, with shaking in a dialyzable beef heart medium that promotes superantigen production [21, 22]. The culture fluids were treated with 4 volumes of 4°C ethanol to precipitate superantigens, the precipitates were resuspended at 5% of the original culture fluid volumes, insoluble material was removed by centrifugation, and superantigens were quantified by Western immunoblot on the basis of a comparison of band density after antibody development, with band densities determined from purified toxins.

The presence of the PVL gene was determined by PCR (forward primer, 5'-GGCCTTTCCAATACAATATTGG-3'; reverse primer, 5'-CCCAATCAACTTCATAAATTG-3') [23]. The presence of PVL protein was assessed by bioassay [24]. Presence of the methicillin-resistance DNA element, *mecA*, was determined by PCR (forward primer, 5'-GGGTACAAGATGATACC-3'; reverse primer, 5'-GGTGCCTTAATATTGCC-3') [23].

RESULTS

Patients with Purpura Fulminans and Staphylococcal Sepsis

Patient 1. A 40-year-old female physician presented to the emergency department with severe shock. She had previously been healthy except for chronic back pain, and she was not menstruating. On the day before hospital admission, she developed nausea, vomiting, diarrhea, and myalgia. She then became tachypneic, cyanotic, and unresponsive. On her arrival at the emergency department, cardiopulmonary resuscitation was initiated, and the patient underwent intubation. Physical examination revealed a heart rate of 150 beats/min and a rectal temperature of 40.3°C (104.5°F); blood pressure was initially unobtainable. Purpura was present on the patient's face, lips, and extremities. She was unresponsive except for expressions of deep pain. Laboratory analysis indicated the following arterial blood gas values: pH, 7.19; partial pressure of carbon dioxide (Pco₂), 42 mm Hg; partial pressure of oxygen (Po₂), 95 mm Hg; bicarbonate level, 16 mmol/L; and base excess (BE), –12 on a fraction of inspired oxygen (Fio₂) of 100%. A complete blood cell count indicated the following values: hemoglobin, 14.8 g/dL; WBC count, 6400 cells/mm³ (59% neutrophils and 33% bands); and platelet count, 30,000 platelets/mm³. The patient had an international normalized ratio of 1.6, an activated partial thromboplastin time of 62 s, and a fibrinogen level of 150 mg/dL. Her blood urea nitrogen level was 30 mg/dL, her creatinine level was 2.9 mg/dL, her lactate level was 10.5 mmol/L, and her creatine phosphokinase (CPK) level was 2757 IU/L. Her chest radiography findings were normal.

The initial clinical diagnosis was fulminant meningococemia. The patient was transferred to the intensive care unit and received intravenous fluids, sodium bicarbonate, calcium, methylprednisolone, dopamine, and dobutamine. Ceftriaxone (2 g iv) was given immediately. Emergency plasmapheresis was initiated because of presumed meningococemia. She remained febrile (temperature, 40.6°C [105°F]), anuric, and unresponsive. Purpura became confluent over the trunk and the distal half of the upper and lower extremities. Her platelet count decreased to 25,000 platelets/mm³, and her CPK level increased to 39,400 IU/L. Cultures of blood samples obtained at the time of hospital admission yielded methicillin-susceptible *S. aureus* (MSSA) that produced SEC (80 µg/mL) but not TSST-1 or SEB. Therapy with nafcillin (2 g iv q4h) and levofloxacin (250 mg q.d.) was started, and ceftriaxone therapy was discontinued. Culture of a sputum sample obtained after intubation also grew much *S. aureus*, which produced SEC and PVL by PCR but not TSST-1 or SEB.

Progressive ischemia of the legs necessitated bilateral below-knee amputations. Blood cultures remained positive for *S. aureus*. Therapy was withdrawn, and the patient died on day 12 of hospitalization. Postmortem examination revealed massive

purpura. Focal infarctions were present in the liver, spleen, left kidney, and heart. Endocarditis was absent. The lungs were edematous without evidence of pneumonitis. Multiple “water-shed” infarctions were present in the brain, as were multiple focal microabscesses.

Patient 2. A 56-year-old female nurse noted a sudden onset of fever and chills accompanied by severe pain in the right lower back and hip area, followed by diffuse myalgia and weakness. Examination in the emergency department revealed the following vital signs: temperature, 36.1°C (97°F); heart rate, 120 beats/min; and blood pressure, 109/54 mm Hg. A diffuse macular rash was noted on the arms, neck, abdomen, and pretibial areas. Laboratory values were as follows: hemoglobin, 12.1 g/dL; WBC count, 14,500 cells/mm³ (92% neutrophils and elevated band forms [not quantified]); platelet count, 47,000 platelets/mm³; serum blood urea nitrogen, 38 mg/dL; creatinine, 2.7 mg/dL; and bicarbonate, 19 mmol/L. Urinalysis revealed 10–25 WBCs/high-powered field (hpf) and moderate levels of bacteria. The CPK level was 947 IU/L, and the findings of chest radiography were normal.

