Case Report

Sphingomonas paucimobilis bacteraemia and septic arthritis in a diabetic patient presenting with septic pulmonary emboli

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Sphingomonas paucimobilis, a yellow-pigmented, aerobic, glucose non-fermenting, Gram-negative bacillus, is a rare cause of human infection normally associated with immunocompromised hosts. We report a case of bacteraemia and septic arthritis in a 47-year-old diabetic man who presented with septic pulmonary emboli due to *S. paucimobilis*. The patient had an initial presentation of fever, right knee pain, coughing, dyspnoea and chest pain. The infection was treated successfully by surgical debridement combined with meropenem plus ciprofloxacin, based on the patient's antibiotic susceptibility profile. To our knowledge, this is the first case report for septic pulmonary emboli having arisen from an *S. paucimobilis* infection.

Introduction

Septic pulmonary embolism is an uncommon disorder in which infected thrombi become lodged within the pulmonary vasculature and give rise to the development of local abscesses. Septic pulmonary embolism often manifests in patients as fever, coughing, chest pains and haemoptysis. Septic pulmonary embolism features are readily imaged by radiology as bilateral, diffuse, peripherally located nodules with or without cavitations (Lee *et al.*, 2007; Wong *et al.*, 2002). Septic pulmonary embolism is usually associated with tricuspid valve endocarditis (mostly in intravenous drug users), septic thrombophlebitis (in the pelvic region or Lemierre's syndrome) or infected intravascular devices (Cook *et al.*, 2005; Lee *et al.*, 2007; Wong *et al.*, 2002). However, septic pulmonary embolism due to *Sphingomonas paucimobilis* has never previously been reported.

S. paucimobilis is an aerobic, glucose non-fermenting, Gram-negative bacillus that is widely distributed in the natural environment such as in soil and water (Smalley *et al.*, 1983). It can be a waterborne clinical pathogen and causes a variety of community-acquired or nosocomial infections, especially in immunocompromised patients (Calubiran *et al.*, 1990; Morrison & Shulman, 1986; Reina *et al.*, 1991). *S. paucimobilis* has only ever been

reported as the cause of septic arthritis and osteomyelitis in a boy with acute lymphoblastic leukaemia and in an intravenous drug user with HIV (Araújo *et al.*, 2000; Charity & Foukas, 2005). Here, we describe a case of *S. paucimobilis* bacteraemia associated with septic pulmonary emboli in a diabetic patient with concomitant septic and gouty arthritis.

Case report

A 47-year-old male patient presented to the emergency room complaining of intermittent fever with chills for 1 week. The patient had been suffering from diabetes mellitus for 3 years, medicated with a single, oral glucose-lowering agent. During regular visits to the local clinic, the post-prandial finger sugar level always exceeded 200 mg dl⁻¹. The patient had a history of gouty arthritis with several attacks over the right metatarsophalangeal joint. Prior to hospitalization, he developed the symptoms of an upper respiratory tract infection with a sore throat and dry cough for about 1 month. He subsequently received intravenous injections at local clinics but could not recall whether he was prescribed any antimicrobial therapy. The patient described a dull right upper abdominal quadrant pain extending to the right chest wall without any correlation to meals, radiating pain or obvious gastrointestinal symptoms, such as vomiting or diarrhoea. He also complained of pain in the right knee with mild

Abbreviation: CT, computed tomography.

swelling and local heat. The patient had received vacuum cupping over the skin of his right knee to relieve the pain just a few days previously. He denied recent travel, dental work, intra-articular injection of the right knee, ingestion of raw food, or contacts with pets, dirty water or springs.

