CASE OF MULTIPLE PNEUMOCOCCAL MANIFESTATIONS

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ABSTRACT

Despite Streptococcus pneumoniae (S. pneumoniae) being the leading cause of community-acquired pneumonia, its other manifestations are far more uncommon. In this article, we report an interesting case of a 66-year old man who acquired a S. pneumoniae endocarditis, with a subsequent admission for a S. pneumoniae septic joint; later complicated by a recurrence of his infective endocarditis and a likely S. pneumoniae brain abscess.

CASE REPORT:

A 66-year old man, Mr FB, was admitted into hospital on New Year’s Eve with a two-day history of being unable to weight-bear on his left lower limb, with increasing pain on flexion of the knee. On examination, he was pyrexial, with a temperature of 39.2°C, and haemodynamically stable. Cardiovascular examination demonstrated a grade 3 pan-systolic heart murmur, whilst his respiratory and abdominal examinations were normal.

The left knee joint was hot on palpation, with a small effusion. A joint aspiration demonstrated frank pus, and was sent for further analysis. Bloods on admission included a white cell count of 12.6x10⁹/L (neutrophil count of 10.6 x10⁹/L, lymphocyte count 1.0 x10⁹/L, monocyte count 1.0 x10⁹/L), international normalised ratio (INR) of 2.4, C-reactive protein (CRP) of 261.5mg/L, with his urea, electrolytes and uric acid all within normal limits. A left knee radiograph was performed, which was unremarkable (Figure 1). A urine dipstick showed blood ++, protein ++, nitrate +, and a sample was sent for microscopy, culture and antibiotic sensitivities. Blood cultures were also taken on admission before the commencement of antibiotic therapy.

The patient was initially treated for septic arthritis of the left knee joint. A regime of intravenous vancomycin (1g twice-daily), clarithromycin (600mg twice-daily) and gentamycin (100mg twice-daily as a synergist) was commenced after discussion with a microbiology consultant. He was treated with regular tramadlol for pain control.

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Prior to this admission, this patient had also been admitted in October 2008. He was diagnosed with a *Streptococcus pneumoniae* (*S. pneumoniae*) mitral valve endocarditis, for which he was treated with four weeks of intravenous benzylpenicillin, then subsequently two weeks of oral amoxicillin. Following this he had a mitral valve repair. His past medical history also included two previous deep vein thromboses, atrial fibrillation and hypertension, for which he was taking warfarin, furosemide and ramipril daily. From a previous admission, it was also documented that he had experienced an unknown adverse reaction to taking penicillin several years ago.

An initial gram-stain of the blood cultures was negative. After 48 hours, *S. pneumoniae* was isolated in both the blood cultures and the knee aspirate. The mid-stream urine sent on admission demonstrated normal white cells and no growth from culture. The patient improved clinically for several days and was able to demonstrate an increased range of movement of the limb, with reduced pain on weight-bearing. In conjunction with an improved clinical picture, there was an improvement of his white cell count, which fell to 7.9x10⁹/L after three days of antibiotic therapy. As the patient had demonstrated a recurrence of an unusual infection, a thorough and detailed history social and sexual history were taken, which did not demonstrate any high-risk behaviours.

Despite these initial improvements, his CRP and INR continued to increase whilst on antibiotics (306.0mg/L and 7.7 after three days, respectively). At this time, the patient had only minor bleeding from a
previous peripheral venous access site and a full neurological examination was unremarkable. A discussion was held with the on-call haematology registrar, who advised administering prothrombin complex concentrate 4000 units intravenously over 24 minutes and rechecking the INR two hours thereafter.

Reversal of warfarin was achieved with his repeat INR being 1.7. Warfarin was discontinued and was to be recommenced once the INR was stable for three days. After discussion with the microbiology consultant, his antibiotic regime was switched to intravenous ceftriaxone 2g twice-daily for two weeks then oral amoxicillin for 4 months, due to a presumed interaction between clarithromycin and warfarin. As he had a documented penicillin reaction, this was to be given with caution.