During the next 24 h, the patient developed significant purpura over the neck, chest, arms, and pretibial areas, in addition to acute respiratory and renal failure. Assisted ventilation and hemodialysis were required. The platelet count decreased to 16,000 platelets/mm³. Multiple blood samples obtained at the time of hospital admission grew MSSA on culture. The organisms were positive for production of SEB (100 µg/mL) and were negative for production of TSST-1 and SEC. Urine culture results were negative. The patient received intravenous nafcillin. The purpura stabilized, and the platelet count normalized. Respiratory and renal failure gradually resolved. MRI revealed several small fluid densities in the right piriformis and obturator internus muscles. Attempted aspiration of these lesions was unsuccessful. Desquamation of the palms, soles, and thigh occurred during the second week after hospital admission. The purpura healed spontaneously, with the exception of the deepest lesions on the leg, which ulcerated and became secondarily infected with methicillin-resistant *S. aureus* (MRSA) and penicillin-susceptible *Enterococcus* species. Therapy was changed to vancomycin, and the infection slowly resolved.

Patient 3. A 34-year-old woman reported having fever, myalgia, and arthralgia for 3 days, followed by extreme weakness and an inability to walk. The patient had a >20-year history of juvenile rheumatoid arthritis. Her medications included leflunomide (20 mg q.d.) and adalimumab (40 mg sc per week). At presentation to the emergency department, she was confused and had a blood pressure of 85/50 mm Hg, a heart rate of 80 beats/min, and a temperature of 35.4°C (95.7°F). Her hemoglobin level was 10.4 g/dL, her WBC count was 11,000 cells/mm³, and her platelet count was 38,000 platelets/mm³. Labo-

ratory studies revealed the following values: serum glucose, 28 mg/dL; serum bicarbonate, 11 mmol/L; calcium, 6.3 mg/dL; albumin, 2.0 g/dL; aspartate aminotransferase, 524 U/L; alanine aminotransferase, 70 U/L; alkaline phosphatase, 524 U/L; bilirubin, 5.5 mg/dL; blood urea nitrogen, 68 mg/dL; serum creatinine, 5.2 mg/dL; lactate, 4.4 mmol/L; international normalized ratio, 2.6; partial thromboplastin time, 86 s; and fibrinogen, 70 mg/dL. Urinalysis revealed a specific gravity of 1.010, 2–5 RBCs/hpf, 0–2 WBCs/hpf, and granular cast of 2–5. The patient’s chest radiography findings were normal. She was administered 50% dextrose, aggressive hydration, and dopamine before transfer to a tertiary care hospital. Physical examination indicated cool extremities with purple toes, petechial lesions over the left Achilles tendon and upper back, rheumatoid nodules over extensor tendon sheaths of elbows, and nonspecific abdominal tenderness. Admission arterial blood gas measurements revealed the following values: pH, 7.27; Pco₂, 19 mm Hg; Po₂, 85 mm Hg; and bicarbonate, 9 mmol/L. Blood cultures yielded MSSA and *Escherichia coli*, and fungal blood cultures grew *Candida albicans*. Urine cultures yielded 10,000–50,000 *S. aureus*/mL and specimens from the left-shoulder and left-knee aspirates also grew *S. aureus*. The *S. aureus* strains were positive for production of SEC (80 µg/mL) and PVL by PCR but were negative for production of TSST-1 and SEB.

The patient was treated with vancomycin, gentamicin, gatifloxacin, and fluconazole, as well as levetiracetam, vitamin K, platelet transfusions, and daily hemodialysis. She developed progressive renal and respiratory failure and coma. Purpura spread over the arms, feet, legs, and trunk (figure 1). On day 10, extensive desquamation was noted on the arms, legs, face, and trunk. CT of the head showed changes compatible with anoxic encephalopathy. The patient died on day 12 of hospitalization.

