The Journal of Laryngology & Otology (2016), ***130*** (Suppl. S4), *S60–S62*.

doi:10.1017/S0022215116008276

CLINICAL RECORD

Melioidosis in a patient with chronic rhinosinusitis

N M PHILLIPS[1], A CERVIN[2,3], J EARNSHAW[2], H E SIDJABAT[4]

[1]ENT Department, Rockhampton Hospital, Queensland, [2]Department of Otolaryngology, Head and Neck Surgery, Royal Brisbane and Women's Hospital, Queensland, [3]Otolaryngology (Rhinology), Faculty of Medicine and Biomedical Sciences, University of Queensland, Brisbane, and [4]Infection and Immunity Research Theme, University of Queensland Centre for Clinical Research, Brisbane, Australia

Abstract

Background: Melioidosis is a serious infection caused by soil-dwelling Gram-negative bacillus *Burkholderia pseudomallei*. It is most commonly reported in Northern Australia, Southeast and Southern Asia, China, and Taiwan.

Methods: A case report and short review of the literature are presented. Presentation, diagnosis including genomic sequencing, and acute and long-term management are discussed.

Results: A 58-year-old female presented with chronic rhinosinusitis secondary to melioidosis. This is the third reported incidence of sinusitis secondary to melioidosis, which occurred in an otherwise well female with no risk factors and no apparent cause of exposure. Treatment involved an acute phase in which meropenem was administered parenterally for two weeks, followed by a prolonged oral course of trimethoprim-sulfamethoxazole for three months, as per recommended guidelines.

Conclusion: In patients presenting with refractory chronic rhinosinusitis, ENT surgeons should consider the presence of unusual causative pathogens such as *B pseudomallei*, particularly in those with recent travel history to Northern Queensland and/or Southeast Asia.

Key words: Burkholderia Pseudomallei; Melioidosis; Rhinitis; Sinusitis

Introduction

Melioidosis is an infection caused by the Gram-negative bacillus *Burkholderia pseudomallei*. It was first recognised in 1911 by Alfred Whitmore, who isolated the bacteria from an opiate addict in Rangoon, Burma.[1] Previously classified under various genera, it was assigned a new genus, burkholderia, by Yabuuchi *et al*. in 1992.[2]

Melioidosis occurs primarily throughout Northern Australia, Southeast and Southern Asia, China, and Taiwan. Thailand reports the highest documented cases of melioidosis, with an estimated 2000–5000 cases each year, compared with only 50 cases reported annually in Singapore and Australia.[3]

B pseudomallei are readily isolated from soil and surface water in endemic areas. Infection is usually via percutaneous inoculation or contamination of wounds or mucosa with soil or surface water. Animal-to-human and human-to-human transmissions are rare. A specific exposure incident is only identified in 6–25 per cent of cases.[4] There have been two outbreaks of melioidosis in Australia that were linked to the contamination of potable water with *B pseudomallei*, which was due to water being unchlorinated or below standard chlorine levels.[5]

Incidence peaks between the ages of 40 and 60 years, with a male-to-female ratio higher than 3:2. The incubation period for acute melioidosis ranges from 1 to 21 days (mean, 9 days). Acute presentations represent 85 per cent of all cases, with chronic presentations representing 11 per cent, and latent infection with reactivation representing 4 per cent.[6,7] There is bacteraemia on admission in 40–60 per cent of cases, septic shock in approximately 20 per cent and pneumonia in over 50 per cent, with some patients experiencing genitourinary and skin infections.[3,5,7,8] Overall mortality rates are between 10 per cent, in Australia, and 40 per cent, in Thailand.

Severity of illness depends on bacterial load, route of administration, pathogenicity of infecting strain and, most importantly, host risk factors. Up to 80 per cent of adults with melioidosis have at least one risk factor, whilst the figure is much lower, between 5 and 15 per cent, in children. Risk factors include diabetes (present in 23–60 per cent of cases), hazardous alcohol use (12–39 per cent), chronic lung disease (12–27 per cent), chronic renal disease (10–27 per cent), thalassaemia (7 per cent), glucocorticoid use and other immunosuppressive therapy (less than 5 per cent), and cancer (less than 5 per cent).[5]

Case report

A 58-year-old female, who had suffered with chronic rhinosinusitis since 2012, presented to an out-patient clinic in Queensland, Australia. She had been managed privately since 2012 by two different ENT surgeons, and had undergone three functional endoscopic sinus surgery operations. The last procedure was performed in late 2013. The operative specimens collected in late 2013 grew methicillin-susceptible *Staphylococcus aureus*.

