DOI：10.6314/JIMT.2016.27(1).07 內科學誌 2016：27：49-54

Pyomyositis and Necrotizing Pneumonia in a Young Soldier Caused by Methicillin-Susceptible *Staphylococcus aureus* of Sequence Type 59 Lineage

Pei-Hsiung Kuo[1], Feng-Jui Chen[2], Ming-Chin Chan[3], Li-Ping Kan[4], Kuo-Ming Yeh[4], Jung-Chun Lin[4], and Sheng-Kang Chiu[4]

[1]Department of Internal Medicine, Kaohsiung Armed Forces General Hospital–Gangshan Branch;
[2]National Health Research Institutes;
[3]Infection Control Office, National Defense Medical Center, Tri-Service General Hospital;
[4]Division of Infectious Diseases and Tropical Medicine, Department of Internal Medicine, National Defense Medical Center, Tri-Service General Hospital

Abstract

We herein report a case involving a 23-year-old male soldier with initial right leg pain that rapidly progressed to life-threatening septic pulmonary emboli, septic shock, and acute respiratory failure. The eventual diagnosis was pyomyositis and necrotizing pneumonia caused by Panton-Valentine leukocidin-producing, sequence type 59 single-locus variant (ST59slv) methicillin-susceptible *Staphylococcus aureus*. This microorganism is common in Taiwan and usually causes non-life-threatening skin and soft tissue infections. This is the first report of a life-threatening condition caused by ST59slv *S. aureus* infection. The patient survived with antistaphylococcal and antitoxic therapy, surgical drainage and debridement, intensive care, and multidisciplinary intervention. (J Intern Med Taiwan 2016; 27: 49-54)

Key Words: Necrotizing pneumonia, Pyomyositis, Panton-Valentine leukocidin, *Staphylococcus aureus*

Introduction

Pyomyositis involves intramuscular suppuration of the skeletal muscles. It is a type of deep-seated subcutaneous tissue infection often caused by *Staphylococcus aureus.* The clinical presentation of pyomyositis is variable and nonspecific, and is usually misdiagnosed as muscle sprain or strain. Delay in the accurate diagnosis and treatment of pyomyositis could lead to life-threatening complications. To our knowledge, in Taiwan, this is the first report of a rare case of hematogenous spread of lethal pyomyositis and necrotizing pneumonia in a young soldier that is caused by a Panton-Valentine

Reprint requests and correspondence：Dr. Sheng-Kang Chiu
Address：Division of Infectious Diseases and Tropical Medicine, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, No. 325 Sec. 2 Cheng-Kung Rd., Neihu 114, Taipei, Taiwan

leukocidin (PVL)-positive methicillin-susceptible *S. aureus* (MSSA) strain of sequence type 59 lineage (ST59).

Case Report

A 23-year-old male soldier was on service in Kinmen County, where he visited a clinic for pain in his right leg. Four days later, the pain worsened, and he developed mild shortness of breath and intermittent low-grade fever. He then visited another clinic and received an intramuscular analgesic. However, the following day, the pain worsened further and he had difficulty standing up. Subsequently, he was brought to a local hospital in Kinmen County where he developed fever, hypotension, respiratory distress, and decreased level of consciousness. Endotracheal intubation was performed immediately, and he was administered intravenous vasopressors. Later, he was transferred by air ambulance to Tri-Service General Hospital, Taipei, Taiwan, and admitted to the intensive care unit.

The patient had no history of trauma, acupuncture, unsafe sexual behavior, exposure to seawater, or handling of seafood. His colleague reported that his recent activities before the onset of leg pain involved vigorous exercise and carrying some heavy objects.

His initial physical examination at Tri-Service General Hospital revealed stupor, a body temperature of 37.5°C, weak and vague pulse, heart rate of 147 beats/min, blood pressure of 46/23 mmHg, and respiratory rate of 35 breaths/min. His Acute Physiology and Chronic Health Evaluation II score was 30. His skin had no ecchymosis or vascular stigmata; however, he had several small (<5 mm) monomorphous raised pustules on his face and chest. The sputum drawn from his endotracheal tube was blood-streaked. Auscultation of the chest revealed diffuse crackles, but no murmurs, rubs, or gallops. His abdomen was distended and had guarding. His genital examination was unremarkable. His right leg was more swollen than the left; however, no signs of compartment syndrome were observed.

