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SHORT REPORT
Changing epidemiology of melioidosis? A case of acute pulmonary melioidosis with fatal outcome imported from Brazil

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SUMMARY

Melioidosis is an infectious disease caused by *Burkholderia pseudomallei*. It is endemic in South East Asia and tropical regions of Northern Australia. Sporadic cases have been described elsewhere. In this article we present a case of acute pulmonary melioidosis with fatal outcome imported from Brazil. The most common pathogen causing severe community-acquired pneumonia in Brazil is *Streptococcus pneumoniae*. Other possible pathogens include *Legionella* spp., *Mycoplasma pneumonia*, Gram-negative rods and viruses. There are few reports of melioidosis in the Americas. This article represents the second known human case of melioidosis from Brazil. Recognition of melioidosis as a possible cause of severe pneumonia, even if a patient has not been travelling in a highly endemic area, is important because of the therapeutic consequences. The epidemiology of melioidosis will be reviewed.

Melioidosis, an infection caused by the Gram-negative bacillus *Burkholderia pseudomallei*, is highly endemic in South East Asia and tropical regions of Northern Australia [1, 2], where it is an important cause of community-acquired pneumonia and sepsis [3, 4]. *B. pseudomallei* is susceptible to chloramphenicol, third-generation cephalosporins, carbapenems, tetracyclines, trimethoprim–sulphamethoxazole and amoxicillin–clavulanate [3]. It is resistant to other penicillins, first-and second-generation cephalosporins, macrolides, rifamycins, colistin, and aminoglycosides [3].

Melioidosis has a broad clinical spectrum, ranging from subclinical disease to acute fulminant sepsis, often in combination with severe pneumonia. The incubation period can be as short as several days; the infection can, however, be latent for many years after exposure, often becoming apparent after a decrease in the host's immunocompetence [5]. For a full description of clinical symptoms and treatment we refer to several recent reviews [1, 3, 4, 6].

Predisposing conditions for this infection include diabetes, excessive alcohol consumption, chronic pulmonary disease and chronic renal disease [4]. Melioidosis should be suspected in any patient with pneumonia, sepsis, or abscesses and a history of past or recent travel to an endemic area, particularly if they have any of the predisposing illnesses described above.

Recognition of melioidosis will have important implications for the choice of antibiotic treatment of the patient. The distribution of melioidosis is, however, not restricted to known endemic areas [2, 6].

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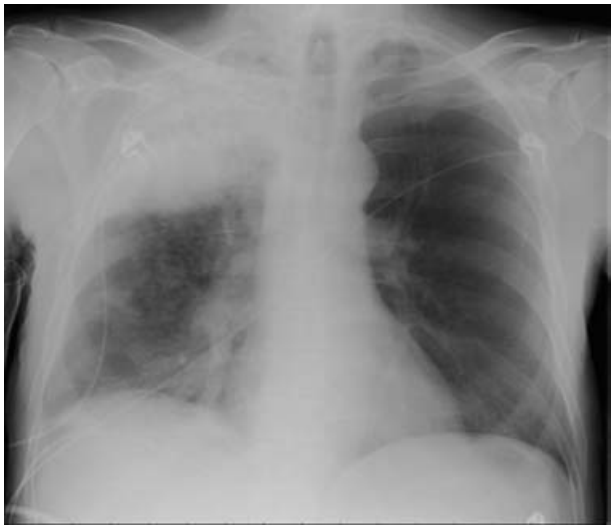

Fig. 1. A chest X-ray showing very dense consolidation in the upper right lobe and diffuse patchy consolidations in the remainder of the right lung.

Below, we describe a case report of a patient who presented with acute fatal septicaemic pneumonia due to *B. pseudomallei* after a visit to Brazil.

A 50-year-old diabetic male with a history of insulin-dependent diabetes presented to our accident and emergency department with a 2-day history of fever, dyspnoea, coughing with production of purulent sputum and pain on the right hemithorax.

His recent history revealed an 8-day trip to Ceará, Brazil, where he had travelled with a group, visiting developed as well as rural areas; the trip included hikes through national parks, swims in the sea as well as in swimming pools and in a freshwater lake, and sightseeing in caves. He had stayed in hotels throughout the trip, which ended 2 days before his admittance to hospital. During his stay in Brazil the weather was sunny with temperatures between 23–30 °C (75–86 F); there was no rainfall. The rainy season in this area runs from February to May, whereas the patient's trip took place in July. He smoked 20 cigarettes a day, drank two units of alcohol a day, and denied use of illicit drugs.

On physical examination we saw a severely ill man who was dyspnoeic and tachypnoeic. His blood pressure was 121/65, his pulse 137/min, his body temperature was 40·7 °C, his respiratory rate was 40/min and his oxygen saturation was 88%. On auscultation of the lungs, crackles and bronchial breathing were heard over the right lower lobe, with abnormal breathing over the remaining part of the right lung. Further physical examination revealed no abnormalities.

A chest X-ray showed a very dense consolidation in the upper right lobe with diffuse patchy consolidations throughout the rest of the right lung (Fig. 1). We diagnosed severe community-acquired pneumonia in a 50-year-old diabetic who had recently travelled to Brazil.

We started treatment with intravenous cefuroxime 750 mg three times daily, erythromycin 1000 mg four times daily and gentamicin 420 mg daily, according to our protocol for treatment of severe community-acquired pneumonia.