Accepted for publication 8 April 2016

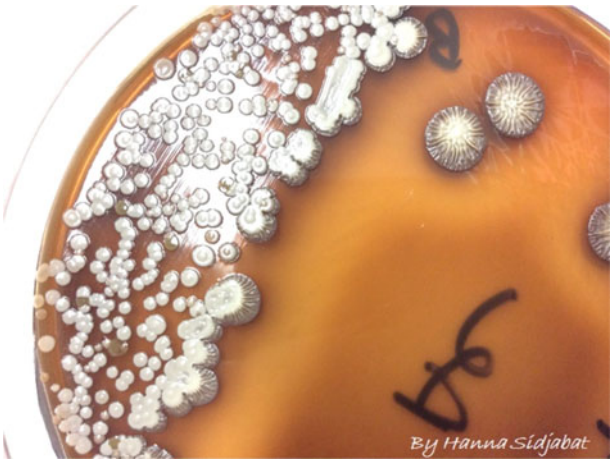

FIG. 1

Horse blood agar culture of *Burkholderia pseudomallei*: there were smooth, creamy, white colonies at 24 hours, transitioning to a dry and wrinkled state at 48 hours. Image courtesy of Hanna Sidjabat.

The patient was reviewed by an infectious disease specialist in 2014, and commenced on rifampicin and fusidic acid. This treatment was stopped after several weeks because of the lack of any improvement and the patient was referred.

Her symptoms did not improve, and she complained of rhinorrhoea, post-nasal drip and mid-facial pain that was more severe on the left at examination in 2015. In addition, the patient reported experiencing subjective fevers during the previous several months, along with intermittent subcutaneous purulent skin eruptions that were not associated with a rash in the distribution of her trunk and arms. She was commenced on clarithromycin, used as an immunomodulator to decrease the inflammatory response in her sinuses.

Nasopharyngeal and pharyngeal swabs were collected. The swabs were cultured aerobically on horse blood agar and mannitol salt agar. Typical morphology of burkholderia spp. dominated the colonies growing on the horse blood agar plate (Figure 1). Few *S aureus* like colonies grew on the horse blood agar. The *S aureus* also grew on the mannitol salt agar.

Both burkholderia spp. and *S aureus* were identified to the species level using matrix-assisted laser desorption/ionisation time-of-flight ('MALDI-TOF') mass spectrometry with a Vitek® MS automated microbial identification system. The burkholderia spp. was initially identified as *Burkholderia vietnamiensis*. The *S aureus* was confirmed as *S aureus* using matrix-assisted laser desorption/ionisation time-of-flight. Given the predominance of burkholderia spp. on the culture from the specimen, the primary causative pathogen in this patient was considered to be burkholderia spp.

Both burkholderia spp. and *S aureus* were whole genome sequenced using a HiSeq™ 2000 sequencing system.[9] The burkholderia spp. was then confirmed as *B pseudomallei* with sequence type 1361. It is important to note that sequence type 1361 has not been found in other patients.[9] This was a case of *B pseudomallei* with a unique sequence type that was not isolated from a melioidosis endemic area. An investigation of the virulence mechanisms of *B pseudomallei* sequence type 1361 in comparison with those of *B pseudomallei* strains from endemic areas is warranted. This may be useful to determine the emergence of new *B pseudomallei* sequence types causing infection in non-melioidosis endemic areas.

The patient's past medical history revealed that she suffered from rheumatoid arthritis (for which she was not on any immunosuppressants), hypertension and gastroesophageal reflux disease, and she had previously received hormone replacement therapy. She had also undergone dacryocystorhinostomy. She had visited Cairns and Cooktown on holidays in 2013, but had not been to any other melioidosis endemic areas. She lived on an acreage and was an avid gardener working extensively with mulch. She had never smoked. Records of her alcohol consumption were not available.

