A Case of Fatal Community-Acquired Necrotizing Pneumonia Caused by Panton-Valentine Leukocidin Positive Methicillin-Sensitive *Staphylococcus Aureus*

Narimon Honarpour and Jenny T. Mao*

Division of Pulmonary & Critical Care, Department of Medicine, David Geffen School of Medicine at UCLA, 10833 Le Conte Avenue, Los Angeles, CA 90095-1690, USA

Abstract: The expression of Panton-Valentine leukocidin (PVL) has been implicated as a virulence factor for community-acquired *Staphylococcus aureus* pneumonia with most reported cases involving methicillin-resistant strains. Here we describe a case of community-acquired, PVL-positive methicillin-sensitive *Staphylococcus aureus* (MSSA) sufficiently virulent to cause rapidly progressive necrotizing pneumonia, massive pulmonary hemorrhage, sepsis, and death in a patient without conventional risk factors (diabetes, advanced age). To our knowledge, this is the first case report of a fatal necrotizing pneumonia caused by PVL-positive MSSA in Los Angeles County.

Keywords: PVL, MSSA, community-acquired necrotizing pneumonia and massive hemoptysis.

CASE REPORT

A 48-year old female with no significant past medical history or recent hospitalization presented to the emergency room with shortness breath and hemoptysis. Her symptoms began four days prior to presentation with rhinorrhea, sore throat, nonproductive cough associated with pleuritic chest pain, and subjective fevers. The day prior to presentation, she had been seen at two separate hospital emergency rooms. Her vital signs and chest X-ray were unremarkable at that time (Fig. **1A**), and she was given the diagnosis of a viral upper respiratory tract infection (URI). No other laboratory work up was pursued at either one of these visits. The patient was discharged home with instructions to take over-the-counter medication as needed for her symptoms.

By the following day, the patient's cough worsened and she developed frank hemoptysis with severe dyspnea, and her family brought her back into the emergency room. At presentation she was found to be in severe respiratory distress using accessory muscles and having paradoxical abdominal movement. Vital signs were remarkable for a temperature of 36^{o}C, pulse of 120 beats per minute, blood pressure of 64/47 mmHg, respiratory rate of 60 per minute, and oxygen saturation of 58% on room air *via* pulse oximetry. She was promptly intubated for hypoxemic respiratory failure.

Upon intubation copious amounts of blood were suctioned from the endotracheal tube. A chest X-ray showed diffuse bilateral opacification (Fig. **1B**). The patient was aggressively resuscitated with intravenous fluids, blood products, pressors, and started on empiric pipercillin/tazobactam and Vancomycin for presumed sepsis and pneumonia. Laboratory values were consistent with sepsis and disseminated intravascular coagulation (DIC), with a low white blood cell count, low platelet count and hematocrit, elevated prothrombin time and low fibrinogen, triple acid-base disorder, and acute renal failure. She then went into pulseless electrical activity (PEA) and was resuscitated. In view of the patient's massive hemoptysis, she was evaluated by interventional radiology for bronchial artery embolization. A probable source of bleeding was identified in the right middle lobe and embolization was attempted; however, the patient again went into PEA arrest during the procedure, and no further attempts were pursued. The massive hemoptysis continued and the patient subsequently expired in spite of continued resuscitation efforts. The case was referred to the Los Angeles County Coroner's Office for autopsy.

Autopsy was remarkable for necrotizing pneumonia in the right middle lobe with high numbers of gram-positive cocci. Blood cultures from the patient grew out MSSA. The isolate was tested at the Center for Disease Control and determined to be positive for PVL by polymerase chain reaction (PCR) and negative for enterotoxins A, B, C, D, E, H, and toxic shock syndrome toxin 1. The cause of death was determined to be massive hemoptysis resulting from community-acquired, PVL-positive, MSSA necrotizing pneumonia.

DISCUSSION

S. aureus is a well-known cause of nosocomial infections (including pneumonia) [1]. More recently, community-acquired methicillin resistant *S. aureus* (MRSA) infections in healthy individuals (e.g. children or young adults) without conventional risk factors (advancing age, diabetes and chronic lung diseases) have been described [2-7]. Interestingly, symptoms of URI often precede the onset of rapidly progressive necrotizing pneumonia and septic shock, which can develop within 24 hours of presentation [2-7]. Most reports focused on the prevalence of MRSA infections in the community and the importance of empiric treatment in suspected cases.

Various factors have been described to account for the virulence of *S. aureus* in addition to antibiotic resistance.