He was transferred to the intensive care unit of another hospital due to lack of such facilities in our hospital at that time. Soon after admission his condition deteriorated; he developed progressive respiratory failure necessitating mechanical ventilation; his course was further complicated by a septic shock syndrome, unresponsive to intravenous fluids and inotropic drugs. On the second day after admittance, he developed an irreversible cardiac arrest. Blood and sputum specimens obtained on the day of admittance grew a Gram-negative rod susceptible to ceftazidime, but resistant to gentamicin, cefuroxime and erythromycin. The bacterium was identified as *B. pseudomallei* with API 20NE and confirmed by 16sRNA PCR sequencing by the National Institute for Public Health and the Environment (RIVM).

B. pseudomallei is a saprophyte living in soil and surface water in endemic areas [3]. Human infection is commonly caused by cutaneous inoculation or by inhalation of contaminated water or soil [1, 3]. The endemic areas are South East Asia and Northern Australia [2, 4]. For a graphic review of the epidemiology of melioidosis see Figure 2. In Thailand, melioidosis was responsible for 23% of all community-acquired septicaemias in one prospective study [7]. *B. pseudomallei* is widespread in soil in Thailand; in one study the bacillus could be isolated from 114 out of 167 (68%) soil samples from different sites (radius 250 km) in north-eastern Thailand [8]. In the Australian Northern Territory, a tropical area, melioidosis is a common cause of fatal community-acquired pneumonia [9]. The incidence of melioidosis in this area is estimated to be 16·8/1 00 000 per year [4]. Outside the Northern Territory, melioidosis is also seen in Western Australia [10, 11], North Queensland [11], including the Torres Strait islands [11, 12], and Papua New Guinea [11, 13]. As reviewed by Dance [2], apart from Thailand, other countries in South East Asia where melioidosis is found to be endemic are Burma, Malaysia [14], Singapore [14], Vietnam [5], Laos, Cambodia, Hong Kong [14], and possibly the Philippines, China and Korea. Melioidosis has also been reported in Indonesia [15], Taiwan [16], Pakistan [17], Bangladesh [17], India [2, 17], as well as in several African countries [2], among which are Ivory Coast, Madagascar, Kenya [18], La Réunion [14], The Gambia [19] and Burkina Faso [14].

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Fig. 2. An illustration of the epidemiology of melioidosis. ■, Endemic areas; □, sporadic cases.

Furthermore, there is evidence of melioidosis in Iran [2, 14] and possibly other countries in the Middle East [2].

Melioidosis as an imported disease was seen in France in the 1970s when animals of the Paris Zoo, several equestrian clubs and other zoos throughout France were affected [2, 3, 6, 14, 20].

There are few reports of melioidosis in Central and South America and the Caribbean. Cases have been described in Puerto Rico [21], Guadeloupe [22], Martinique [23], Haiti [14] and Aruba [24]. Dance reviewed additional cases from Ecuador, Panama, Mexico, Peru and El Salvador [2]. Recently, a case of infection with *B. pseudomallei* was reported from Brazil [25]. This concerned a 10-year-old boy from Ceará, Brazil developing fatal septic shock syndrome, who was found to have positive blood cultures for *B. pseudomallei*. Interestingly, our patient had also been to this particular region of Ceará. To our knowledge, this article by Miralles et al. and our case report are the only publications thus far on human cases of melioidosis in Brazil. It is quite possible that these sporadic cases are in fact indicative of endemic infections, not yet acknowledged as such.

In the 1980s, Galimand et al. isolated *B. pseudomallei* from soil in Brazil [14]. There are no known cases of melioidosis in animals in Brazil [25]. An interesting consideration is where our patient was infected; on several occasions there could have been contact with fresh surface water. A specific inoculating event could, however, not be identified. Although there seems to be a preponderance of cases during the wet season in endemic areas [7, 9], it must be noted that our patient's trip took place outside the rainy season. To our knowledge, he had not visited any other countries in the months preceding his illness.

In retrospect, his travel history revealed a trip to Vietnam 4 years prior to his recent trip to Brazil. He had not been ill during or after that trip. According to family, he might, however, have fallen in a rice paddy due to hypoglycaemia during that trip. His only health problem at that time was diabetes mellitus, which was generally well regulated with insulin. Since reactivation can present as a fulminant sepsis, there is a theoretical possibility that he was infected 4 years before in Vietnam. Clinically, however, this seems unlikely.

The diagnosis of melioidosis was not suspected in our patient since he had not travelled to a known endemic area. On admission, a vast range of pathogens causing this severe community-acquired pneumonia was considered; in Brazil, the most common pathogens of (severe) community-acquired pneumonia include *Streptococcus pneumoniae*, *Legionella* spp., *Mycoplasma pneumoniae*, *Haemophilus influenzae*, *Chlamydia pneumoniae*, Gram-negative rods, and respiratory viruses [26–28]. Based on the low prevalence of penicillin-resistant pneumococci in Brazil [28], the guidelines for the treatment of community-acquired pneumonia as provided by the Brazilian Society for Infectious Diseases recommend third-or fourth-generation cephalosporins plus a macrolide

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intravenously as first-choice treatment for severe pneumonia [26]. Interestingly, this regimen also covers *B. pseudomallei*.

Despite optimal antibiotic treatment, melioidosis is still associated with significant mortality; Currie et al. found an overall mortality of 19% in their Australian study [4]. The role of recombinant G-CSF as adjunctive therapy combined with antibiotics remains to be elucidated [4], although preliminary results did not show a significant benefit [29].

Our patient was treated with a combination of cefuroxime, erythromycin, and gentamicin according to our protocol for severe community-acquired pneumonia. Unfortunately, *B. pseudomallei* is not susceptible to any of these antibiotics [3]; the infection could, thus, follow its natural course. Our case illustrates the importance of awareness of *B. pseudomallei* as a possible pathogen. In a patient who has visited tropical areas, even if these are not considered to be highly endemic for this disease, melioidosis should be included in the differential diagnosis.

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