Septic Pulmonary Embolism: Analysis of Twenty-Eight Cases

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Abstract

Septic pulmonary embolism (SPE) is an uncommon disease with a diverse epidemiology. The purpose of this study was to investigate the clinical characteristics of SPE in northern Taiwan. A retrospective review of hospitalized patients with SPE from January 1, 2001 to December 31, 2005 was conducted in a medical center in northern Taiwan. The clinical presentations, radiographic findings, microbiological data, treatment and outcomes were analyzed. Twenty-eight patients were included in the final analysis. Their mean age was 44 years, and 16 patients were men. The most common septic source was infective endocarditis of the tricuspid valve (n=14), followed by liver abscess (n=5). Staphylococcus aureus was the causative microorganism in 16 patients, followed by Klebsiella pneumoniae in 9 patients. Bacteremia occurred in 19 patients. All patients were treated with appropriate antibiotics and 4 had a valve replacement for infective endocarditis, 1 had a fasciotomy for necrotizing fasciitis, and 1 had percutaneous drainage of a liver abscess. Respiratory failure developed in 5 patients and 3 patients died. Tricuspid valve endocarditis and liver abscess were the main contributing risk factors in patients with SPE in northern Taiwan, while Staphylococcus aureus and Klebsiella pneumoniae were the causative pathogens in these 2 conditions, respectively. (J Intern Med Taiwan 2013; 24: 1-7)

Key Words: Endocarditis, Liver abscess, Pulmonary embolism

Introduction

Septic pulmonary embolism (SPE) is an uncommon disease without a specific clinical presentation and may present with an insidious onset of fever, cough or hemoptysis. The diagnosis is based on the presence of certain risk factors such as intravenous drug use, tricuspid valve bacterial endocarditis, thrombophlebitis, indwelling catheters or devices, osteomyelitis, or soft tissue infection, combined with characteristic radiographic findings of multiple peripheral lung nodules with or without cavitation. The primary foci of infection responsible for SPE differ in the literature. Although the incidence has declined, infective endocarditis is a considerable embolic source of SPE in Western countries. Sakuma et al also reported that infective endocarditis was a common extrapulmonary septic source, followed by pneumonia and sepsis of unknown origin in Japan. In contrast, Lee et al

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reported 21 cases of SPE in Korea, but infective endocarditis was only seen in 3 cases, liver abscess in 2, central venous catheter infection in 2, and soft tissue infection or arthritis in the remainder. Wang et al reported 10 children with SPE in northern Taiwan and the most common embolic source was soft tissue infection, followed by bone infection, suppurative otitis media, and catheter-related infection. Seven of these patients had community acquired staphylococcal infections and bacteremia. To identify the clinical characteristics of SPE in adult patients in northern Taiwan, we retrospectively analyzed the clinical presentations, microbiological and image studies, therapeutic modalities and outcomes in these patients.

Materials and Methods

A retrospective chart review was conducted in a 2800-bed medical center in northern Taiwan. The collected data were sourced from January 1, 2000 through December 31, 2005. We reviewed the medical records of 201 patients with ICD-9 code 415.1 (pulmonary embolism and infarction) and ICD-9 code 415.19 (other pulmonary embolism and infarction) to identify patients with septic pulmonary embolism. The definition of SPE was (1) the presence of multiple round or wedge-shaped densities in the lung periphery; (2) resolution of pulmonary lesions after administration of antimicrobial agents or death due to sepsis, with a clearly infectious cause; and (3) the presence of active extrapulmonary infection as a potential embolic source. In the absence of septic sources, SPE was also suggested by the presence of intravenous drug use or an underlying immunocompromised condition. The causative microorganism was defined as the identified microorganism from blood culture and/or sputum cultures with good quality on a sputum smear (defined as epithelial cells < 10/HPF and polymorphonuclear cells > 25/HPF), or a specimen from a septic source. Patients under 18 years old were excluded. All data were obtained by reviewing patients’ histories, physical examinations, chest radiographs (CXR), and computed tomography (CT). The analysis included patient age, sex, clinical symptoms and signs, results of examinations, treatment programs, and outcomes. This study was approved by the Institutional Review Board.

Results

Patients

Twenty-eight patients who fit the inclusion criteria of SPE were included in the final analysis, of whom 5 have already been reported in the literature. Seven patients with multiple peripheral lung densities on CXR indicating SPE were not further examined with chest CT. The clinical data of the patients are shown in Table 1. Their mean age was 44 years (range 18-87). Sixteen were men. The mean duration between appearance of symptoms and diagnosis of SPE was 11 days (range 1-28), while the average duration of hospitalization was 43 days (range 3-110). Ten patients were intravenous drug users, while 8 had diabetes mellitus. Fever developed in 19 patients, followed by cough in 9 patients, dyspnea in 8 patients, and chest pain in 3 patients. Chest auscultation showed crackles in 8 patients, wheezing in 1, and clear breath sounds in the remainder.