*Address correspondence to this author at the Division of Pulmonary and Critical Care Medicine, David Geffen School of Medicine at UCLA, 37-131 CHS, 10833 Le Conte Avenue, Los Angeles, California 90095-1690, USA; Tel: 310-825-3100; Fax: 310-206-2442; E-mail: jmao@mednet.ucla.edu

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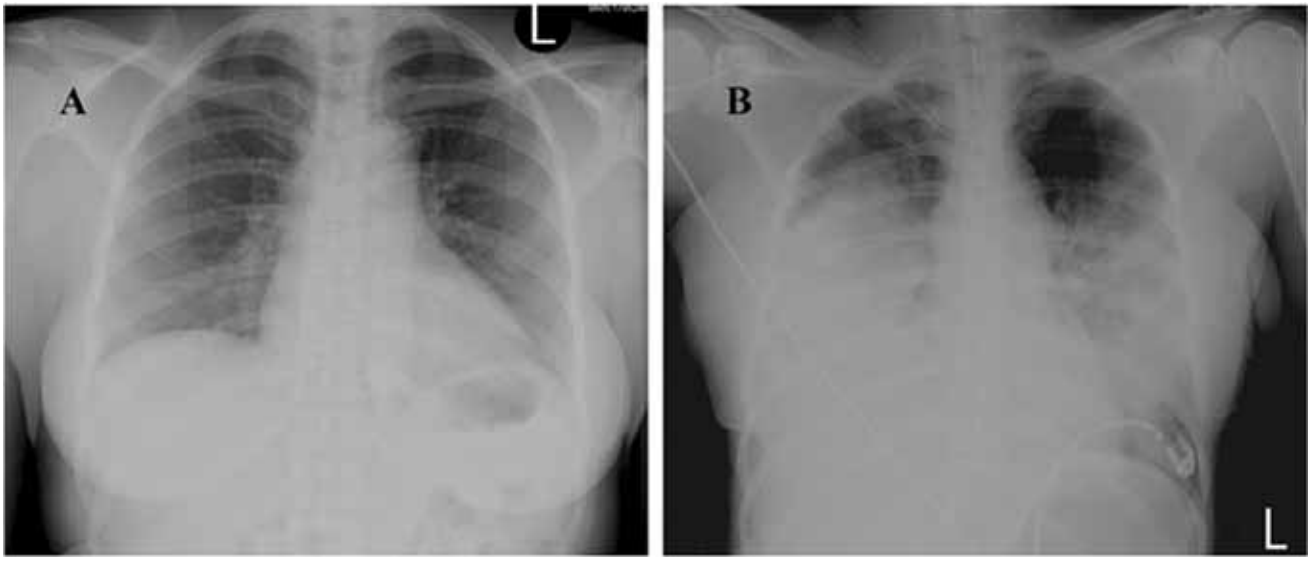

Fig. (1). A) Posteroanterior chest radiograph at initial presentation when patient presented with symptoms of upper respiratory tract infection. **B**) Posteroanterior chest radiograph on the following day when patient presented with acute respiratory failure, massive hemoptysis, and development of diffuse opacification in both lungs.

These include elaborations of exotoxins, adhesion molecules, hemolysins, leukotoxins, and leukocidins [8, 9]. Specifically, production of leukocidins such as PVL, have been recently linked to rapidly progressive necrotizing soft tissue infections and pneumonia in many European and North American communities, including the Los Angeles area [2, 3, 4-7, 10]. PVL is a pore-forming cytotoxin that targets mononuclear and polymorphonuclear cells. Gillet *et al.* reported that patients with PVL-positive *S. aureus* pneumonia were younger, often had preceding influenza-like symptoms, and had poorer prognoses than PVL-negative patients [8]. These PVL-positive patients were also more likely to develop hemoptysis and leukopenia. The majority of the reported PVL-positive cases have been associated with MRSA. These community-acquired MRSA strains are genetically distinct from hospital-acquired strains [11]. In our case, the patient had community-acquired, PVL-positive MSSA. The organism was sufficiently virulent to cause rapidly progressive necrotizing pneumonia, massive pulmonary hemorrhage, bacteremia, sepsis, and death. To our knowledge, this is the first case report of a fatal necrotizing pneumonia caused by PVL-positive MSSA in the Los Angeles County.

The true prevalence of PVL-positive MSSA is largely unknown because testing is not routinely performed. Holmes *et al.* recently reported that approximately 1.6% of the isolates tested for the PVL locus in the United Kingdom were positive, of which 47% of the isolates tested were methicillin-resistant [12]. These isolates were mostly associated with necrotic infections of the skin and soft tissue but were also detected in patients with community-acquired pneumonia. In our case, PVL was the only toxin found in the MSSA isolate and appeared to play a key role in the severity of the disease. The initial URI symptoms suggest that a viral infection could have set the stage for the bacterial infection, particularly in an otherwise immunocompetent patient. To this end, studies have demonstrated that the toxic effect of PVL results from the synergistic action of two exoproteins, LukS-PV and LukF-PV. These proteins are encoded by two contiguous and cotranscribed genes (*luk*S-PV and *luk*F-PV) [9] that are carried on temperate bacteriophages [13]. Whether or not the patient's URI symptoms are caused by a virus or directly by the MSSA is unclear.

