Involvement of Methicillin-Susceptible *Staphylococcus aureus* Related to Sequence Type 25 and Harboring *pvl* Genes in a Case of Carotid Cavernous Fistula after Community-Associated Sepsis


Hospital Pedro Ernesto, State University of Rio de Janeiro, and Instituto de Microbiologia Paulo de Góes, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil

*Staphylococcus aureus* encoding Panton-Valentine leukocidin (PVL) genes has become the cause of life-threatening infections. We describe a case of carotid cavernous fistula after bacteremia in a 12-year-old male, caused by a methicillin-susceptible *S. aureus* isolate carrying the *pvl*, *fnbA*, and *ebpS* genes and related to sequence type 25 (ST25). The patient’s condition was complicated by pleural empyema and osteomyelitis in the right femur. The patient was discharged in good clinical condition after 160 days of hospitalization.

**CASE REPORT**

A previously healthy 12-year-old male who practices kung fu was admitted on 5 December 2009 to the adolescent unit of a hospital located in Rio de Janeiro, Brazil. He was admitted with a history of 7 days of fever and muscle pain in his right thigh. Clinical signs and symptoms observed at the time of admission revealed severe sepsis and pyomyositis. During a physical examination, his axillary temperature was 37.9°C, with blood pressure of 180/90 mm Hg, a pulse of 136 beats per min, and respiration of 60 per min. Jaundice, abdominal pain, and dehydration were also observed. There was also focal pain in the right ankle and thigh. On admission, the laboratory findings revealed leukocytosis with 23% bands, a hematocrit level of 25%, a hemoglobin level of 140,000/mm³, and a platelet count of 140,000/mm³. The blood biochemical test results were as follows: glucose, 62 mg/dl; aspartate aminotransferase, 52 U/liter; alanine aminotransferase, 40 U/liter; bilirubin total level, 9.73 mg/dl; uric acid, 62 mg/dl; creatinine, 1.2 mg/dl; urea, 62 mg/dl; creatinine, 1.2 mg/dl. Amylase, γ-glutamyltransferase, alkaline phosphatase, and creatine phosphokinase (CPK) were normal. Arterial blood gas results were as follows: carbon dioxide tension (pCO₂), 31; oxygen tension (pO₂), 66; HCO₃⁻, 20; base excess (BE⁺), 2.8; oxyhemoglobin saturation (sat O₂), 93%; pH (hydrogen ionic potential), 7.43. A chest X-ray showed bilateral interstitial infiltrate. After blood cultures and se-rologic tests (cytomegalovirus [CMV], Epstein-Barr virus [EBV], HIV, hepatitis viruses, syphilis, and toxoplasmosis) were obtained, intravenous therapy was initiated with vancomycin at 1 g every 12 h (q12h), ceftriaxone at 1 g q12h, and clindamycin at 600 mg q6h. Continuous positive airway pressure (CPAP) was started for ventilatory support. Additional exams with computed tomography (CT) scan imaging showed multiple areas of pulmonary consolidation and pleural effusion. Ultrasonography confirmed myositis in the right thigh, and a transthoracic echocardiogram showed no valve vegetation. In the second day after his admission, a *S. aureus* strain (confirmed by catalase and coagulase tests) was isolated from two blood culture sets. Antimicrobial susceptibility testing (3) revealed that the isolates were susceptible to all the antimicrobials tested, including oxacillin. The antibiotics were changed to oxacillin. As the patient persisted with fever, tachypnea, and focal pain, he was transferred to the intensive care unit on 9 December 2009. After 72 h of intravenous administration of oxacillin, 12 g/day in continuous-infusion, the blood culture was still methicillin-susceptible *S. aureus* (MSSA) positive. The patient’s condition was complicated with pleural empyema and osteomyelitis in the proximal third of the right femur. Thoracocentesis facilitated removal of the pleuritic fluid exudates, which showed negative cultures. Two hundred milliliters of bloody and purulent secretion was drained from bone, of which bacterial culture showed results similar to those for the blood cultures. After 7 days of intravenous therapy with oxacillin, the blood culture remained positive. Then, rifampin was added to the treatment. On the 10th day of antibiotic treatment, he developed proptosis in the right eye, which suggested cavernous sinus thrombosis. Arteriography and CT angiography were performed, and a carotid cavernous fistula (CCF) was observed (Fig. 1). Endovascular repair of the CCF was successful. Thirteen days after his admission, the blood cultures were negative, but the patient remained with fever until the 18th day. The total time of antibiotic therapy was 6 weeks. The results of serological tests were all negative, and the patient was discharged in good clinical condition after 160 days of hospitalization.

The MSSA isolate was sent to a reference laboratory to search for virulence and resistance genes and to determine the clonality of the isolate. Bacterial DNA was extracted, and a PCR to amplify the *mecA* resistance gene (11) and virulence genes, lukS-PV and lukF-PV (*pvl*), as well as the *tst*, *sea*, *seb*, *eta*, *etb* (11), *friB*, *friB*, *cna*, and *ebpS* genes (10), was carried out. The isolate was typed by multilocus sequence typing (MLST), as previously described (5).