The laboratory results were as follows: white blood cell count, 1.13×10^3 cells/mL; hemoglobin, 11.5 g/dL; platelets, 24×10^9/L; creatinine, 2.6 mg/dL; lactate, 5.0 mmol/L; C-reactive protein, 20.18 mg/dL; aspartate aminotransferase, 364 U/L; alanine aminotransferase, 116 U/L; creatine phosphokinase, 13,766 U/L; electrolytes, normal; arterial blood gas analysis, metabolic acidosis; coagulation, impaired (international normalized ratio, 1.4). He tested negative for human immunodeficiency virus. His chest radiograph (Fig. 1A) showed multiple, opaque, and diffuse nodules in both the lungs, suggesting septic emboli or metastatic lesions. A computed tomography (CT) image (Fig. 1B) showed hypodense areas in the right iliacus and gluteal muscles, suggesting pyomyositis. Transthoracic echocardiography results were normal.

On day 1, treatment with teicoplanin, imipenem, and clarithromycin was initiated. A diagnostic incision and drainage in the right iliac region was performed immediately. Gram staining of the specimen from the incision and drainage procedure showed numerous gram-positive cocci and polymorphic neutrophils. The antibiotics were then changed to intravenous oxacillin (2 g every 4 h) and intravenous linezolid (600 mg every 12 h). On day 3, culture of the initial 2 blood samples yielded MSSA. A culture of the specimen from surgical debridement also yielded MSSA, which was consistent with the presence of pustules on the face and chest wall. Thus, surgical debridement was repeated. On day 6, the patient developed spontaneous hemopneumothorax. Simultaneously, the ventilator was set such that the tidal volume was 6–8 mL/kg and the peak inspiratory pressure was 16 cm H_2O. A chest CT (Fig. 1C) image showed loculated pleural fluid, the split-pleura sign, and severe subcutaneous emphysema in most anterior region of the chest wall. The consultant surgeon performed bilateral video-

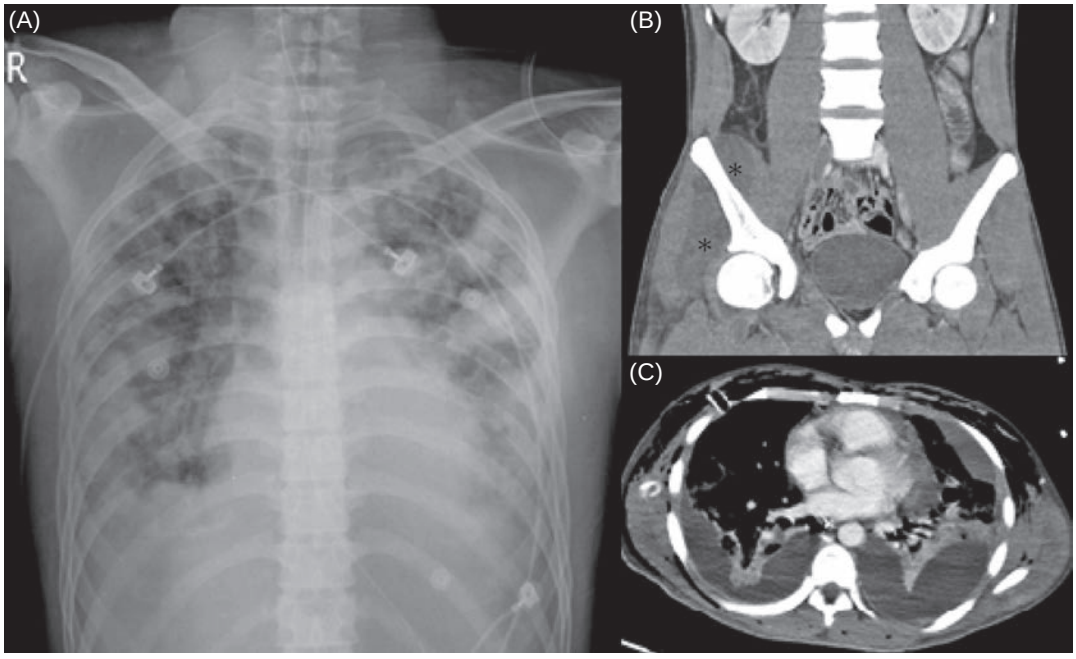

Figure 1. (A) The chest radiograph shows opaque diffuse nodules in both the lungs. (B) Coronal computed tomogram shows enlargement and decreased attenuation of the right iliacus and gluteal muscles (asterisks) and effacement of the fat planes, which suggest infectious myositis. (C) Contrast-enhanced computed tomogram shows loculated pleural fluid and split-pleura sign (which indicate exudative pleural effusion), subcutaneous emphysema in most anterior region of the chest wall, and small cavitary lesions in both the lungs.

assisted thoracoscopic decortication and drainage of the lungs. Histopathological examination of the biopsy specimen from the lung tissue showed necrosis, inflammation, and MSSA colonies.