Clinicians need to maintain a heighten awareness that both community acquired MRSA and MSSA can cause rapidly progressive, necrotizing infections such as fasciitis or pneumonia. Close monitoring, timely modification of empiric antimicrobial coverage, adequate duration of therapy, and additional testing for PVL or other MRSA or MSSA associated toxins should be considered as a part of clinical practice. Testing for the presence of toxins such as PVL, in addition to antimicrobial resistance profiles, may need to be incorporated into diagnostic panels to help stratify patient's risk for more invasive disease. Furthermore, close surveillance of these strains is essential in monitoring their spread and association with disease. In view of the severity of the illness, patients who present with rapidly progressive community acquired pneumonia should be suspected of having PVL-positive *S. aureus* infections and may need to be placed in isolation to limit transmission and colonization between close contacts and affected individuals [14, 15].

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REFERENCES

[1] Diekema D, Pfaller M, Schmitz F, *et al*. Survey of infections due to Staphylococcus species: frequency of occurrence and antimicrobial susceptibility of isolates collected in the United States, Canada,

Latin America, Europe, and the Western Pacific region for the SENTRY Antimicrobial Surveillance Program, 1997-1999. Clin Infect Dis 2001; 32 Suppl 2:114-32.

[2] Boussaud V, Parrot A, Maynaud C, *et al*. Life-threatening hemoptysis in adults with community acquired pneumonia due to Panton-Valentine leukocidin-secreting Staphylococcus aureus. Int Care Med 2003; 29: 1840-43.

[3] DuFour P, Gillet Y, Bes M, *et al*. Community-acquired methicillin resistant *Staphylococcus aureus* infections in France: Emergence of a single clone that produces Panton-Valentine Leukocidin. CIN 2002; 35: 819-24.

[4] Francis J, Doherty M, Lopatin U, *et al*. Severe Community-Onset Pneumonia in Healthy Adults Caused by Methicillin-Resistant *Staphylococcus aureus* Carrying the Panton-Valentine Leukocidin Genes. CID 2005; 40:100-7.

[5] Gillet Y, Issartel B, Vanhems P, *et al*. Association between *Staphylococcus aureus* strains carrying gene for Panton-Valentine leukocidin and highly lethal necrotising pneumonia in young immunocompetent patients. Lancet 2002; 359: 753-59.

[6] Hsu L, Koh T, Anatham D, Kurup A, Chan K, Tan B. Panton-Valentine Leukocidin-positive Staphylococcus aureus, Singapore. Emerg Inf Dis 2004; 10: 1509-10.

[7] Lina G, Pietmont Y, Godail-Gamot F, Bes M, *et al*. Involvement of Panton-Valentine Leukocidin-Producing *Staphylococcus aureus* in primary skin infections and pneumonia. CID 1999; 29:1128-32.

[8] Panton P, Valentine F. Staphylococcal toxin. Lancet 1932; 1: 506-8.

[9] Miller L, Remington, F, Rieg G, Mehdi S, *et al*. Necrotizing fasciitis caused by community-acquired methicillin-resistant *Staphylococcus aureus* in Los Angeles. N Engl J Med 2005; 352: 445-53.

[10] Vandenesch F, Naimi T, Enright M, *et al*. Communit-acquired methicillin-resistant *Staphylococcus aureus* carrying Panton-Valentine Leukocidin genes: Worldwide emergence. Emerg Inf Dis 2003; 9: 978-984.

[11] Holmes A, Ganner M, McGuane S, *et al*. *Staphylococcus aureus* isolates carrying Panton-Valentine leucocidin genes in England and Wales: frequency, characterization, and association with clinical disease. J Clin Microbiol 2005; 43: 2384-90.

[12] Prevost G, Couppie P, Prevost P, *et al*. Epidemiological data on *Staphylococcus aureus* strains producing synergohymenotropic toxins. J Med Microbiol 1995; 42: 237-45.

[13] Kaneko J, Kimura T, Kawakami Y, Tomita T, Kamio Y. Panton-valentine leukocidin genes in a phage-like particle isolated from mitomycin C-treated *Staphylococcus aureus* V8 (ATCC 49775). Biosci Biotechnol Biochem 1997; 61: 1960-2.

[14] Boubaker K, Dieboold P, Blanc D, *et al*. Panton-Valentine Leukocidin and staphylococal skin infections in school children. Emerg Inf Dis 2004; 10: 121-24.

[15] Osterlund A, Kahlmeter G, Bieber L, Runehagen A, Breider J. Intrafamilial Spread of Highly Virulent *Staphylococcus aureus* Strains Carrying the Gene for Panton-Valentine Leukocidin. Scand J Infect Dis 2002; 34: 763-87.

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