Upon admission, blood investigations were as follows: leukocyte count, $4.3 \times 10^3 \mu\text{l}^{-1}$ (86.8% neutrophils); haemoglobin level, 10.1 g dl^{-1} ; platelet count, $9.2 \times 10^3 \mu\text{l}^{-1}$; C-reactive protein level, $231.9 \mu\text{g ml}^{-1}$ (normal range <5). Biochemical serum analysis showed that all levels were within their normal limits apart from glucose, measured as 396 mg dl^{-1} . The level of haemoglobin A1c was 10.9%. Urinalysis showed neither pyuria nor the presence of ketone bodies. Plain X-rays were taken of the right knee joint and of the chest shortly after admission and both appeared normal. Abdominal computed tomography (CT) showed only diverticulosis of the ascending colon and no solid organ abscess was found. An empiric antibiotic was administered along with cefmetazole 1 g every 8 h initially for suspected diverticulitis of the ascending colon, as apparent from the abdominal CT scan. However, the patient still suffered from high fever with chills of up to 40°C for several days. Two sets of blood culture were taken which both yielded *S. paucimobilis* by the BacT/Alert 3D System (bioMérieux) and the isolates were identified by ATB ID 32 GN (bioMérieux) and by the dideoxynucleotide chain-termination method with the Microseq 500 16S ribosomal rRNA bacterial sequencing kit (PE Applied Biosystems) and analysed on an ABI PRISM 310 Genetic Analyzer (PE Applied Biosystems). Standardized disc diffusion of the organism by the CLSI method showed susceptibility to amikacin, aztreonam, piperacillin/tazobactam, imipenem, trimethoprim/sulfamethoxazole and ciprofloxacin. The MICs of the blood isolates determined by the VITEK2 System (bioMérieux) were: gentamicin $\geq 16 \mu\text{g ml}^{-1}$, tobramycin $\geq 64 \mu\text{g ml}^{-1}$, amikacin $8 \mu\text{g ml}^{-1}$, ampicillin $\geq 32 \mu\text{g ml}^{-1}$, amoxicillin/clavulanate $16 \mu\text{g ml}^{-1}$, piperacillin/tazobactam $\leq 4 \mu\text{g ml}^{-1}$, aztreonam $8 \mu\text{g ml}^{-1}$, cefazolin $\geq 64 \mu\text{g ml}^{-1}$, cefoxitin $\geq 64 \mu\text{g ml}^{-1}$, ceftriaxone $16 \mu\text{g ml}^{-1}$, cefepime $\geq 64 \mu\text{g ml}^{-1}$, tigecycline $\geq 8 \mu\text{g ml}^{-1}$, trimethoprim/sulfamethoxazole $\leq 20 \mu\text{g ml}^{-1}$, imipenem $\leq 1 \mu\text{g ml}^{-1}$, nitrofurantoin $\geq 512 \mu\text{g ml}^{-1}$, ciprofloxacin $0.5 \mu\text{g ml}^{-1}$, levofloxacin $2 \mu\text{g ml}^{-1}$. The test for extended-spectrum β -lactamase was negative. Based on the culture report, we replaced cefmetazole with piperacillin/tazobactam 4.5 g every 6 h plus amikacin 1 g once daily.

Despite treatment, the patient's right knee suffered from progressive swelling, becoming hot, erythematous and tender, and the symptoms extended to the leg and resulted in a decreased range of movement within 7 days after admission. Meanwhile, the dry cough and dyspnoea became aggravated and a follow-up chest X-ray (Fig. 1a) revealed septic pulmonary emboli over the bilateral lower lung field. Arthrocentesis was applied to the right knee and analysis of the synovial fluid revealed a leukocyte count of $27\,000 \mu\text{l}^{-1}$ with 86% polymorphs and 14% lymphocytes and crystals of monosodium urate (negatively birefringent

Fig. 1. (a) Chest X-ray showing septic pulmonary emboli in bilateral lung fields. (b) High-resolution computed tomography of the chest showing a cavitary lesion over the right lower lobe.

by polarized light microscopy). However, no microorganisms were identified by Gram staining, or by aerobic or anaerobic culturing. We supplemented the patient's treatment with oral colchicine against acute gouty arthritis. Transthoracic and transoesophageal echocardiograms revealed no vegetations upon the mitral or tricuspid valves. Magnetic resonance imaging (Fig. 2) showed fluid collection within the right knee joint space with significant