We collected and sent the samples of the colonies to the National Health Research Institutes for microbiological analysis. The toxin and resistance genes were detected using polymerase chain reaction assay, and the genotype of the *S. aureus* strain was confirmed using multilocus sequence typing (MLST). The strain was a PVL-positive, *mecA*-negative, sequence type 59 single-locus variant (ST59slv).

In the following days, the patient underwent debridement of the infected muscle region 3 more times, and it was finally covered with a pedicled rectus femoris muscle flap and a myocutaneous skin graft. He was administered linezolid for 7 days and oxacillin for 6 weeks, and was then discharged and sent for the rehabilitation program.

Discussion

Pyomyositis is a deep-seated and complicated soft tissue infection, predominantly caused by *S. aureus*[1]. Other microorganisms such as gram-negative organisms, anaerobes, mycobacteria, and fungi are also implicated[2]. Infection by a gram-negative organism is more common among patients with underlying medical diseases and by an opportunistic pathogen is probable in immunocompromised patients. The mechanism underlying the pathogenesis of pyomyositis remains unclear. It is possibly caused by transient bacteremia, and intensive exercises or local trauma could be risk factors[2]. In the first stage, the muscle demonstrates gradual swelling and pain because of bacterial seeding and reproduction, and the final stage involves septicemia, metastatic abscess, and multi-organ dysfunction with high mortality[2]. The diagnosis of pyomyositis requires a high clinical suspicion and radiolog-

ical imaging studies such as ultrasound, CT scan, or magnetic resonance imaging[2]. Successful management requires prompt diagnosis, timely surgical debridement or drainage, and appropriate antibiotics therapy[1].

S. aureus has various virulent factors such as hemolysins and leukocidins. The amount of toxin production may contribute to the pathogenesis of *S. aureus* infection[3]. PVL has been suggested as a valuable marker and target to screen the virulence of some strains of *S. aureus.* PVL is a pore-forming toxin that destroys the host leukocytes and induces cells lysis[4]. Approximately, 5–50% of *S. aureus* isolates produce PVL causing tissue necrosis and extensive severe infections[5]. Gillet et al. first reported about a community-acquired pneumonia caused by *S. aureus.* They observed that the patients infected with PVL-positive *S. aureus* were younger, without risk factors, and presented more often with hemoptysis, high fever, tachycardia, tachypnea with diffuse bilateral infiltrates, and pleural effusion[6]. Khanafer et al. reported that severe leukopenia in PVL-positive infections was associated with high mortality[7]. Sicot et al. proposed that methicillin resistance was not always a predictor of the severity in *S. aureus* pneumonia; however, airway hemorrhages were more frequently associated with PVL-MSSA pneumonia[8]. Both MSSA and methicillin-resistant *S. aureus* (MRSA) can secrete PVL; however, PVL is predominantly expressed in MRSA[9]. A recent study showed that PVL could cause significant damage to the muscles, but not to the skin, and was associated with increased incidence of myositis[9]. Therefore, PVL testing should be performed if the aforementioned characteristic is evident in *S. aureus* infections.

Currently, there are no guidelines for the management of PVL-positive *S. aureus* infections[10]. An *in vitro* study of the antibiotics for PVL-positive strains revealed that oxacillin enhanced PVL release, while clindamycin, linezolid, fusidic acid, and rifampicin were inhibitory[11]. It would be beneficial to use oxacillin in combination with clindamycin, rifampicin, or linezolid to treat PVL-positive *S. aureus* infections. Intravenous immunoglobulins can be used in severe cases owing to the *in vitro* evidence that it neutralizes the toxic action of PVL on polymorphonuclear cells[12].

The MLST method has been developed for bacterial genotyping to explore the genes and their epidemiologic distribution. According to the literature in Taiwan, sequence type 188 was predominant in MSSA infections, while ST59 was the common type in MSSA and MRSA[13]. Chen et al. published the first report showing that PVL-positive ST59 *S. aureus* was a successful clonal lineage in both MRSA and MSSA[14]. PVL-positive ST59 MSSA has a similar genetic profile as the PVL-positive ST59 MRSA strains[14].

Our report presents a case of a young healthy man with no risk exposure who presented with hemoptysis and severe leukopenia, and was diagnosed with a rare deep-seated infection with hematogenous spread of the pathogen leading to septic shock and multi-organs dysfunction. To our knowledge, this is the first case report of pyomyositis and necrotizing pneumonia caused by ST59slv *S. aureus.* We successfully treated the patient by administering combined antibiotic therapy using oxacillin and linezolid, surgical drainage and debridement, intensive care, and multidisciplinary intervention.

