Tropical Biomedicine 37(3): 560–565 (2020)

A fatal case of primary melioidotic prostatic abscess: the peril of poor drug compliance

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Received 6 November 2019; received in revised form 4 May 2020; accepted 6 May 2020

Abstract. Primary prostatic melioidosis is a rare presentation of melioidosis even in melioidosis endemic areas. We report a case of a 58-year-old man with underlying diabetes mellitus who presented with a 5-day history of high-grade fever associated with lower urinary tract symptoms. Suprapubic tenderness and tender prostatomegaly were noted on examination. An abdominal computed tomography (CT) scan confirmed the presence of a prostatic abscess. Both blood and prostatic pus cultures grew *Burkholderia pseudomallei*. He was initially started on intravenous ceftazidime, followed by an escalation to intravenous meropenem. He was discharged home with oral amoxicillin-clavulanate and doxycycline after completing 12 days of meropenem. Unfortunately, his compliance to oral antibiotic therapy was poor, and he succumbed to the disease.

INTRODUCTION

Melioidosis is caused by a saprophytic gram-negative bacillus known as *Burkholderia pseudomallei*. This bacterium is commonly found in moist soil and pooled surface water. Northeast Thailand, Malaysia, Singapore, and northern Australia are considered highly endemic areas (Dance, 2000). The pathogenesis of this infection is mainly based on its ability to invade phagocytes and survive intracellularly (Wiersinga *et al.*, 2012). Lungs are the main organ involved in this infection but extrapulmonary manifestations do occur occasionally (How *et al.*, 2005). Involvement of the prostate is rare, particularly as a primary focus of melioidosis. Prostatic abscesses have been reported to occur in about 13% of the cases, as primary and secondary foci of melioidosis (Kingsley *et al.*, 2016).

CASE REPORT

A 58-year-old Malay man with underlying type 2 diabetes mellitus presented with high-grade fever for 5 days. This was associated with suprapubic pain and dysuria. He did not complain of any other symptoms. He was a retired factory supervisor. Since retiring, he spent his time gardening around his house. On clinical examination, he was febrile with a temperature of 38.5°C and tachycardic with a pulse rate of 130 beats/min. His blood pressure and glucometer readings were 130/90 mmHg and 6.4 umol/L, respectively. He had tenderness at the suprapubic region. A digital rectal examination revealed an enlarged and tender prostate. The rest of the clinical examination was unremarkable.

Laboratory investigations revealed the presence of leukocytosis, with a predominance of neutrophils (87.9%), a high

C-reactive protein and pyuria. Other laboratory results were within their reference ranges, as shown in Table 1. His chest X-ray was unremarkable, with no radiological evidence of a pulmonary infection. A transrectal ultrasound showed the presence of hypoechoic lesions in the prostate suggestive of an abscess, as shown in Figure 1. CT scans of the pelvis and abdomen were performed to confirm the lesions. The CT scan revealed an enlarged prostate with a localized hypodense lesion measuring 55 mm x 54 mm x 69 mm, which was consistent with an abscess. There was no radiological evidence of a hepatic or splenic abscess.

A decision was made to drain the prostatic abscess and a transrectal ultrasound (TRUS)-guided needle aspiration was performed. The pus specimen was sent for bacterial culture. Both pus and blood samples (taken earlier) grew *B. pseudomallei* that was susceptible to ceftazidime, meropenem, trimethoprim-sulfamethoxazole (TMP-SMX), amoxicillin-clavulanic acid and tetracycline, as shown in Table 2. The identification of *Burkholderia pseudomallei* was accomplished biochemically using the API 20 NE kit (bioMérieux, France). A urine specimen was also sent for culture but it yielded no growth.

He was empirically started on IV ceftazidime 2 g q8h, which was continued after the culture results were available on Day-3 of admission. However, he did not demonstrate significant clinical improvement after five days of therapy. His condition deteriorated further with the development of respiratory distress, necessitating intensive care unit admission. However, repeated chest X-rays did not show any new or significant changes. His sputum was also sent for microbiological culture, but no bacterial growth was recorded. Repeated blood cultures were still positive for *B. pseudomallei*, with an antibiogram similar to that of the initial isolate. The antimicrobial therapy was escalated to IV meropenem 1 g q8h. His fever gradually subsided and he was subsequently weaned off oxygen supplementation. He completed 12 days of meropenem therapy and was discharged home with oral amoxicillin-clavulanate 1 g bd and oral doxycycline 200 mg od for three months. Oral TMP-SMX was not prescribed

