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Case Report

Melioidosis presenting as pneumonia and left parietal lobe focal meningitis with a subdural collection: a case report

Nisanthan Selvaratnam, Sanchayan Thananchayan, Sivagamasundary Uthayakumaran, Ghetheeswaran Srivickneswaran

Teaching Hospital, Jaffna, Sri Lanka.

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Corresponding Author: Nisanthan Selvaratnam, E-mail:< nisanjhc@yahoo.com > https://orcid.org/0000-0002-8955-9868

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Introduction

Melioidosis is caused by *Burkholderia pseudomallei,* which is a facultative intracellular Gram-negative bacterium. The organism is largely found in soil and fresh surface water in endemic regions. The modes of transmission include percutaneous inoculation, inhalation, aspiration, and, occasionally, ingestion [1,2]. The predominant mode of transmission is via percutaneous inoculation when exposed to wet soil during the rainy season [3]. The organism can reach virtually any site via the haematogenous route which is evident by well documented cases of pneumonia following presumptive inoculating skin injuries are well documented [4]. Diabetes, hazardous alcohol use, chronic kidney disease and chronic lung disease are the most important risk factors for melioidosis [3]. Rainfall in the two weeks prior to onset of symptoms may be an independent risk factor for a pneumonic presentation, septic shock, and death [5].

The incubation period following an inoculating injury range from 1 to 21 days (mean nine days) [6,7]. Acute disease is defined as symptoms lasting for less than two months before diagnosis. Chronic disease is defined as symptoms persisting for longer than two months. [7] Chronic melioidosis includes pneumonia, resembling tuberculosis, or a non-healing skin ulcer or deep-seated abscess. Infection with *B. pseudomallei* can remain latent in the body and subsequently activate, similar to tuberculosis. Diagnosis mainly relies on isolation of the organism from clinical samples with subsequent high melioidosis serology titres supporting the diagnosis [3].

Beta-lactams, carbapenems and, trimethoprim-sulfamethoxazole, are the main therapeutic options for melioidosis, depending on the phase of treatment. Following acute treatment eradication therapy is considered mandatory to prevent relapse. Close

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follow-up is needed to monitor the clinical response and to detect any adverse drug effects [8].

Case presentation

A 27-year-old, farmer with diabetes mellitus and chronic ethanol usage, was transferred from the local hospital to Teaching Hospital, - Jaffna for further evaluation of fever with confusion. Initially, he presented with a history of fever, dry cough, myalgia, and loss of appetite for 10 days, and headache, nausea, and, vomiting for 3 days and confusion for 2 days. He denied any history of shortness of breath, chest pain, palpitation, or seizure. His urine output and bowel habits were normal. There was no contact history of tuberculosis. He strongly denied a history of high-risk sexual behavior. He did not have focal symptoms of malignancy or-symptoms of autoimmune connective tissue diseases.

On examination, he was febrile with a documented temperature of 102° F. His Glasgow coma scale was12/14. His pulse rate and blood pressure were 108 bpm and 80/50 mmHg, respectively. Auscultation of the lungs revealed coarse crepitations with reduced breath sounds over the right middle zone. Examination of the abdomen and heart were largely normal. There were no focal neurological signs or papilloedema. Blood was taken for culture and other basic investigations. He was resuscitated with intravenous fluids and empirical broad-spectrum antibiotics, ceftriaxone 2 g IV b.d and doxycycline 100 mg per oral b.d. were commenced.

Initial blood work at the local hospital revealed neutrophilia (7.60×10^9/l), thrombocytopaenia (79×10^9/l), elevated inflammatory markers (C-reactive protein-283.7 mg/L, erythrocyte sedimentation rate-104 mm/1st hour), raised aspartate aminotransferase (215 IU/L), raised alanine aminotransferase (163 IU/L) and normal renal function tests. He had chest radiography which showed right upper lobe consolidation (Figure 1).