With the patient now stable, apyrexial and with improved mobility, he was referred to the cardiology team to rule out recurrence of his previous \textit{S.pneumoniae} endocarditis. A trans-thoracic echocardiogram was unable to definitively rule out new valvular vegetations. He was seen by a cardiology consultant, who felt that infective endocarditis was unlikely and a trans-oesophageal echocardiogram (TOE) was not indicated at this time.

The patient deteriorated over the next 48 hours and again became pyrexial with a temperature of 38.2°C, but he remained alert and orientated. His antibiotics were switched to intravenous vancomycin 1g twice-daily and synergistic gentamycin 100mg twice-daily on further microbiologist advice.

During the following three days, he became increasingly disorientated in place, person and time. His analgesia was reviewed as a possible cause, and his tramadol was replaced with nefopam. Repeat blood tests demonstrated an elevated INR of 5.0. This was discussed with the regional on-call haematology team, who recommended administering 1mg of vitamin K intravenously.

During the next 24 hours, the patient developed an expressive dysphasia and became increasingly confused. A neurological examination demonstrated no limb weakness or facial droop, and his pupils remained equal and reactive to light. His Glasgow Coma Score (GCS) was 13/15 (eyes – 4, voice – 3, motor – 6). An urgent computer tomography (CT) scan was performed, which demonstrated a “bi-locular lesion in the deepness of the left brain hemisphere, which accounted for the fresh bleed into the lesion”. The radiologist felt that the lesion could “represent any kind of true mass lesion, such as two ring-like abscess formations, or two ring-like focal lesions of other (malignant) aetiology.” (Figure 2). Further discussion was held with the on-call haematology team, which recommended the administration of a further 4000 units of prothrombin complex concentrate intravenously over 24 minutes, followed by 20mg of vitamin K.

He was transferred urgently to a local tertiary neurological centre. On arrival, he had developed a right-sided hemiparesis and a reduced GCS of 12/15 (eyes – 3, voice – 3, motor – 6). Subsequently he attended theatre and underwent an image-guided burr hole aspiration of a temporal
haematoma/abscess cavity, with a simultaneous left knee washout. Tissue and pus samples were taken from both sites, but no organisms were isolated after three weeks of incubation. Whilst in theatre, a TOE was also performed, with the radiologist being “suspicious that there is active endocarditis” due to a “lesion on [the] anterior mitral leaflet”.

Figure 2 – CT brain demonstrating bi-locular lesion

His course of vancomycin was continued, with intravenous ceftriaxone 2g twice-daily being restarted. For three days post-operatively, a nasogastric (NG) tube was used due to a poor swallowing reflex, but this gradually improved and the NG tube was removed. He steadily became more mobile, and was deemed medically fit to be transferred to a rehabilitation ward. There, he was mobilised with the physiotherapy team, who felt that he was improving daily. The microbiologist advised continuing intravenous antibiotics for a further two weeks before switching to oral amoxicillin for at least 6 weeks dependent on response. He continued to improve clinically and was discharged on oral antibiotics, with follow-up organised by the neurosurgical and cardiology teams.

A follow-up CT scan was performed five weeks after the initial CT scan. It demonstrated a significant improvement, with no evidence of intra- or extra-axial haemorrhage. There was a hypodense area in the left temporal lobe consistent with a previous abscess. The patient also felt much better in himself, with improved mobility and a normal swallow.
DISCUSSION

Mr FB initially presented with infective endocarditis caused by *S. pneumoniae*. Two years later, he was readmitted with *S. pneumoniae* septic arthritis, a probable recurrence of *S. pneumoniae* endocarditis, and a likely *S. pneumoniae* brain abscess. *S. pneumoniae* is a well-known cause of bacteraemia in both uncompromised and immunosuppressed patients. There have been over 95 different presentations documented of a *S. pneumoniae* infection; including septic arthritis, endocarditis, meningitis and various abscesses[1,2]. Following a thorough and relevant literature search, the authors have been unable to find a similar case to Mr FB, demonstrating several presentations of *S. pneumoniae* separated in both time and space.

