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Burkholderia pseudomallei in cystic fibrosis and treatment complications

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Abstract

A healthy 29-year-old Australian man with cystic fibrosis (CF) grew *Burkholderia pseudomallei* on a routine sputum culture 1 month after returning from holiday in Thailand. He underwent a 12-month treatment regime with multiple antibiotics resulting in a number of adverse events. Sputum cultures were cleared of the pathogen and remain negative 8 years post-treatment. There were no clinical sequelae and no deterioration in lung function. Few reports have been published to date on melioidosis in CF patients. The proposed management for this infection includes multiple antibiotics regimens for prolonged periods of time, which may result in adverse events. Optimal treatment and length of treatment are currently determined on an individual basis.

Introduction

Melioidosis is caused by the bacteria *Burkholderia pseudomallei*, a gram-negative bacterium that is found in soil and water mainly in Southeast Asia, Asia, and Northern Australia. In endemic areas, it causes fulminant pneumonia and septicemia but may present in subacute or chronic forms in non-endemic areas. Infection occurs by direct inoculation of the skin, inhalation, or ingestion with the majority of infected hosts having some underlying immunodeficiency or risk factor [1].

There are few published case reports/series of *B. pseudomallei* in cystic fibrosis (CF) patients [1–4]. These cases vary in their presentation, the antibiotics used to treat them, and their outcomes in terms of mortality and pathogen eradication. Here we present only the third known case of *B. pseudomallei* eradication in a patient with CF.

Case Report

Our patient is a 29-year-old Australian with CF who was previously well with predicted forced expiratory volume in 1 s of 120%. One month after returning from Thailand, routine sputum sample on one occasion isolated *B. pseudomallei* without any clinical evidence of infection. Given the pathogenic nature of this bacteria, he was treated aggressively with a 6-week course of intravenous (i.v.) antibiotics consisting of meropenem 2 g three times daily (tds), ceftazidime 3 g tds, nebulized tobramycin 80 mg tds, and oral trimethoprim/sulfamethoxazole (TMP-SMZ) 160/800 mg two tablets bi-daily (bd). Note in Australia at this time TOBI® (Novartis Pharmaceuticals Corporation, East Hanover, New Jersey; tobramycin) was not routinely available.

On day 3 he developed nausea, vomiting, and diarrhea. Stool cultures and *Clostridium difficile* toxin tests were negative, and his symptoms settled with anti-emetic medication. On day 10 he developed a pruritic erythematous rash on his hands, feet, and trunk. TMP-SMZ dose was reduced to one tablet bd. On day 11 he spiked a temperature of 38°C with a negative septic screen; ceftazidime and TMP-SMZ were ceased with resolution of symptoms.

He was discharged with home i.v. meropenem for 6 weeks and oral doxycycline for several months. Doxycycline use was complicated by photosensitivity resulting

in a change to amoxicillin/clavulanic acid, one tablet tds. Nausea and vomiting developed and the dose was decreased to one tablet bd with resolution of symptoms. A total of 12 months of treatment was completed with no further growth of the bacteria, maintenance of adequate lung function, and no further adverse events. The patient remains well with stable lung function 8 years post-treatment.

Discussion

Most patients described in case reports of CF with *B. pseudomallei* present with an acute febrile illness or deterioration in lung function after isolation of the pathogen and receive prolonged treatment. However, cases of well patients with isolation of the pathogen on routine testing are much less common and have been described in only two case series.

One patient grew *B. pseudomallei* after contact with her sibling but was clinically well. Treatment with TMP-SMZ was complicated by bone marrow suppression and doxycycline was substituted. Eradication was not achieved although duration of treatment was not reported [2]. Another healthy individual with CF who was a friend of the mentioned patient grew *B. pseudomallei* on a routine culture. She was commenced on treatment with ceftazidime and bactrim for 14 days, followed by TMP-SMZ for 3 months, for presumed colonization. This patient was able to clear the pathogen [2]. Finally a recent report of a 15-year-old boy who had *B. pseudomallei* isolated for 10 years received no treatment and remained well with mild bronchiectasis only [1].

Our patient was asymptomatic and, in addition, had normal lung function. Most of the reports of treatment of melioidosis are in patients who are acutely unwell. There is minimal experience in the literature to guide the treatment of stable patients with incidental isolation of this pathogen.

It is important to note that the treatment for most of the reported cases in CF patients have differed in terms of antibiotic choice and duration with varied outcomes in terms of mortality and pathogen clearance. Suggested treatment regimes by Currie *et al*. include ceftazidime (or meropenem or imipenem) ± TMP-SMZ for a minimum of 14 days, followed by an eradication regime for 3 months of TMP-SMZ ± doxycycline [5].

A more recent Cochrane review comparing treatments for melioidosis also suggest i.v. therapy regimens should contain ceftazidime, imipenem, or the newer beta-lactam/beta-lactamase inhibitors and oral therapy containing a combination of chloramphenicol, doxycycline, and TMP-SMZ treatment for approximately 20 weeks. Total duration of therapy is based on clinical judgment. Of note the studies comprised in the Cochrane review included all cases of melioidosis, mostly with underlying disorders such as diabetes and renal failure. The applicability of these treatment regimes may vary in CF patients where antimicrobial resistance, virulence, and host factors may play an important part in treatment outcomes.

Additionally, it should be kept in mind that treatment with a multitude of antibiotics may result in decreased adherence to therapy, antimicrobial resistance, and side effects, as in the case of our patient. Further understanding of the virulence of these bacteria in CF patients may help differentiate the intensity of treatment that is necessary in different patients. A larger case series may help differentiate patterns of treatment and outcomes in these patients.

Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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