Patients with Purpura Fulminans Who Did Not Have Staphylococcal Sepsis

Patient 4. A 21-year-old, previously healthy man developed mild coryza and cough. Four days later, his condition suddenly worsened, with onset of fever, chills, dyspnea, and, later, nausea, vomiting, and diarrhea. He was brought to the emergency department. His vital signs were as follows: temperature, 37.9°C (100.1°F); heart rate, 172 beats/min; blood pressure, 91/72 mm Hg; and respiratory rate, 32 breaths/min. Initial examination revealed marked respiratory distress, no petechiae, supple neck, no heart murmur, decreased breath sounds in the right lower lung field, no abdominal tenderness, and no focal neurologic findings. The patient’s blood pressure decreased to 81/36 mm Hg. Initial arterial blood gas studies revealed the following values: pH, 7.22; Pco₂, 30 mm Hg; Po₂, 91 mm Hg; bicarbonate, 12 mmol/L; and BE, –13 on an Fio₂ of 95%. Complete blood cell count values were as follows: WBC count, 2500 cells/mm³ (10%



Figure 1. Lower extremity purpura in patient 3

neutrophils, 30% bands, 12% metamyelocytes, and 10% myelocytes); and platelet count, 140,000 platelets/mm³. The serum creatinine level was 3.3 mg/dL, and the blood urea nitrogen level was 25 mg/dL. A chest radiograph showed an extensive infiltrate in the right lower lobe. The patient underwent intubation in the emergency department; started receiving intravenous fluids, levarterenol, sodium bicarbonate, cefotaxime, and azithromycin; and was transferred to the intensive care unit.

The patient rapidly developed hypotension, anuria, and worsening metabolic acidosis, despite receipt of aggressive fluid resuscitation and levarterenol. His skin became mottled, and purpura developed over his lips and knees. Additional coagulation studies revealed an international normalized ratio of 3.8, an activated partial thromboplastin time of 140 s, and a platelet count of 43,000 platelets/mm³. Gatifloxacin was added to the therapy regimen. During the ensuing 12 h, the purpura progressed to cover his entire body. Attempts were made to procure activated protein C concentrate (i.e., drotrecogin [Xigris; Eli Lilly]) on a compassionate-need basis, but the patient died within 24 h after intubation, before the drotrecogin arrived.

Sputum samples that had been obtained for culture after intubation yielded large numbers of MRSA (also positive for *mecA*) that was susceptible to erythromycin, clindamycin, levofloxacin, trimethoprim-sulfamethoxazole, tetracycline, and vancomycin. The *S. aureus* appeared to be a community-associated MRSA strain; it produced SEC (~80 µg/mL) but not TSST-1 or SEB, and it produced PVL and contained the PVL

gene, as determined by PCR. Blood cultures were negative for *S. aureus*. Serological studies revealed no detectable IgM antibodies to influenza viruses A or B. Postmortem lung tissue specimens were negative for viruses on culture, but they yielded the same strain of MRSA as the sputum samples. Postmortem examination revealed diffuse purpura of the skin and diffuse acute necrotizing pneumonia.

Patient 5. A 43-year-old woman presented to a hospital with a 5-day history of sore throat, nausea, vomiting, arthralgia, and myalgia. At admission, dyspnea and cyanosis were present, and the patient's blood pressure was unobtainable. The patient had been healthy and was not menstruating. Physical examination revealed that her face and lips were cyanotic. There was faint erythema present in both flanks. Laboratory studies revealed the following values: hemoglobin, 13.8 g/dL; WBC count, 23,100 cells/mm³; platelet count, 149,000 platelets/mm³; international normalized ratio, 1.35; partial thromboplastin time, 47.2 s, fibrinogen/fibrin degradation products (FDP), >20 µg/mL; serum creatinine, 2.8 mg/dL; blood urea nitrogen, 25 mg/dL; calcium, 6.0 mg/dL; and CPK, 7378 IU/L. Arterial blood gas measurements revealed the following values: pH, 7.07; Pco₂, 36 mm Hg; and Po₂, 436 mm Hg on an Fio₂ of 100% by mask. The serum lactic acid level was 7.0 mmol/L. Initial chest radiographs showed subtle central interstitial infiltrates. Examination of endotracheal secretions revealed >25 WBCs/hpf and <10 epithelial cells/hpf and grew 70% MSSA and 30% other bacteria. The *S. aureus* strains were positive for production of

TSST-1 (16 $\mu\text{g}/\text{mL}$) and were negative for production of SEB and SEC. Blood cultures grew coagulase-negative staphylococci in 1 bottle only. The patient received a 2-L fluid flush but remained hypotensive and dyspneic. She underwent intubation, and therapy with vancomycin, clindamycin, and levarterenol was initiated. Her blood pressure improved.