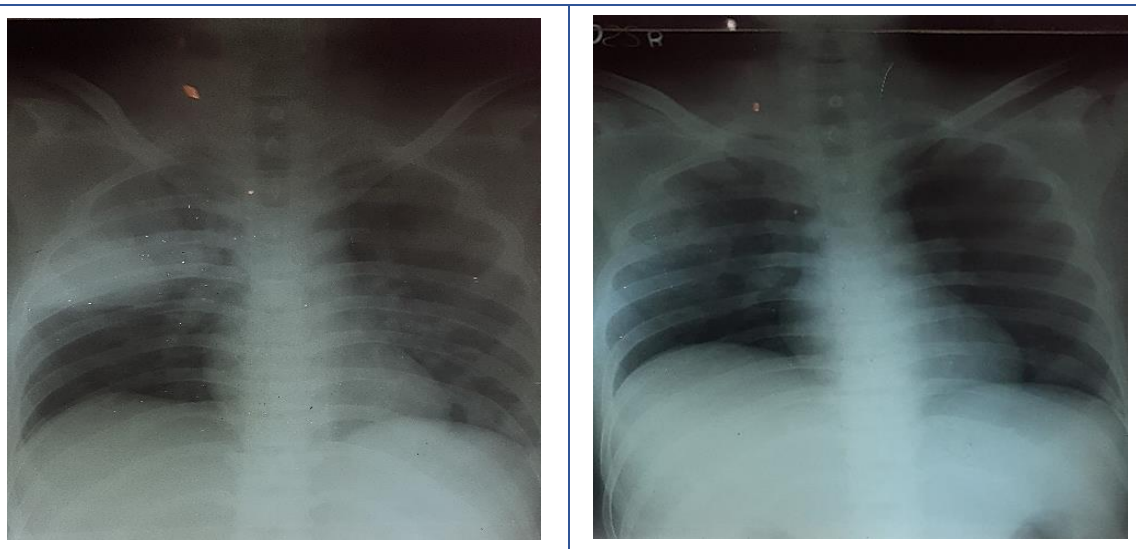

Figure 1: Chest Xray – right upper lobe consolidation (left), complete resolution of consolidation after two weeks of treatment (right).

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The Mantoux test was negative and sputum studies could not be carried out since the sputum sample was sub optimal. Trans thoracic two-dimensional echocardiogram showed no evidence of infective endocarditis. His urine full report and culture were normal. Ultrasound scan of the abdomen demonstrated only a simple liver cyst. Blood picture did not reveal any overt hematological malignancy. He had continuous fever and reduced level of consciousness despite broad spectrum antibiotics so that an urgent non-contrast computer tomography of brain was arranged, which showed a left parietal subdural collection with mild mass effect. Vancomycin 1 g IV t.d.s was added to the antibiotic regime to cover methicillin resistant *Staphylococcus aureus* (MRSA)considering that this presentation could be due to disseminated *S. aureus* infection. Lumbar puncture as not performed as he had thrombocytopenia, coagulopathy, and a mass effect in the brain. He had negative HIV and VDRL. MRI of the brain showed focal meningitis with a subdural collection in the left parietal region (Figures 2 & 3).