At the time of examination in 2015, she was afebrile and appeared well. There was mucopurulent post-nasal drip, and fibre-optic nasendoscopy demonstrated significant mucosal crusting bilaterally, which was worse on the left side and involved the central maxillary meatus and ostia. There were no cutaneous manifestations of the disease.

Chest radiography findings, immunoglobulin levels, lymphocyte subsets and full blood count were all unremarkable, indicating no immunocompromise and demonstrating no sign of systemic melioidosis.

The patient was treated with 2 weeks of intravenous (IV) administration of meropenem as an in-patient and discharged on trimethoprim-sulphamethoxazole (Bactrim®) 160 mg/800 mg twice daily for 14 weeks.

The latest cultures of nasopharyngeal swabs collected several months later were negative for *B pseudomallei*. Therefore, the administration of Bactrim was ceased. Despite an excellent response with initial improvement in symptoms at the latest follow up, several months after discharge, the patient continued to suffer headache, mild facial pain and increasing green nasal discharge. This was confirmed on fibre-optic nasendoscopy, and significant crusting was observed. Computed tomography of the sinuses was planned and a follow-up appointment for one month later was arranged.

Discussion

This is an atypical case of chronic rhinosinusitis secondary to melioidosis with regard to clinical presentation, with a fluctuating course of disease. The patient presented with typical symptoms, along with endoscopic and radiological evidence of chronic rhinosinusitis. However, the refractory nature of the disease to medical and surgical intervention was not consistent. Concurrent relapsing fever and intermittent subcutaneous purulent skin eruptions are not normally encountered in chronic rhinosinusitis patients and were important in raising suspicion of the underlying pathology.

In this case report, the patient had no risk factors, decreasing the likelihood of an acute presentation and instead indicating cutaneous disease resistant to common methods of treatment. Isolation of *B pseudomallei* by culture remains the 'gold standard'. The first several cultures were negative for *B pseudomallei*, which led to a significant delay in diagnosis and the administration of subsequent treatment. Serological testing with an indirect haemagglutination assay was performed to further confirm the diagnosis.[5]

B pseudomallei is resistant to the majority of antibiotics, but is susceptible to newer beta-lactam antibiotics, especially ceftazidime and meropenem which have the lowest minimum inhibitory concentrations against *B pseudomallei*.[10] The patient was treated according to guidelines; this

https://doi.org/10.1017/S0022215116008276 Published online by Cambridge University Press

entails initial intensive therapy consisting of 2 weeks of meropenem (IV 25 mg/kg, up to 1 g every 8 hours) or ceftazidime (IV 50 mg/kg, up to 2 g every 6 hours) administration, followed by eradication therapy for 3 months consisting of trimethoprim and sulfamethoxazole administration. Relapse generally occurs in up to 23 per cent of patients and is more common with severe disease; however, this is reduced to less than 10 per cent with prolonged oral antibiotic administration following parenteral treatment.[8] Long-term follow up is required to detect relapse. In addition, susceptibility tests should be carried out on isolates obtained during or after treatment in order to detect resistance to trimethoprim-sulfamethoxazole, which occurs in up to 2.5 per cent of cases.[11] Nevertheless, this treatment is considered the initial eradication agent of choice.[5]

- **Melioidosis is caused by Gram-negative bacillus *Burkholderia pseudomallei***
- **Melioidosis is most prevalent in Northern Australia, Southeast and Southern Asia, China, and Taiwan**
- **The overall mortality is 10–19 per cent in Australia, with a recurrence rate of approximately 13 per cent**
- **This is the third reported case that involved the sinuses**
- **The patient was treated with intravenous meropenem during the acute phase, followed by three months' oral trimethoprim-sulfamethoxazole**

A literature review was performed with Ovid Medline and Embase databases using the Medical Subject Heading terms 'melioidosis' or 'Burkholderia pseudomallei' and 'sinusitis'. The search identified two separate cases of sinusitis associated with melioidosis. A single case of orbital cellulitis and sinusitis was described in a 42-year-old, previously healthy gentleman from Singapore, in 1996.[12] The most recent case was in a 51-year-old male, who presented with nasal cellulitis and sinusitis on a background of poorly controlled diabetes, hepatitis B and alcohol abuse, with suspected contraction in Vietnam.[13]