Primary focus of infection

Infective endocarditis of the tricuspid valve was the primary focus of infection in 14 patients. The other septic origins included 5 cases of liver abscesses, 1 case each of arteriovenous shunt infection, facial cellulitis, parotitis, necrotizing fasciitis, osteomyelitis, and 4 with an undetermined source. Echocardiography was performed in 22 patients. Four patients with liver abscess, 1 with necrotizing fasciitis, and 1 with osteomyelitis did not undergo echocardiography. Fourteen patients underwent transthoracic echocardiography (TTE) without transesophageal echocardiography (TEE)
which showed vegetations in 10. Four underwent TEE without TTE which showed vegetations in 2. Four underwent both TTE and TEE which showed vegetations in 2. Abdominal ultrasonography was performed in 19 patients which showed liver abscesses in 5 patients. All 4 patients with undetermined septic foci underwent abdominal ultrasonography examinations, of which 2 underwent TEE only, 1 underwent TTE only, and 1 underwent both TTE and TEE.

Microbiological studies

*Staphylococcus aureus* was the causative microorganism in 16 patients, of which 2 were oxacillin-resistant *Staphylococcus aureus* isolates. Thirteen had infective endocarditis, 1 had facial cellulitis, 1 an arteriovenous shunt infection and 1 intravenous drug user had an undetermined source. *Klebsiella pneumoniae* was the causative microorganism in 9 patients, including 5 with liver abscess, 1 with necrotizing fasciitis and 3 with an undetermined source. Bacteremia occurred in 19 patients, of which 15 had *Staphylococcus aureus* and 4 had *Klebsiella pneumoniae*. Only one patient with facial cellulitis caused by *S. aureus* had no bacteremia, and had no evidence of infective endocarditis as demonstrated by TEE. Four of five patients with *Klebsiella pneumoniae* but without bacteremia received abdominal ultrasonography and/or abdominal CT. Three was diagnosed as liver abscesses.

Imaging examinations

CXR were done in all 28 patients, and disclosed peripheral nodules in 21 patients (Fig. 1A), non-nodular infiltration in 19 patients, cavity lesions in 4 patients (Fig. 1B), wedge-shape peripheral infiltration in 1 patient (Fig. 1C), and pleural effusion in 3 patients. CT of the chest was done in 20 patients, while CT of abdomen including the lower chest was done in 1 patient with a liver abscess. Peripheral nodules were demonstrated in all 21 patients undergoing CT examination (Fig. 2A), while a feeding vessel sign was seen in 18 patients (Fig. 2B), peripheral wedge-shape infiltration in 13 patients (Fig. 2C), cavity lesions in 13 patients (Fig. 2D), and pleural effusion in 7 patients. There were a total of 539 pulmonary parenchymal lesions identified on CT, including nodular lesions with or without cavitation,
peripheral wedge infiltration and non-nodular infiltration. Nodular lesions with or without cavitation were noted in 492 (91.3%) of these lesions, peripheral wedge infiltration in 22 (4.1%), and non-nodular infiltration in 25 (4.6%). Fifty-seven of the 539 (10.6%) parenchymal lesions showed cavitation, and 96 (17.8%) displayed a feeding vessel sign. Table 2 shows different image findings on chest radiograph and chest CT.
All patients were initially treated with empiric antibiotics, which were shifted to appropriate antibiotics if indicated after obtaining the results of cultures and sensitivity tests. Six patients underwent surgical or radiological intervention for primary infection foci, of which 4 had a tricuspid valve replacement for infective endocarditis, 1 had a fasciotomy for necrotizing fasciitis, and 1 had percutaneous drainage of a liver abscess. Respiratory failure developed in 5 patients and 3 patients died because of sepsis, including 1 with infective endocarditis and 2 with liver abscess.

### Discussion

The underlying causes of SPE differ in reports. Ten of our patients were intravenous drug users and 14 patients had infective endocarditis. Drug addiction was the greatest risk factor for SPE decades ago. Lately, there has been a decline in intravenous drug abuse causing SPE in Western countries. Cook et al reported on 14 patients with SPE and only 1 was an intravenous drug user, while Lemierre syndrome (4), central venous infection (3), prosthetic valve infection (2), pacemaker infection (2), dental abscess (1) and perinephric abscess (1) were the remaining underlying conditions. Better needle hygiene and the increasing use of indwelling catheters and devices has contributed to the changing epidemiology of SPE in Western countries.