During a fourteen year study at St Thomas’s Hospital, London, *S. pneumoniae* accounted for 13.3% of all episodes of bacteraemia [3]. Approximately two-thirds of deaths caused by *S. pneumoniae* bacteraemia occur within 72 hours of hospital admission, with the overall mortality rate being approximately 17% [4].

*S. pneumoniae* was first described as a cause of infective endocarditis by Osler in 1881 [5] and identified as a cause of septic arthritis in 1888 [6]. It is a common pathogen in the respiratory system, with studies showing that it is
the causative organism of community-acquired pneumonia in 20-70% of cases when an organism is found [7]. In contrast, the other manifestations of the pathogen are far more unusual. Brain abscesses due to \textit{S. pneumoniae} are a complication rarely recognised in modern practice, and are estimated to be less than 1% of all pyogenic brain abscesses [8].

Two United Kingdom-based studies have demonstrated that the rate of septic arthritis caused by \textit{S. pneumoniae} to be 8.2%-9.7%[9,10] (n=32/389 and n=112/1158, respectively). It is an uncommon complication of a \textit{S. pneumoniae} bacteraemia, with one study demonstrating only 2 out of 444 cases being complicated by joint involvement [11]. The knee is the most common site of \textit{S. pneumoniae} septic arthritis. A 2003 study demonstrated that 32% (n=35/108) of those with a monoarticular \textit{S. pneumoniae} septic arthritis had knee joint involvement, with the next most common monoarticular septic arthritis involving the hip joint (7%, n=8/108). A two year population-based study in the Netherlands demonstrated that \textit{S. pneumoniae} was the cause of bacterial endocarditis in 1% of cases (n=5/419) [12]. The rate \textit{S. pneumoniae} endocarditis fell rapidly following the discovery of penicillin, with this new and effective treatment often preventing progression of the disease onto endocarditis [13]. The potential structural complications of \textit{S. pneumoniae} endocarditis were illustrated by a French multi-centre study, which demonstrated valve perforation (20%, n=6/30), ring abscesses (13.3%, n=4/30), and valvular vegetations (96.7%, n=29/30), with valvular disease often leading to congestive heart failure (63.3%, n=19/30) [14]. Alcoholism is a common associated medical problem, identified in 28.1% of cases by a 1998 meta-analysis [15].

Clinical resistance to penicillin in \textit{S. pneumoniae} was first reported in the mid-1960s, with the first outbreak of resistant infections occurring in South Africa in 1977 [16]. Transferable glycopeptides resistance has been demonstrated in streptococci, which may transfer to \textit{S. pneumoniae} [17]. Despite the increase in cases of \textit{S. pneumoniae} with demonstrable antibiotic resistance, several studies have shown that this is not associated with an increased mortality in those affected patients [18,19].

As supported by James [20] and advised by the hospital microbiologist, Mr FB was treated with a one-week course of intravenous antibiotics followed by oral antibiotics, as it was felt he had an uncomplicated monoarthritis septic arthritis. Repeat knee aspirate and brain abscess cultures did not isolate \textit{S. pneumoniae}, which may be due to the patient having had several days of intravenous antibiotic therapy. After his clinical picture demonstrated a likely \textit{S. pneumoniae} endocarditis, with its high associated mortality rate of 28-60% [21], intravenous antibiotics were restarted. In its Guidelines for the Antibiotic Treatment of Endocarditis in Adults (2004) [21], the British Society for Antimicrobial Chemotherapy recommended that those patients with infective endocarditis require antibiotic therapy for a total of four to six weeks.

Early antibiotic therapy as advised by a microbiologist or infectious disease specialist is crucial. As the number of antibiotic resistant strains of \textit{S.}}
pneumoniae is ever-increasing, improved knowledge of this pathogen is essential to ensuring its effective management.

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REFERENCES