Conclusion

This single case of chronic rhinosinusitis secondary to *B pseudomallei* is the third such case in the literature and the first case to show the potential emergence of *B pseudomallei* in non-melioidosis endemic areas. In patients presenting with refractory chronic rhinosinusitis, ENT surgeons need to consider the possible presence of *B pseudomallei*, particularly in those who have recently travelled to Northern Queensland or Southeast Asia. Patients with concurrent pneumonia, or genitourinary or cutaneous skin infections, especially those with diabetes, a history of excessive alcohol consumption or immunocompromise, should raise suspicion. Diagnosis is critical given the potentially serious consequences and complex treatment regime required.

References

1 Whitmore A. An account of a Glanders-like disease occurring in Rangoon. *J Hyg (Lond)* 1913;**13**:1–34.1
2 Yabuuchi E, Kosako Y, Oyaizu H, Yano I, Hotta H, Hashimoto Y *et al*. Proposal of Burkholderia gen. nov. and transfer of seven species of the genus Pseudomonas homology group II to the new genus, with the type species Burkholderia cepacia (Palleroni and Holmes 1981) comb. nov. *Microbiol Immunol* 1992;**36**:1251–75
3 Cheng AC, Currie BJ. Melioidosis: epidemiology, pathophysiology, and management. *Clin Microbiol Rev* 2005;**18**:383–416
4 Chantratita N, Wuthiekanun V, Limmathurotsakul D, Vesaratchavest M, Thanwisai A, Amornchai P *et al*. Genetic diversity and microevolution of Burkholderia pseudomallei in the environment. *PLoS Negl Trop Dis* 2008;**2**:e182
5 Currie BJ. Melioidosis: evolving concepts in epidemiology, pathogenesis, and treatment. *Semin Respir Crit Care Med* 2015;**36**:111–25
6 Currie BJ, Fisher DA, Howard DM, Burrow JN, Lo D, Selva-Nayagam S *et al*. Endemic melioidosis in tropical northern Australia: a 10-year prospective study and review of the literature. *Clin Infect Dis* 2000;**31**:981–6
7 Currie BJ, Ward L, Cheng AC. The epidemiology and clinical spectrum of melioidosis: 540 cases from the 20 year Darwin prospective study. *PLoS Negl Trop Dis* 2010;**4**:e900
8 Currie BJ, Fisher DA, Anstey NM, Jacups SP. Melioidosis: acute and chronic disease, relapse and re-activation. *Trans R Soc Trop Med Hyg* 2000;**94**:301–4
9 Sidjabat HE, Cottrell K, Cervin A. Draft genome sequences of Burkholderia pseudomallei and Staphylococcus aureus, isolated from a patient with chronic rhinosinusitis. *Genome Announc* 2015;**3**:e01075–15
10 Smith MD, Wuthiekanun V, Walsh AL, White NJ. Susceptibility of Pseudomonas pseudomallei to some newer beta-lactam antibiotics and antibiotic combinations using time-kill studies. *J Antimicrob Chemother* 1994;**33**:145–9
11 Piliouras P, Ulett GC, Ashhurst-Smith C, Hirst RG, Norton RE. A comparison of antibiotic susceptibility testing methods for co-trimoxazole with Burkholderia pseudomallei. *Int J Antimicrob Agents* 2002;**19**:427–9
12 Wong PK, Ng PH. Melioidosis presenting with orbital cellulitis. *Singapore Med J* 1996;**37**:220–1
13 Lim RS, Flatman S, Dahm MC. Sinonasal melioidosis in a returned traveller presenting with nasal cellulitis and sinusitis. *Case Rep Otolaryngol* 2013;**2013**:920352

Address for correspondence:
Dr Nicholas M Phillips,
PO Box 1676,
Noosa Heads,
Queensland, Australia

E-mail: Nicholas.phillips@uqconnect.edu.au

Dr N M Phillips takes responsibility for the integrity of the content of the paper
Competing interests: None declared

https://doi.org/10.1017/S0022215116008276 Published online by Cambridge University Press