

Septic Superficial Femoral Vein Thrombophlebitis Causing Pulmonary Emboli and Respiratory Failure: Case Report and Review of the Literature

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Abstract

Septic pulmonary emboli rarely cause respiratory failure that requires mechanical ventilation. The most common causes of septic pulmonary emboli are related to intravenous drug abuse, indwelling intravenous catheters, endocarditis and septic pelvic thrombophlebitis. In addition, soft tissue injury-related thrombophlebitis rarely causes septic pulmonary emboli. We describe a unique case of a 43-year-old man who developed septic thrombophlebitis of the femoral vein following soft tissue injury from trauma to the shin with ensuing septic pulmonary emboli which necessitated endotracheal intubation and mechanical ventilation. The patient required mechanical ventilation for eleven days, developed empyema and grew out methicillin-resistant *Staphylococcus aureus* on blood cultures. A transesophageal echocardiogram was normal, and there was no indication of bacterial endocarditis. In addition to eleven days of mechanical ventilation, the patient was treated with intravenous heparin, cefepime and clindamycin. These medications were then discontinued and the patient was treated with weight-adjusted vancomycin. Following the return of cultures, the patient was treated for six weeks with ceftaroline 600 mg IV twice a day. In addition, the patient received bilateral thoracentesis followed by chest tube drainage until resolution of the pleural effusions. The patient made a complete recovery. We describe this case and the implications for differential diagnosis and treatment of these two uncommon conditions.

Keywords

Septic Thrombophlebitis, Pulmonary Emboli, Respiratory Failure, Critical Care

1. Introduction

Septic pulmonary embolism (SPE) is a variant of nonthrombotic pulmonary embolism in which a thrombus containing microorganisms causes an inflammatory reaction [1]. These thrombi can cause infarction and metastatic abscesses. SPE is a rare but serious condition that can pose as a difficult diagnostic challenge due to its nonspecific clinical and radiographic features, often leading to delayed diagnosis [2]. SPE has been associated with Lemierre's syndrome and periodontal disease [3] [4]. CT findings of SPE include peripheral nodules with or without cavitation, a feeding vessel sign, and wedge shaped peripheral lesions abutting the pleura (Figure 1) [2] [5] [6] [7]. Diagnosis of SPE is based on the presence of these CT findings and clinical evidence of infection [2].

In a systematic review of SPE from 1978 to 2012, the most common causative organism was *Staphylococcus aureus*, being responsible for 85% of cases [8]. This review of SPE found that most cases are associated with the use of intravenous drugs (26%), the use of an indwelling catheter (13%), or the presence of infectious endocarditis (12%). Less common causes include those associated with soft tissue infections (6%). The article cited three papers, documenting five patients in total with SPE originating from septic thrombophlebitis (ST) of the femoral vein. Of these five cases, three were associated with intravenous drug abuse, one case was associated with pyomyositis, and one was associated with a soft tissue infection following trauma to the great toe [9] [10] [11]. A recent case study also described, the papers cited above were referred to in past tense a case of SPE caused by an infected central venous port [12]. Search of the literature available on PubMed since 2012 shows no additional instances of SPE due to femoral vein thrombophlebitis. A search of the literature has also shown that SPE is

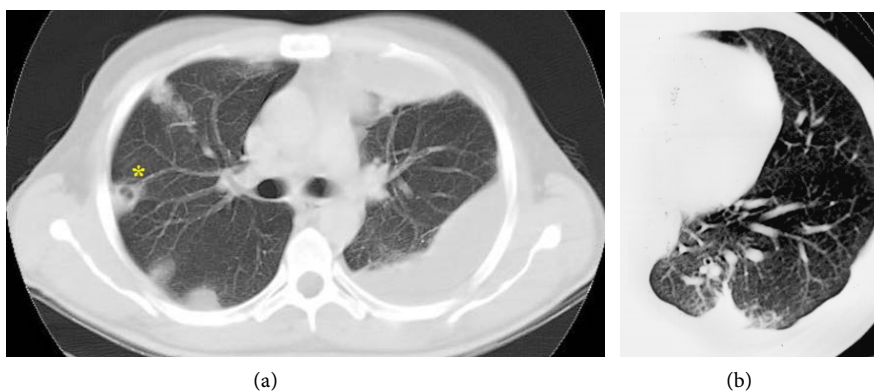


Figure 1. CT findings seen in SPE. (a) Multiple peripheral nodules, and a feeding vessel sign (Asterix); (b) Wedge shaped peripheral lesion abutting the pleura [7].

rarely associated with respiratory failure [8]. We report a case of a man with SPE due to femoral vein thrombophlebitis that is not associated with intravenous drug use.