Fig. 2. Magnetic resonance T2-weighted image of the right knee showing fluid collection within the joint space, synovial enhancement, periarticular soft tissue oedema, and suspected osteomyelitis involving the distal femur.

hyperintensity on T2-weighted images, prominent synovial enhancement, and oedematous change with heterogeneous enhancement over periarticular soft tissue. Also apparent were heterogeneous signal intensities in the right distal femoral bone marrow which correlated with septic arthritis and soft tissue inflammation, hence osteomyelitis could not be ruled out. Furthermore, the spiking fever persisted, so the antibiotic regime was switched to meropenem 1 g every 6 h and levofloxacin 750 mg daily. Blood cultures taken at this time were sterile.

On the twelfth day after admission, the patient received surgical debridement and the synovial pathology showed necrotic debris and microabscess formation consistent with septic arthritis. After the operation, the febrile condition did not improve, so we switched from levofloxacin to ciprofloxacin 600 mg every 12 h.

After 20 days of hospitalization, the patient was still suffering from an intolerable dry cough. A chest CT was performed (Fig. 1b), which also allowed further examination of the septic pulmonary emboli previously identified by chest X-rays. The chest CT scan revealed multiple peripherally located septic emboli (some with cavitations). A CT-guided biopsy identified necrotizing inflammation and acellular necrotic tissue with some neutrophil infiltration, which was compatible with septic embolism. Bacterial culture results for the CT-guided lung biopsy specimen were also negative. The patient became afebrile and the inflammatory markers gradually resolved. After the 4-week course of meropenem and the 3-week course of ciprofloxacin had been completed, the patient was discharged on a maintenance therapy of oral ciprofloxacin 750 mg every 12 h and trimethoprim (trimethoprim 80 mg/sulfamethoxazole 400 mg) 3 tabs every 6 h. Immune function was also

analysed during hospitalization and tests for HIV antibodies, anti-nuclear antibodies and rheumatoid factor all proved negative. Furthermore, immunoglobulin and complement counts were within their normal limits. When the patient was followed up 6 months later, his diabetes was well under control and his right knee had gradually recovered a full range of motion. A chest X-ray showed residual post-inflammatory changes over the right lower lung field (data not shown).

Discussion

S. paucimobilis, previously called *Pseudomonas paucimobilis*, is a yellow-pigmented, aerobic, glucose non-fermenting, Gram-negative bacillus that is widely distributed in the natural environment (Smalley *et al.*, 1983). It also contaminates water supplies, hospital equipment and indwelling devices such as mechanical ventilators or catheters, causing nosocomial infections. *S. paucimobilis* can cause a variety of infections including bacteraemia (Casadevall *et al.*, 1992; Kilic *et al.*, 2007; Slotnick *et al.*, 1979; Southern & Kutscher, 1981), catheter-related infection (Al-Anazi *et al.*, 2008; Decker *et al.*, 1992; Perola *et al.*, 2002; Salazar *et al.*, 1995), septic arthritis, osteomyelitis (Araújo *et al.*, 2000; Charity & Foukas, 2005), meningitis (Hajiroussou *et al.*, 1979), wound infection, urinary tract infection, intra-abdominal infections, ventilator-associated pneumonia (Calubiran *et al.*, 1990; Morrison & Shulman, 1986; Reina *et al.*, 1991), continuous ambulatory peritoneal dialysis-associated peritonitis (Dervisoglu *et al.*, 2008) and postoperative endophthalmitis (Seo *et al.*, 2008). Most of the infections are associated with immunocompromised hosts or patients fitted with indwelling devices. To date, no deaths have been reported in the literature associated with infections from *S. paucimobilis*. This organism lacks the lipopolysaccharide components in the outer membrane of the cell wall usually found in Gram-negative organisms and which are associated with endotoxin activity. The absence of these components may therefore explain the favourable prognosis seen in the previously reported cases (Kawasaki *et al.*, 1994).

