CASE REPORT

A RAPIDLY FATAL CASE OF PANTON-VALENTINE LEUKOCIDIN POSITIVE *STAPHYLOCOCCUS AUREUS* NECROTIZING PNEUMONIA IN AN HIV-INFECTED PATIENT

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Abstract. This article reports a rare case of necrotizing pneumonia caused by Panton-Valentine leukocidin (PVL) positive *Staphylococcus aureus* in an HIV-infected patient presenting with severe back pain and rash. The back pain progressed to excruciating abdominal pain which was misleading, resulting in an investigation on intraabdominal conditions. He developed massive hemoptysis and died within 2 days of the first clinical symptoms. Recognizing the emergence of PVL-producing *S. aureus* is important in both immunocompetent and immunocompromised patients. This organism was transmitted from his wife.

INTRODUCTION

Staphylococcus aureus, producing Panton-Valentine leukocidin, a cytotoxin that causes destruction of leukocytes and tissue necrosis has been reported to cause rapid, extensive necrotizing pneumonia in immunocompetent children and young adults (Gillet *et al*, 2002). To our knowledge, this is the first case report of PVL-producing *S. aureus* in an HIV-infected Thai patient with a fatal outcome.

CASE REPORT

A 38-year-old Thai male, presented to the emergency department of Srinagarind Hospital at 08:50 PM on August 29, 2004, with a generalized rash he had experienced for the previous 9 hours. He had also developed acute back pain 11 hours prior to hospitalization. He took 2 tablets of piroxicam 20 mg, 2 hours after which he developed a burning rash, fever, abdominal pain, and watery diarrhea.

He had been diagnosed with HIV infection in 1994 and had a history of tuberculous colitis, candida esophagitis, cryptococcus lymphadenitis, and pulmonary rhodococcosis sequentially over the previous two years. He received treatment for all these opportunistic infections along with antiretroviral drugs. The latter was started in May 2002. His initial antiretroviral treatment regimen was comprised of stavudine, lamivudine and efavirenz, but was changed in October 2002 to GPO-VIR - a fixed dose combination of stavudine, lamivudine, and nevirapine. He responded well to the treatment. His viral load decreased from

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174,475 copies/ml to <400 copies/ml and the CD4 cell count increased from 27 cells/mm^3 to 292 cells/mm^3 on August 24, 2004 five days prior to admission at a routine clinic visit. His final medication was GPO-VIR only.

On physical examination, he had a temperature of 38.8ºC, a blood pressure of 115/63 mmHg, a pulse rate of 115 beats/min, and a respiratory rate of 28 breaths/min. He had a generalized erythematous rash with questionable target-like lesions and minimal crepitations at the base of the lungs. Presuming a piroxicam allergy, the patient was treated with dexamethazone 10 mg, chlorpheniramine 4 mg intravenously, and adrenaline 0.5 ml subcutaneously. He was discharged with oral chlorpheniramine and domperidone and scheduled for routine follow-up.

The patient was brought back to the emergency at 04:16 AM the next morning with severe abdominal pain in the left upper quadrant, aggravated by inspiration. Generalized guarding and tenderness of the left upper abdomen and the presence of bowel sounds were noted. There was a minimal infiltration of the right middle, right lower and left middle lung fields on chest radiography taken at 06:46 AM (Fig 1).

Blood tests indicated: a leukocyte count of 3.10 x 10^9/l, platelet count of 177 x 10^9/l, hemoglobin level of 15.8 g/dl, prothrombin time of 14.9 sec, and an activated prothrombin time of 44.6 sec, BUN of 32.7 mg/dl, and creatinine of 2.3 mg/dl. The liver function was normal with an alanine aminotransferase of 31 U/l, aspartate aminotransferase of 55 U/l and an alkaline phosphatase of 69 U/l. The serum albumin and bilirubin levels were within normal range. An arterial blood gas on room air showed the following abnormal results: pH 7.295, PCO_2 49.2 mmHg, PO_2 57.2 mmHg, and HCO_3 23.4 mmHg.