2. Case Description

A 43-year-old man presented to the emergency department with sudden onset malaise accompanied by swelling and pain in the right leg. Four days prior to admission, he hit his right shin on a trailer hitch in his garage causing bruising but no bleeding. The following day after returning home from work, he noticed a new onset rash on the right leg and acute onset malaise. Over the next two days, the patient slept the majority of the time, before seeking medical care. He has a history of underlying bilateral leg edema that began in 2015 following a right total hip arthroplasty, according to the patient's report. He admitted to marijuana usage but denied any intravenous drug use. Written consent was given by the patient for publication of this case report.

On presentation, his vitals were: temperature of 102°F, heart rate of 65, respiratory rate of 16, blood pressure of 117/86, and oxygen saturation of 98% on room air. He had bilaterally swollen lower extremities, more prominent on the right, with a large area of erythema and multiple bullae over the lateral right thigh and knee. The right mid-thigh was exquisitely tender to palpation but without crepitus. Right dorsalis pedis pulse was diminished and capillary refill was delayed. Breath sounds were decreased bilaterally and no murmurs were present. Over the next five hours, his vitals decompensated to a temperature of 102°F, heart rate of 152, respiratory rate of 42, blood pressure of 102/73 and oxygen saturation of 92% on room air.

Initial labs demonstrated thrombocytopenia (105,000 platelets/ μ L), hyponatremia, a lactic acid level of 4.5, and an erythrocyte sedimentation rate of 38 mm/hr. However, there was no indication of leukocytosis. Blood, sputum, wound, and urine cultures were obtained. CT of the right lower extremity demonstrated edema, no gas, and a non-occlusive deep vein thrombosis of the right femoral vein; CT angiography of the chest demonstrated small filling defects of the right upper lobe segmental pulmonary artery as well as extensive abnormal lung nodularity of mixed solid and semisolid appearance (**Figure 1**). Transthoracic and transesophageal echocardiograms showed no valvular abnormalities.

He was initially placed on vancomycin, cefepime, and clindamycin and was intubated due to hypoxemic respiratory failure. Heparin drip was held until the first day of hospitalization when an MRI could be obtained to rule out brain emboli (no head CT with contrast at the time of admission was obtained since the patient had underlying chronic kidney disease and had already received contrast for lower extremity and chest CT). The MRI of the head showed no arterial occlusion, allowing heparin to be started. After being placed on antibiotics, he became afebrile on his first day of hospitalization. Blood, wound, and sputum cultures were positive for methicillin-resistant *S. aureus* (MRSA) and urine culture was positive for multiple gram-positive flora; therefore, cefepime and clindamycin were discontinued and the patient was treated with weight-adjusted van-

comycin which was given with a bolus dose of 30 mg/kg followed by a daily dose of 15 mg/kg that provided therapeutic levels.

The patient developed new onset leukocytosis which peaked at 16,910/ μ L on the sixth day of hospitalization. On the seventh day of hospitalization, the patient required bilateral chest tube placement for pleural effusions and to rule out and subsequently treat empyema. Additionally, ceftaroline 600 mg every 12 hours was added to his medication regimen. His leukocytosis resolved on the eighth day of hospitalization despite little clinical evidence of improvement. Fluid culture from his bilateral pleural effusion was positive for MRSA and a blood culture on the ninth day of hospitalization was positive for *Aerococcus viridans*. The patient began having negative blood cultures on the tenth day of hospitalization and was extubated on the eleventh.

Anticoagulation was switched to warfarin on the fourteenth day of hospitalization. Erythema tracking along the course of the great saphenous vein was still seen on the sixteenth day of hospitalization (**Figure 2**). However, an ultrasound demonstrated resolution of the femoral vein thrombosis but with complete occlusion of the saphenous-femoral junction. By this time, the patient's respiratory distress had completely resolved, and he was saturating in the high 90's on room air. The patient was treated with antibiotics for 6 weeks and made a full recovery. In the final follow up, the patient was able to return to independent living.