Acknowledgements

This report was supported by research grants from Tri-Service General Hospital, Taiwan (TSGH-C13-04 and MAB101-2).

References

1. Dryden MS. Complicated skin and soft tissue infection. J Antimicrob Chemother 2010; 65 (Suppl 3): 35-44.
2. Crum NF. Bacterial pyomyositis in the United States. Am J Med 2004; 117: 420-8.
3. Varshney AK, Martinez LR, Hamilton SM, et al. Augmented production of Panton-Valentine leukocidin toxin in methicillin-resistant and methicillin-susceptible Staphylococcus

aureus is associated with worse outcome in a murine skin infection model. J Infect Dis 2010; 201: 92-6.
4. Kaneko J, Kamio Y. Bacterial two-component and hetero-heptameric pore-forming cytolytic toxins: structures, pore-forming mechanism, and organization of the genes. Biosci Biotechnol Biochem 2004; 68: 981-1003.
5. Vandenesch F, Naimi T, Enright MC, et al. Community-acquired methicillin-resistant Staphylococcus aureus carrying Panton-Valentine leukocidin genes: worldwide emergence. Emerg Infect Dis 2003; 9: 978-84.
6. 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: 753-9.
7. Khanafer N, Sicot N, Vanhems P, Dumitrescu O, Meyssonier V, Tristan A, et al. Severe leukopenia in Staphylococcus aureus-necrotizing, community-acquired pneumonia: risk factors and impact on survival. BMC Infect Dis 2013; 13: 359.
8. Sicot N, Khanafer N, Meyssonnier V, et al. Methicillin resistance is not a predictor of severity in community-acquired Staphylococcus aureus necrotizing pneumonia--results of a prospective observational study. Clin Microbiol Infect 2013; 19: E142-8.
9. Tseng CW, Kyme P, Low J, et al. Staphylococcus aureus Panton-Valentine leukocidin contributes to inflammation and muscle tissue injury. PLoS One 2009; 4: e6387.
10. Morgan MS. Diagnosis and treatment of Panton-Valentine leukocidin (PVL)-associated staphylococcal pneumonia. Int J Antimicrob Agents 2007; 30: 289-96.
11. Dumitrescu O, Badiou C, Bes M, et al. Effect of antibiotics, alone and in combination, on Panton-Valentine leukocidin production by a Staphylococcus aureus reference strain. Clin Microbiol Infect 2008; 14: 384-8.
12. Gauduchon V, Cozon G, Vandenesch F, et al. Neutralization of Staphylococcus aureus Panton Valentine leukocidin by intravenous immunoglobulin in vitro. J Infect Dis 2004; 189: 346-53.
13. Chen FJ, Siu LK, Lin JC, Wang CH, Lu PL. Molecular typing and characterization of nasal carriage and community-onset infection methicillin-susceptible Staphylococcus aureus isolates in two Taiwan medical centers. BMC Infect Dis 2012; 12: 343.
14. Chen FJ, Hiramatsu K, Huang IW, Wang CH, Lauderdale TL. Panton-Valentine leukocidin (PVL)-positive methicillin-susceptible and resistant Staphylococcus aureus in Taiwan: identification of oxacillin-susceptible mecA-positive methicillin-resistant S. aureus. Diagn Microbiol Infect Dis 2009; 65: 351-7.

序列型59的金黃色葡萄球菌在一個年輕軍人所導致的化膿性肌炎和壞死性肺炎

郭培雄[1] 陳逢叡[2] 詹明錦[3] 甘麗平[4] 葉國明[4] 林永崇[4] 邱勝康[4]

[1]國軍高雄總醫院岡山分院 內科
[2]國家衛生研究院
[3]三軍總醫院 感染控制室
[4]三軍總醫院 感染及熱帶醫學科

摘 要

我們在此報告一名23歲的男性士兵，最初始於右腿疼痛，後來快速發展到危及生命的感染性肺栓塞，感染性休克，急性呼吸衰竭的情況。最後的診斷是由甲氧西林敏感之金黃色葡萄球菌所引起的化膿性肌炎和壞死性肺炎，此菌株可製造潘頓 - 瓦倫丁殺白細胞素(PVL)，屬於序列型59單基因變異 (ST59slv)。這類微生物在台灣是普遍的，通常是無生命危險的皮膚和軟組織感染症。這是序列型59金黃色葡萄球菌感染所造成生命威脅的第一份報告。病人經由抗葡萄球菌和抗毒素藥物，手術引流及清創，重症監護，和多重專科合併治療之後存活。