Received 12 May 2011 Returned for modification 19 June 2011 Accepted 2 November 2011

Published ahead of print 16 November 2011

Address correspondence to Kátia R. N. dos Santos, santoskrn@micro.ufrj.br.

P.V.D. and R.C.C. contributed equally to this work.

Copyright © 2012, American Society for Microbiology. All Rights Reserved.

doi:10.1128/JCM.00972-11
The MSSA isolate was positive for the PVL genes and for the adhesion genes fibrA and ebpS, which encode fibronectin A and elastin binding protein, respectively. The MLST revealed the allelic profile 4-1-4-1-5-5-239, which was included in a new sequence type, ST2104 (alteration in the yqiI allele), a single variant locus (SLV) of ST25 (CC25).

Staphylococcus aureus isolates carrying Panton-Valentine Leukocidin (PVL) genes have most often been related to skin and soft tissue infections, necrotizing pneumonia, osteomyelitis, and purpura fulminans (4). In this report, we have described a spontaneous carotid cavernous fistula (CCF) developed after severe sepsis caused by MSSA carrying the PVL genes in a previously healthy 12-year-old male, who practices kung fu and suffered an injury when he exercised. A CCF has been described as an abnormal communication between the internal or external carotid artery and the cavernous sinus (9) and may be divided into spontaneous or traumatic (in relation to cause) and direct or dural (in relation to angiographic findings) (2). The most common etiology of direct CCF is trauma (2). Primarily, the patient showed sepsis and pyomyositis, an infection related to a complication of transient bacteremia, which is associated with a concomitant muscle tissue structure abnormality after trauma or exercise creating a locus minoris for bacteria implantation (8).

The organism isolated carried the pvl, fnbA, and ebpS genes, while the mecA gene was not found. Adhesin-encoding genes have been commonly detected in S. aureus isolates, and they have been more associated with endocarditis, septic arthritis, and osteomyelitis (7, 10). On the other hand, S. aureus isolates harboring the PVL genes are less frequent, and these organisms could be considered as a cause of severe and invasive infections (4). Here we have described a case of an S. aureus isolate causing an uncommon pathology that had never been found in the literature. We hope that this case report can be a pioneer documentation of new complications related to PVL S. aureus infections.

A study conducted in 2006 by Bocchini and coworkers (1) showed that patients infected with S. aureus carrying the PVL genes are more likely to present concomitant myositis or pyomyositis and often had blood culture positive for the organism compared with patients presenting infection by a pvl-negative isolate.

Direct causality between PVL-positive MSSA and CCF has never been reported. Nevertheless, when physicians observe peri-orbital swelling, proptosis, chemosis, and a dysfunction or paralysis of cranial nerves III, IV, or VI in a teenager, supportive intra-crinal thrombophlebitis should be considered. This pathology usually develops after secondary bacteremia caused by Gram-positive cocci, Gram-negative aerobic bacilli, or anaerobes affecting the paranasal sinuses or facial site (6). Our case shows a carotid cavernous fistula (CCF) secondary to bacteremia caused by S. aureus of metastatic spread from the musculoskeletal system. We observed the classic Dandy’s triad, which is pathognomonic of CCF. CT angiography of the skull corroborated the diagnosis (2, 9).

The S. aureus isolate harboring the PVL genes identified in this study was related to ST25 by MLST typing. In Brazil, most S. aureus isolates carrying the pvl genes are related to ST30 (12). To our knowledge, this is the first report of the presence of an ST25-related MSSA strain carrying PVL genes worldwide. Furthermore, this ST had not been described as causing infection in a patient in our country. It has been detected in United Kingdom bovine and human isolates (13).

According to Smith and coworkers (13), there is a closer evolutionary relationship between ST25 and ST97, another uncommon sequence type that was associated with a pvl-positive MRSA isolate detected in a study conducted by us in Rio de Janeiro city (data not published). This may indicate that isolates associated with these rare STs are acquiring pvl genes and spreading in the environment, being able to cause severe infections.

The reason for PVL-positive S. aureus clustering in young patients needs to be elucidated. Its complications are challenging, but the prognosis can be favorable in adolescents when aggressive medical and surgical management are applied. In conclusion, this is the first case report of carotid cavernous fistula (CCF) in a young patient after an overwhelming septic infection caused by an MSSA isolate carrying the pvl genes and related to ST25.

ACKNOWLEDGMENTS

This study was supported by grants from CAPES, CNPq, and FAPERJ, Brazilian governmental institutions.

REFERENCES

5. Enright MC, Day NP, Davies CE, Peacock SJ, Spratt BG. 2000. Multi-

FIG 1 CT angiography of skull. The arrow indicates carotid cavernous fistula in the right superior medial border of the posterior knee of the cavernous portion of the right internal carotid artery, measuring approximately 6 mm in diameter, with immediate filling of ipsilateral cavernous sinus, which is dilated, measuring approximately 12 by 10 mm.