3. Discussion

Case reports of SPE have increased recently in conjunction with a change in etiology [13]. In the 1970's, 76% - 78% of SPE cases were found in intravenous



Figure 2. The extremity at day 27 demonstrating thrombus filled great saphenous vein with branches. This venous obstruction of the great saphenous vein developed after thrombosis of femoral vein and during treatment. The healing wounds on the knee are the site of entry of the MRSA into the vascular system.

drug users; this association dropped to 26% in cases reported from 1978-2012 [13] [14] [15]. During this time frame, a majority of SPE cases were caused by *S. aureus* as previously stated. Specific strains of *S. aureus* contain the virulence factor Panton-Valentine Leukocidin (PVL), which is a cytotoxin that destroys leukocytes by its pore forming activity [16]. The presence of the PVL gene is associated with increased virulence, inflammation, and increased rates of ST and is found more commonly in MRSA than methicillin-sensitive *S. aureus* [16] [17]. With the increase in MRSA infections since its emergence in the 1970's, we propose that the increase of case reports could be due to increased rates of MRSA infection resulting in increased SPE rates in the non-intravenous drug using population [18] [19].

The mainstay of treatment for venous thromboembolism due to infectious causes is antibiotics, with or without the use of heparin [20]. There have been a limited number of studies (only one trial consisting of 15 patients) examining the treatment of ST and/or SPE with or without anticoagulation in conjunction with antibiotics with most data being present in the form of case studies. Falagas *et al.* stated that heparin may be used with good outcomes and minimal adverse effects in patients with ST but noted that many patients do well on antibiotics alone. However, our patient already had pulmonary emboli before the time of placement and was therefore restarted on heparin.

Vancomycin has been the mainstay parenteral drug of choice for treatment of MRSA. When started on vancomycin, our patient showed mild improvement by resolution of fever, however he continued to require ventilatory support. This lack of resolution of SPE with vancomycin alone is possibly attributable to its inflammation-dependent, variable tissue penetration and could explain our patient's delayed recovery until after the addition of ceftaroline [21]. An additional regimen that could have been attempted after prolonged MRSA SPE is daptomycin and rifampin. Reports have shown resolution of SPE in patients who fail vancomycin treatment when switched to a combination of daptomycin and rifampin [22].

A thrombectomy with vein excision was considered during the illness. Surgical intervention in patients with septic thrombi who fail to respond to initial medical management can be lifesaving [23]. However, by the time this patient came under our care, his pulmonary emboli had become a nidus of infections; therefore, it was unlikely that removing the septic thrombus in the right leg would have resolved his symptoms. Thus, no surgical intervention was pursued in order to avoid the stress of surgery in a toxic patient.

Previous descriptions of SPE in adults have been associated with either immunologic suppression due to diabetes or intravenous drug abuse. In addition, most cases have been presented with systemic symptoms such as fever, chills, pleuritic chest pain, and dyspnea. The extrapulmonary sources for the pulmonary emboli have been described as coming from pyelonephritis, vertebral osteomyelitis, paraspinal abscesses, pyomyositis, abscess of the thigh, cellulitis, ST, indwelling venous catheters, and endocarditis [9]. Similarly to our patient, patient,

CT scans have often showed cavitory nodules bilaterally, and vegetations were often not present on echocardiogram [9]. Compared to other cases in the literature of SPE, this case is unique in that the source of the septic pulmonary embolus was the superficial femoral vein (**Figure 2**).

In discussing this case, we present it as a patient who has no recent history of intravenous drug abuse. The source of his infection, while still definitively unknown, could have been caused by hitting his leg on the trailer hitch in his garage. He did not report any skin breaks as would be expected to provide an entry for the MRSA. However, there is evidence in the literature that blunt trauma (toe trauma) can result in SPE. Therefore, we propose that our patient's source of infection was likely introduced from his trailer hitch contusion resulting in a soft tissue infection with subsequent development of ST and SPE.

4. Conclusion

SPE is an uncommon disorder with an insidious onset that is difficult to diagnose. We present a case of rapidly progressive SPE from femoral vein thrombophlebitis due to soft tissue injury that required immediate endotracheal intubation and mechanical ventilation. Initial chest CT and X-ray revealed multiple nodular opacities peripherally without cavitation, making the diagnosis difficult in this patient with otherwise normal laboratory values. ST with SPE often presents with protean clinical manifestations and nonspecific radiologic patterns. The diagnosis can be difficult to establish and relies on the presence of a febrile illness, multiple modular lung infiltrates peripherally on CT scan of the chest, and predisposing factors. We describe an unusual case of superficial femoral vein thrombophlebitis causing SPE which required endotracheal intubation and mechanical ventilation due to respiratory failure, which is uncommon in SPE. This case emphasizes the importance of early diagnosis of SPE and appropriate treatment.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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