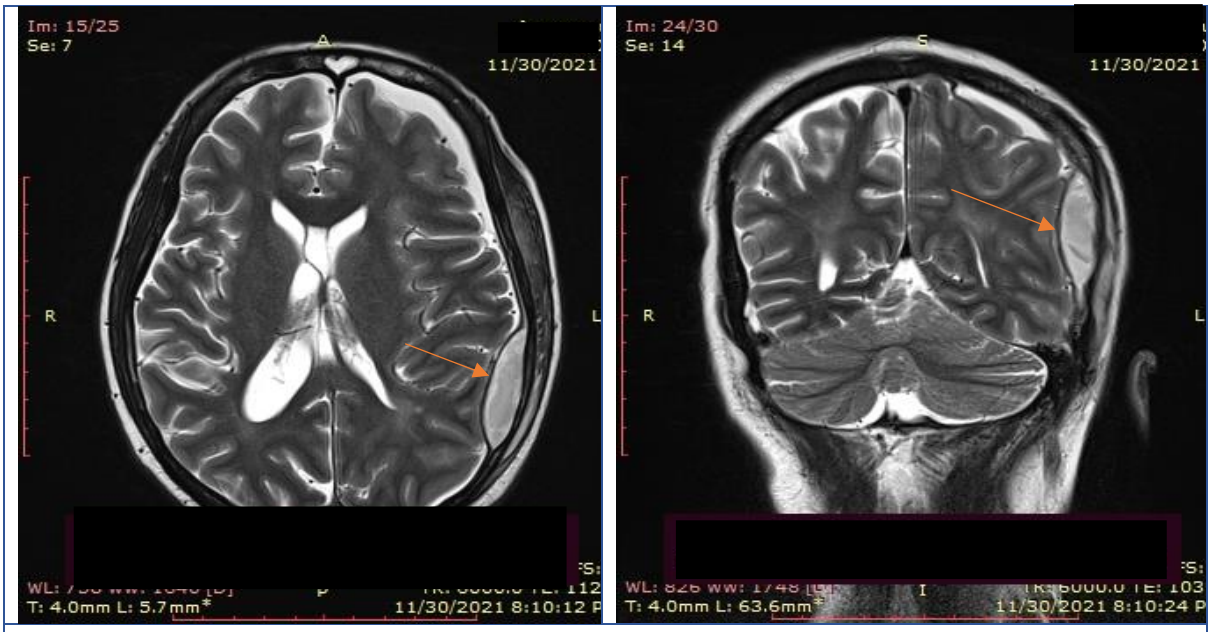

Figure 2: T2 weighted MRI of brain- axial view(left)and coronal view(right) shows lentiform shaped extra axial fluid collection in the subdural space of the left parietal region which exerts a mild mass effect on gyri and sulci. Adjacent meninges are thickened and enhanced.

Surgical drainage of subdural collection was done, and sample was sent for culture and antibiotic sensitivity testing. Meantime, blood culture had yielded *Pseudomonas* species, which was sensitive to meropenem and co-amoxiclav, but resistant to gentamycin. This unusual sensitive pattern raised suspicion of melioidosis, and the isolate was sent to the Faculty of Medicine, University of Colombo for identification along with serum for melioidosis antibodies. He was commenced on meropenem 2 g IV t.d.s and co-trimoxazole 1920 mg per oral b.d. Pus culture also isolated a similar bacterium. Indirect hemagglutination assay for melioidosis antibody was positive at a titre of 1:80 and the blood culture isolate were confirmed as *Burkhoderia pseudomallei* and the diagnosis of melioidosis was finally made. Initial intensive phase therapy was continued for 8 weeks

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until clinical improvement was evident with resolution of inflammatory markers. Repeat blood culture was sterile after 2 weeks of treatment. Neurological symptoms and fever resolved completely. Repeat chest X-ray showed normal lung fields. (Figure 1) He was discharged home on eradication therapy with co-trimoxazole 1920 mg per oral b.d and folic acid 5 mg oral daily for 6 months. He is being followed up by the medical and microbiology teams.