S. paucimobilis has been reported to be usually susceptible to tetracycline, chloramphenicol, trimethoprim/sulfamethoxazole, carbapenems and aminoglycosides; its susceptibility to other antimicrobial agents including third-generation cephalosporins and fluoroquinolones is variable. In addition, the organism is usually resistant to penicillins and to first-generation cephalosporins (Hsueh *et al.*, 1998; Reina *et al.*, 1991; Smalley *et al.*, 1983). The published results of susceptibility tests suggest that imipenem alone or an aminoglycoside plus a third-generation cephalosporin should be the agents of choice in the treatment of these infections in the Taiwan area (Hsueh *et al.*, 1998). In our case, we initiated treatment against the infection with piperacillin/tazobactam plus amikacin, based on the susceptibility profile, followed by meropenem plus levofloxacin. Eventually, the patient was

successfully treated with meropenem plus ciprofloxacin. Even though the disc diffusion method demonstrated that the pathogen was susceptible to piperacillin/tazobactam, amikacin and levofloxacin, the initial poor responses to these antibiotics indicated that the MICs derived by screening were necessary for guiding the antimicrobial therapy.

Despite *S. paucimobilis* bacteraemia being most commonly observed in patients fitted with indwelling devices or who are severely immunocompromised, especially with haematological malignancy (Al-Anazi *et al.*, 2008; Kilic *et al.*, 2007; Perola *et al.*, 2002; Salazar *et al.*, 1995), the patient presented here belonged to neither category. Instead, our patient was suffering from an underlying status of poorly controlled diabetes mellitus. The clinical circumstances and microbiological investigations determined that the patient had developed bacteraemia from *S. paucimobilis*. Although *S. paucimobilis* was not isolated from either the patient's synovial fluid or the CT-guided biopsy of the septic emboli, the histological findings from these sites strongly suggest an infective process, and the failure to yield bacteria may be due to the patient already receiving antimicrobial treatment. It is reasonable to assume that the *S. paucimobilis* isolated in blood culture was the cause of the sequela followed by seeding of the right knee joint space with septic arthritis and of the pulmonary vessels, resulting in septic emboli. To our knowledge, this is the first case report of a patient presenting with *S. paucimobilis* bacteraemia leading to septic pulmonary emboli. As for the source of bacteraemia, we considered that it was most likely due to intravenous injection at local clinics with contaminated equipment, or bacteria being introduced during vacuum cupping over the skin of the right knee, since the patient denied any contact history.

Septic arthritis can be concomitant with crystal-induced arthritis (Gupta *et al.*, 2003; Yu *et al.*, 2003). Moreover, an animal model manifested that the inflammatory process induced by joint infection may release crystals from the cartilage and synovium, a process referred to as 'crystal shedding and strip mining' (Gordon *et al.*, 1986). Therefore, it is essential to demonstrate the presence of monosodium urate crystals or calcium pyrophosphate dehydrate crystals by polarized light microscopy, although the positive identification of crystals cannot rule out concomitant septic arthritis. Microbiological examinations should be performed routinely once crystal-induced arthritis has been established. The patient had received piperacillin/tazobactam plus amikacin for 3 days prior to arthrocentesis, which could inadvertently have caused the negative result for the synovial fluid culturing.

In conclusion, this rare case demonstrated that *S. paucimobilis* bacteraemia associated with septic arthritis and septic pulmonary embolism can occur in a relatively non-immunocompromised host, such as a diabetic. We successfully treated the patient with surgical debridement and intravenous meropenem plus fluoroquinolone for 4

weeks according to the MICs for *S. paucimobilis*. Septic pulmonary embolism is rarely due to glucose non-fermenting Gram-negative bacilli and develops very uncommonly in patients who are not intravenous drug users, or who lack intravascular infections or infected intravascular devices. Septic pulmonary embolism can complicate diagnosis and mislead the initial appropriate antibiotic treatment and so comprehensive microbiological studies and susceptibility testing are crucial to ensure a successful outcome.

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