While obtaining a surgical consultation, the patient experienced progressive dyspnea and hypoxemia requiring intubation at 12:25 PM. Ceftriaxone and metronidazole were administered intravenously for possible intra-abdominal infection. Since the patient had protracted abdominal pain, computed tomography of abdomen was requested at 01:00 PM. The study revealed thickening of the bowel wall of the ascending colon and the small bowel loops with evidence of peri-mesenteric fat stranding and small para-aortic lymphadenopathy, and pneumonia of the right middle lobe, the left lingular lobe and the basal segments of both lower lungs. By 02:00 PM, the patient had developed profuse massive hemoptysis and became hypotensive at 04:00 PM. There was diffuse bilateral infiltration on chest radiography taken at 03:41 PM (Fig 2). The hemoptysis persisted and the hypotension did not respond to inotropic drugs. The patient died at 06:00 PM.

An autopsy was not permitted but a necropsy of the lungs was allowed. Two specimens on blood culture, the sputum culture and lung necropsy culture grew a methicillin sensitive strain of *S. aureus*. The pathology of the necropsy lung parenchyma revealed massive alveolar hemorrhage. The alveoli were filled with erythrocytes, sparse inflammatory cells, and numerous clusters of cocci.

Since the patient had experienced a severe pulmonary hemorrhage, PVL-producing *S. aureus* was suspected and the isolates were tested for the presence of PVL genes using polymerase chain reaction (PCR) with previously described primers (Lindberg ***et al***, 2004). For confirmation of the specificity of the PCR products, DNA sequencing from amplification of the isolate was performed. The results were 99% identical to the X72700 sequence (Lindberg ***et al***, 2004), and were therefore submitted to Gen Bank (Accession no. DQ 1518097).

The possibility of intra-familial transmission was suspected and an investigation

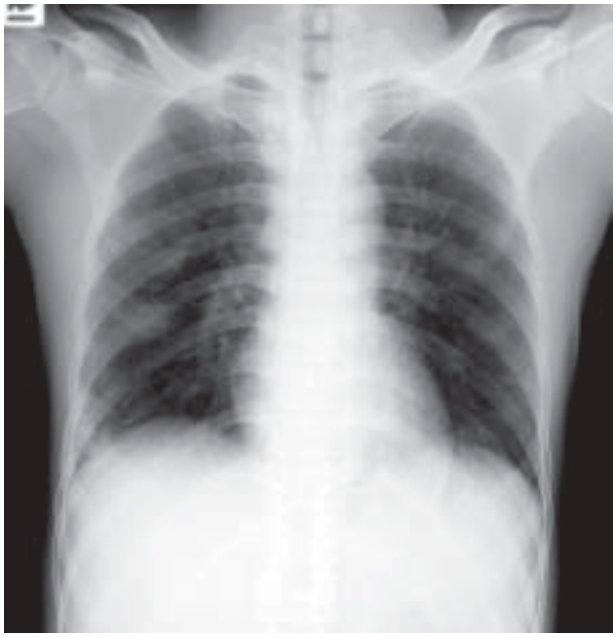

Fig 1–Chest radiograph of the patient at 06:46 AM on August 29, 2004 shows minimal infiltration of the right middle, right lower, and left middle lung fields.