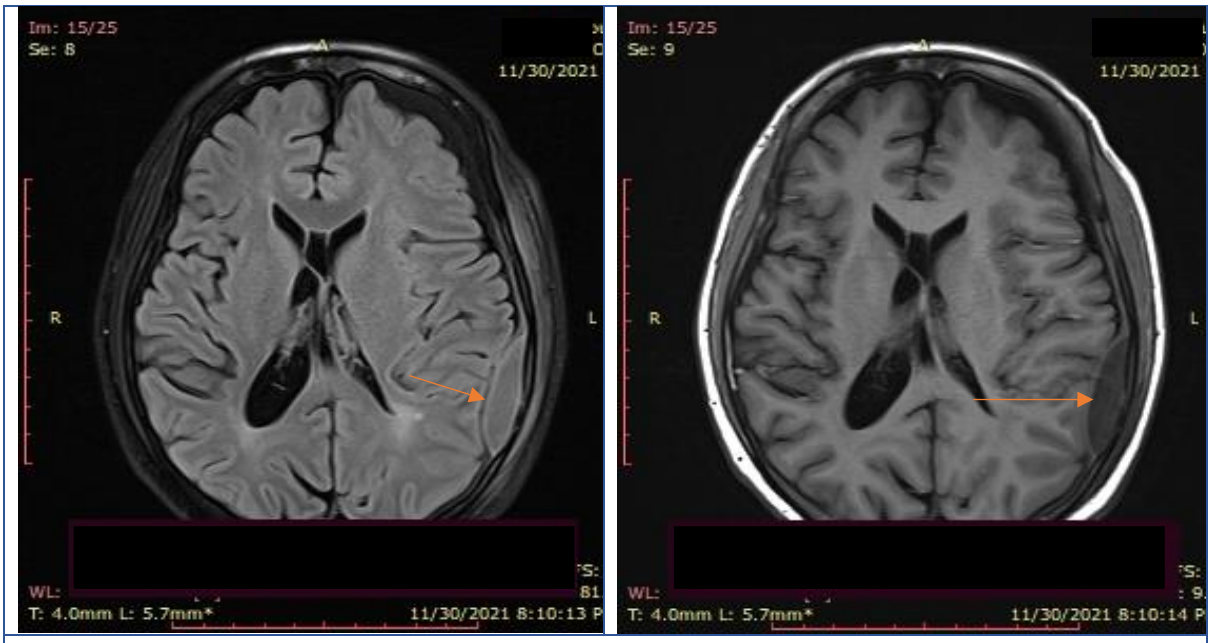

Figure 3: T 1 weighted FLAIR (left) and T 1 weighted (right)

Discussion

The clinical spectrum of melioidosis ranges from acute pyogenic suppuration to chronic granulomatous inflammation. The lung is the most common organ involved and infection may manifest as acute lobar pneumonia, bronchopneumonia, empyema, or lung abscess [9]. With 50% of all patients being bacteraemic and up to a quarter presenting with septic shock [10,11]. Acute pulmonary manifestations include high fever with chills and rigors, cough, sputum, and respiratory distress with or without shock. A subacute or chronic pulmonary involvement may present with cough, purulent sputum, haemoptysis, and night sweats, resembling tuberculosis [12].

Neurological melioidosis is rare (seen in about 5%), and may present with brain or epidural abscesses, encephalomyelitis, aseptic meningitis, dural venous sinus thrombosis or transverse myelitis. Isolated subdural collections associated with melioidosis are rarely reported [13].

Melioidosis is more common in diabetics and is acquired by exposure to contaminated soil and water. Our patient, too, had poorly controlled diabetes and had a history of exposure to wet soil.

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Culture is the gold standard for diagnosis with subsequent high melioidosis serology titres supporting the diagnosis. Serologic testing alone is not sufficient to arrive at diagnosis [3]. False-negative serology has been reported in acute sepsis [14].
B. pseudomallei grows in routine culture media but is easily mistaken for *Pseudomonas* spp in inexperienced hands. The unusual antibiotic sensitivity pattern gives an important clue to the diagnosis; *B. pseudomallei* is characteristically sensitive to the antimicrobials such as penicillin, ampicillin, first or second-generation cephalosporins, and meropenem, but is resistant to gentamicin [13].

Melioidosis is treated with ceftazidime, carbapenems, and trimethoprim-sulfamethoxazole, depending on the phase of treatment [8]. Patients who are suspected or confirmed to have melioidosis without neurological manifestation and who do not have severe disease are treated with intravenous ceftazidime 1g eight hourly as intensive therapy [15]. Intravenous meropenem 1 g eight hourly is recommended as initial intensive therapy for patient with severe disease who require ICU care [16]. Neurological melioidosis is treated with a doubled dose of meropenem. Trimethoprim-sulfamethoxazole is added to ceftazidime or meropenem if patients have infections other than pulmonary involvement. Initial intravenous intensive therapy is given for at least 14 days [8]. However longer durations of four to eight weeks are recommended in certain cases, especially in neurological melioidosis [17].

Eradication therapy, consisting of oral trimethoprim-sulfamethoxazole is considered mandatory to prevent relapse of melioidosis, and begins immediately following the initial intensive antibiotic regimen. Folic acid is added to prevent toxicity. Minimum three months duration is recommended for eradication therapy, but more than six months is considered necessary for neurological manifestations [8].

Close follow-up is important for monitoring the clinical response and for detecting adverse drug effects. We perform complete blood count and kidney and liver function tests twice weekly initially, and then reduced to weekly, then monthly checks, depending on patient circumstances [17].

Since the patient had presented with septic shock with pulmonary and neurological manifestations, he was treated with intravenous meropenem 2 g eight hourly and trimethoprim-sulfamethoxazole 1920 mg per oral b.d for eight weeks as initial intensive therapy and the same dose of trimethoprim-sulfamethoxazole alone was continued for six months as eradication therapy.

Conclusion

Melioidosis with neurological manifestations, is a rare life-threatening infection. Early diagnosis and prompt treatment saves lives. Long term follow up is warranted since relapse is common, especially if patient is not promptly treated with appropriate antibiotics for the optimum duration.

Acknowledgements

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