Septic pulmonary embolism is a common complication in intravenous drug users with staphylococcal endocarditis and radiography is a helpful modality for an early clinical diagnosis in this situation. Intravenous drug addiction, staphylococcal septicemia, and SPE are considered a triad pathognomonic for tricuspid valve endocarditis. Because of the growing epidemic of intravenous drug use in Taiwan, clinicians should be familiar with the radiographic characteristics of SPE in order to detect underlying disease early, avoid unnecessary investigation, and provide appropriate therapy. *Staphylococcus aureus* was the causative microorganism in our patients with tricuspid infective endocarditis complicated by SPE. We suggest TTE or TEE in the patients with SPE caused by *Staphylococcus aureus*.

In this analysis, liver abscess was the second leading septic source of SPE. Although not usual, liver abscess should be considered a possible septic source of SPE in Taiwan. Six of nine patients with *Klebsiella pneumoniae* infection had diabetes mellitus. All 5 patients with liver abscess had *Klebsiella pneumoniae*, which is a common pathogen in diabetic patients with liver abscess in Taiwan. Sakuma et al reported that 65 of 247 patients with SPE had definite extrapulmonary infection sources, of which twenty-eight patients had infective endocarditis, followed by 10 with liver abscess. Liver abscess is prevalent in diabetic patients in Taiwan, and the incidence of septic metastases is
6.7-12.3%\textsuperscript{7,13-15}. Endophthalmitis, lung abscess, empyema, SPE, brain abscess, meningitis, prostate abscess, osteomyelitis, septic arthritis, psoas muscle abscess, spleen abscess, chest wall abscess, and necrotizing fasciitis have been reported as metastatic foci\textsuperscript{7,13-15}. Diabetes mellitus, \textit{Klebsiella pneumoniae} infection and bacteremia are risk factors contributing to septic metastasis\textsuperscript{13-15}. The reported incidence of SPE in patients with liver abscess is 2.2-5.3%\textsuperscript{7,13,14}, which indicates that SPE is an unusual but not rare complication in patients with liver abscess. Septic pulmonary embolism should be considered if such a patient complains of cough or dyspnea or presents with hypoxemia.

CXR demonstrated the characteristic radiographic findings in our patients. The typical findings on CXR are peripheral nodules, some featuring cavity lesions, and even non-specific findings\textsuperscript{2}. Hilar or mediastinal lymphadenopathy, pleural effusion, and pneumothorax have also been found in patients with SPE\textsuperscript{16}. Chest CT is a more valuable radiologic modality then chest radiography when SPE is suspected. The CT features in the studied patients included multiple peripheral nodules, wedge-shaped peripheral lesions, cavitation of nodules, and a feeding vessel sign and were consistent with previous reports\textsuperscript{17}.

Most of our patients recovered uneventfully, which is consistent with previous reports. The prognosis of SPE has improved with appropriate antibiotic therapy and effective control of the primary infection focus\textsuperscript{2,6}. Valve replacement for infective endocarditis or thoracotomy for empyema may be needed in some patients who fit the indications\textsuperscript{2}.

In conclusion, tricuspid valve endocarditis and liver abscess were the main contributing risk factors in patients with SPE in northern Taiwan, and \textit{Staphylococcus aureus} and \textit{Klebsiella pneumoniae} were the causative pathogens in these 2 conditions, respectively.

References

敗血性肺栓塞：28位病例分析

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摘 要

敗血性肺栓塞並不常見，且其流行病學因地而異。本研究之目的為探討北台灣敗血性肺栓塞病患的臨床特徵。我們回溯性分析台灣北部某醫學中心自2001年1月1日至2005年12月31日的敗血性肺栓塞病患，分析資料包括病患的臨床表現、放射線學與微生物學檢查、治療以及預後。共有28位病患，平均年齡為44歲，16位男性。最常見的原發感染病灶為三尖瓣心內膜炎 (14位)，其次為肝膿瘍 (5位)。最常見的致病菌為金黃色葡萄球菌 (16位)，其次為克雷伯氏肺炎菌 (9位)，19位病患患有菌血症。全部病患均接受適當的抗生素治療，4位接受心臟瓣膜置換手術，1位接受筋膜切開術，1位接受肝膿瘍經皮引流。5位病患發生呼吸衰竭，最後3位因敗血症而死亡。感染性心內膜炎與肝膿瘍是北台灣的肺部敗血性栓塞病患最常見的原發感染源，其致病菌分別是金黃色葡萄球菌與克雷伯氏肺炎菌。