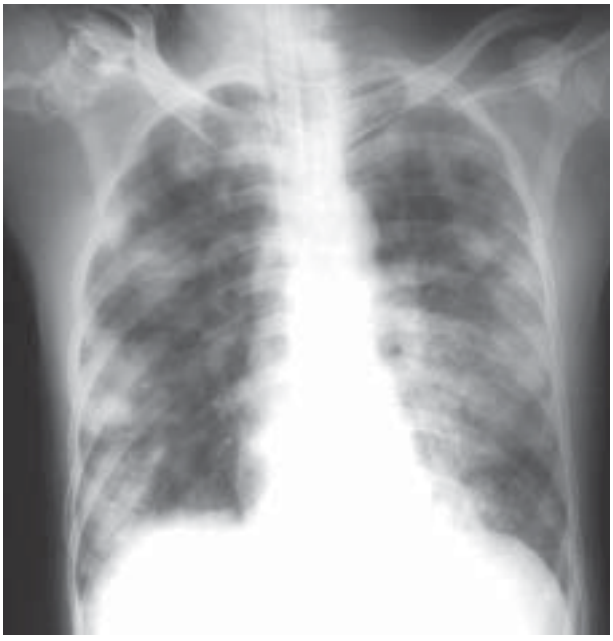

Fig 2 - Chest radiograph of the patient at 03:41 PM on August 29, 2004 shows diffuse bilateral infiltrations of both lungs.

revealed that the patient's wife had 2 subcutaneous abscesses of her right flank 4 days prior to the patient's illness. Examination on September 15, 2004, revealed abscesses. Methicillin-sensitive *S. aureus* with the same antibiogram as the patient's isolate was identified from the abscesses. The isolate was positive for the PVL gene.

To assess the genetic relationship between the *S. aureus* isolates from the patient and his wife, they were typed by randomly amplified polymorphic DNA (RAPD), using three different primers (Garcia-Hermoso *et al*, 1999; Lindberg *et al*, 2000, 2004) and a repetitive sequence based PCR (Rep-PCR) (Francis *et al*, 2005). The strains from the patient and his wife had identical RAPD and Rep-PCR patterns. Genomic typing of these strains revealed that the patient and his wife were infected with the same strain.

The abscesses were responsive to oral antibiotic and the wife did not develop any serious staphylococcal infection. The patient's wife was also HIV-infected with a CD4 cell count of 385 cells/mm^3 on June 30, 2004, which had decreased to 278 cells/mm^3 on September 15, 2004. Antiretroviral treatment was therefore initiated to which she responded well.

DISCUSSION

This report describes a rare case of PVL-producing methicillin-sensitive *S. aureus* infection in an HIV-infected patient. The infection is usually reported in immunocompetent patients (Del Vecchio *et al*, 1995; Gillet *et al*, 2002). Making a correct diagnosis in this case was difficult because the patient presented with atypical signs and symptoms of rash, fever, and severe abdominal pain. The PVL-producing *S. aureus* infection was suspected after: 1) discovering a known pathogen in the blood; 2) the necropsy of the lung culture; and, 3) a retrospective review of the clinical course

of the patient.

Massive hemoptysis was rare (4%) among the 50 HIV-infected patients that presented with hemoptysis reported by Nelson and Forman (1996). One was caused by pulmonary aspergillosis and another by *Pseudomonas aeruginosa* pneumonia. Community-acquired PVL-producing *S. aureus* infections have been reported worldwide (Vandenesch *et al*, 2003; Mulvey *et al*, 2005; Tenover *et al*, 2006). To date, there have been no reported PVL-positive *S. aureus* in Thailand. The patient probably developed the *S. aureus* strain from his wife.

Most cases of skin and soft tissue infections in one study (Lina *et al*, 1999) (93% of furunculosis) were reported as being due to PVL-producing *S. aureus*. Transmission of PVL-producing *S. aureus* has been reported in close contacts, from breast feeding (Le Thomas *et al*, 2001), among post-partum women (Saiman *et al*, 2003), among professional football players (Kazakova *et al*, 2005), during the resuscitation of a child by a physician (Chalumeau *et al*, 2005), and between pets and their owners (Strommenger *et al*, 2005; van Duijkeren *et al*, 2005).

This study demonstrates that in HIV-infected patients during the process of immune recovery with antiretroviral therapy, PVL-producing *S. aureus* infection can occur with devastating results. The incidence and clinical significance of PVL-producing *S. aureus* should be explored and monitored. Whether HIV infection is a risk factor for predicting clinical severity of this organism needs further evaluation.

ACKNOWLEDGEMENTS

We thank Mr Bryan Roderick Hamman for his assistance with the English-language presentation.

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