The next day, extensive purpura was noted on the patient's extremities, with scattered lesions on the torso. Her platelet count decreased to 39,000 platelets/ mm^3 , her international normalized ratio was 16.9, her partial thromboplastin time was 75.6 s, and her FDP remained $>20 \mu\text{g}/\text{mL}$. The patient developed acute respiratory distress syndrome and acute renal failure, and she remained pressor dependent. She started receiving activated protein C (i.e., drotrecogin; 24 mg/kg/h infusion for 96 h). The patient's condition improved. The purpura progressed to skin necrosis of the fingertips, toes, and soles of her feet (figure 2). Acute- and convalescent-phase serological tests were negative for both influenza A and B viruses. The patient was discharged to a rehabilitation unit, and she was subsequently readmitted to the hospital for bilateral below-knee leg amputations.

A summary of findings for these 5 patients is presented in table 1.

DISCUSSION

This study describes 5 patients with *S. aureus* purpura fulminans and toxic shock syndrome. These patients were seen in the Minneapolis–St. Paul area during the period of 2000–2004. Four of the patients were previously healthy, and 4 of the patients were women. Three patients had blood cultures positive for superantigen-producing *S. aureus*, but 2 of the patients had negative blood culture results; these 2 patients tested positive for superantigen-producing *S. aureus* in the respiratory tract. We hypothesize that the clinical features of purpura fulminans and toxic shock syndrome seen in these patients resulted from massive cytokine release induced by the *S. aureus* strains.

The term “purpura fulminans” was initially used to describe the rapid onset of overwhelming purpura and skin necrosis that occurred in children and that was associated with bacterial infection [25, 26]. Meningococemia is, by far, the infection most commonly attributed to purpura fulminans, followed by streptococcal infection [27]. Recent studies indicate that this syndrome can be the result of autoimmune protein S or C deficiency [27–29]. Over time, the term has also been applied to cases of purpura fulminans that occur in the face of overwhelming sepsis (i.e., “sepsis-associated purpura fulminans”) [30]. There are 4 primary features of this syndrome: large,

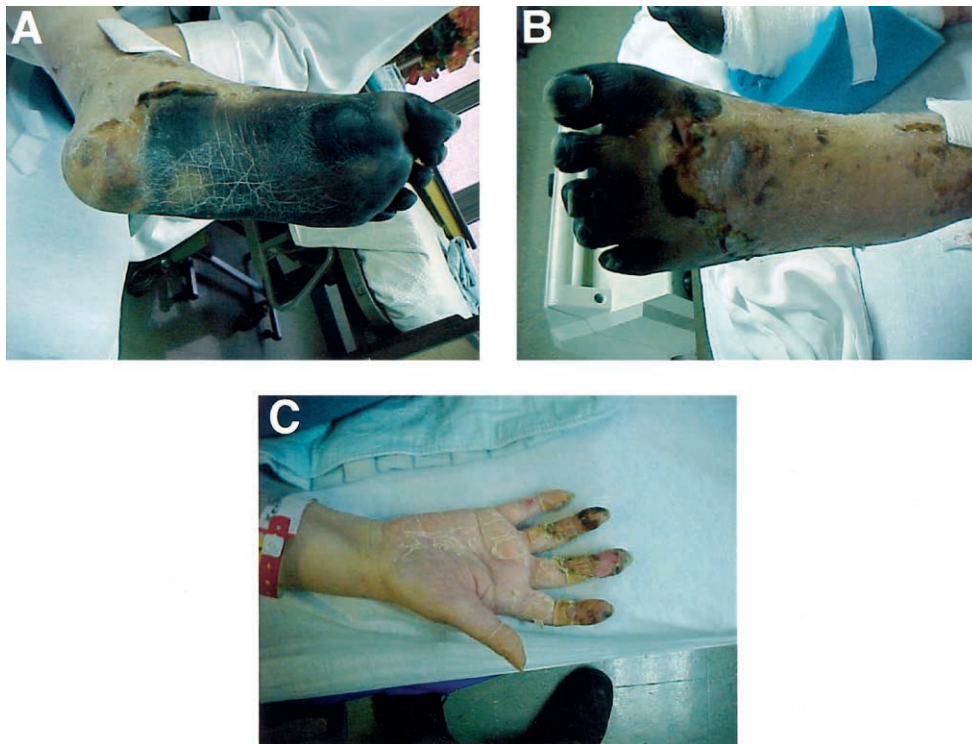


Figure 2. Skin necrosis of the bottom of the foot (A), the top of the foot (B), and the hand (C) of patient 5, following purpura associated with her illness.

Table 1. Description of 5 patients with purpura fulminans.

Patient	Age in years/sex	Culture results	Toxin(s) produced ^a	Treatment	Symptoms	Outcome(s)
1	40/F	MSSA on blood and sputum cultures	SEC, PVL	Ceftriaxone, nafcillin, levofloxacin	Purpura of extremities and torso	Patient underwent bilateral below-knee amputations; patient died
2	56/F	MSSA on blood culture	SEB	Nafcillin	Purpura of neck, breasts, arms, and chest	Patient had respiratory and renal failure; patient survived
3	34/F	MSSA on blood, urine, and left-shoulder and left-knee aspirate cultures; <i>Escherichia coli</i> on blood culture; <i>Candida albicans</i> on blood culture	SEC, PVL	Vancomycin, gentamicin, gatifloxacin, fluconazole	Purpura of extremities and trunk, anoxic encephalopathy, oliguria, hypotension	Patient died
4	21/M	MRSA on sputum culture; negative blood culture results	SEC, PVL	Cefotaxime, azithromycin, gatifloxacin	Necrotizing pneumonia; purpura over entire body	Patient died
5	43/F	MSSA on sputum culture; coagulase-negative staphylococci on blood culture	TSST-1	Vancomycin, clindamycin, drotrecogin	Purpura of hands and feet	Patient underwent bilateral below-knee amputations; patient was rehabilitated

NOTE. MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *S. aureus*; PVL, Pantone-Valentine leukocidin; SEB, staphylococcal enterotoxin serotype B; SEC, staphylococcal enterotoxin serotype C; TSST-1, toxic shock syndrome toxin-1.

^a In tests for production of SEB, SEC, PVL, and TSST-1. All toxins were detected by antibody reactivity, except for PVL, which was detected by PCR and/or bioassay.

purpuric skin lesions; fever; hypotension; and disseminated intravascular coagulation [27, 31].

The 5 cases of purpura fulminans reported here suggest that *S. aureus* infections are also now associated with purpura fulminans with accompanying toxic shock syndrome. One case was caused by a community-associated strain of MRSA [23, 32–34]. Typical of such MRSA strains, the organism produced the superantigen SEC and had the gene for PVL [23, 33, 34]. It is hypothesized that one or both of these staphylococcal exotoxins caused this patient's necrotizing pneumonia and toxic shock syndrome-like symptoms. The other 4 patients also had symptoms consistent with toxic shock syndrome or probable toxic shock syndrome, and their staphylococcal isolates produced TSST-1, SEB, or SEC [35, 36]. These 3 toxins are superantigens that cause most cases of toxic shock syndrome [5–8]. Superantigens induce toxic shock syndrome through induction of massive proinflammatory cytokines from T cells and macrophages [1, 2]. The hypotension and shock associated with toxic shock syndrome are considered to be due to TNF- α and TNF- β [1, 3]. Fever is almost certainly dependent on IL-1 β [1, 3]. Finally, the release of massive cytokines likely initiates multiple inflammatory pathways, including the procoagulant cascade, which, in its severest form, manifests as purpura fulminans [31]. Surprisingly, only 1 of our 5 patients developed the typical "sunburn" rash emblematic of toxic shock syndrome [36, 37]. Thus, the purpuric rash seen in our patients may be indicative of a more severe form of toxic shock syndrome.

The clinical presentations of all 5 patients were identical to those seen for patients with fulminant meningococemia, and this was the initial clinical diagnosis in 2 cases. Patients with fulminant meningococemia are known to have markedly re-

duced plasma levels of activated protein C as a result of dysfunction of the endothelial protein C activation pathway [38]. Activated protein C is not only an anticoagulant but also an important modulator of the inflammatory response [31]. Meningococemia is generally much more predisposed than other types of bacteremia to cause a dysfunction of the activated protein C pathway [39]. However, the cases reported in this study suggest that *S. aureus* illnesses increasingly lead to an identical clinical syndrome. Because *S. aureus* illnesses are not notifiable, we do not know the precise rate of occurrence of purpura fulminans caused by this organism. Moreover, some of these strains were MRSA. On the basis of our experience, we strongly recommend that patients who present with purpura fulminans receive antibiotic therapy active not only against *Neisseria meningitidis* and streptococci, but also against MRSA. Consideration should also be given to early administration of activated protein C (i.e., drotrecogin) in an attempt to minimize purpuric skin injury and to down-regulate the inflammatory cascade before irreparable tissue injury occurs [31, 38, 39]. Finally, because toxic shock syndrome is mediated by superantigens, it is possible that intravenous immunoglobulin therapy may be indicated, because these preparations contain significant antibodies against the causative exotoxins [40].

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