Table 1. Laboratory investigation results on the day of presentation

Parameters	Result	Normal Range
Full Blood Count:		
Hemoglobin	12.3	11.6–15.1 g/dL
White cell count	12.9 x 10^9/L	4.1–11.4 x 10^9/L
Platelet	215 x 10^9/L	171–399 x 10^9/L
C-reactive protein	11.8	< 0.5 mg/dL
Liver Function Test:		
Total Protein	68	64–83 g/L
Albumin	41	35–50 g/L
Alkaline Phosphatase	62	40–150 U/L
Alanine transaminase	21	0–55 U/L
Renal profile:		
Sodium	138	136–145 mmol/L
Potassium	4.5	3.5–5.2 mmol/L
Urea	5.2	3.2–7.4 mmol/L
Creatinine	77.9	63.6–110.5 umol/L
Urinalysis:		
Red blood cell	Negative	
Leukocyte	Positive (2+)	
Nitrate	Negative	
Glucose	Negative	
Ketone	Negative	

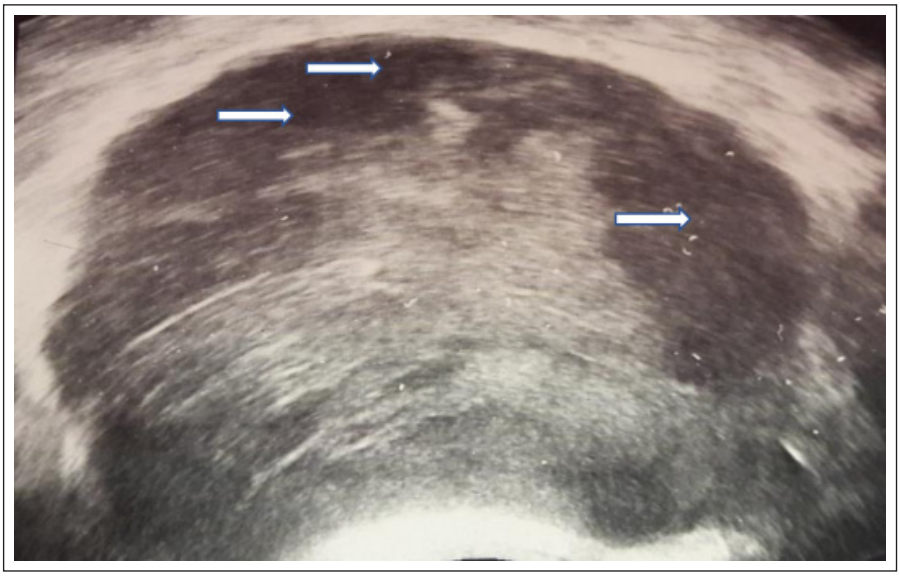

Figure 1. Ultrasound of the prostate showing the presence of an abscess (arrows).

Table 2. Antibiotic susceptibility testing result for this *Burkholderia pseudomallei* isolate

Antibiotic	Minimum inhibitory concentration (MIC) µg/mL	MIC Range Reference (µg/mL)*		
		Sensitive	Intermediate	Resistant
Amoxicillin-clavulanic acid	2	8	16	32
Ceftazidime	1.5	8	16	32
Imipenem	0.38	4	8	16
Trimethoprim-sulfamethoxazole (TMP-SMX)	2	2	–	4
Doxycycline	2	4	–	–

* Based on the Clinical and Laboratory Standards Institute (CLSI) Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria. 3rd ed. CLSI guideline M45.

because the patient was allegedly allergic to this antibiotic.

Three months after being discharged home, the patient did not turn up for his scheduled follow up in Kuala Lumpur General Hospital. It was learnt that the patient was not compliant to his antibiotics and was admitted to another hospital. Alas, he succumbed to the infection.

DISCUSSION

The incidence of melioidosis varies widely between regions, depending on its geographical and agriculture activities. Its incidence in Malaysia was reported to be between 6.1 to 16.35 cases per 100,000 population in the various states (How *et al.*, 2005; Hassan *et al.*, 2010). The infection is acquired mainly through inhalation or direct penetration of a pre-existing skin condition. Thus, occupational and recreational activities that have direct or regular contact with contaminated soil or water are considered risk-related activities (Hassan *et al.*, 2010; Currie *et al.*, 2010). Diabetes mellitus is one of the most important risk factors associated with melioidosis, as previously reported by many authors (How *et al.*, 2005; Zueter *et al.*, 2016). Coming back to our patient, his underlying diabetes

mellitus and regular soil exposure through gardening activities were his most likely risk factors for contracting melioidosis.

Melioidosis may mimic many other conditions as multi-organ involvement is common. An acute presentation is reported in the majority of cases, with bacteraemia being a common occurrence (Kingsley *et al.*, 2016; Currie *et al.*, 2010). Similarly, our patient had acute symptoms and bacteraemia. Although genitourinary involvement in melioidosis is not common, prostatic abscess has been reported before (Kingsley *et al.*, 2016; Currie *et al.*, 2010). A prostatic abscess in melioidosis frequently presents as a secondary infection (as part of systemic melioidosis) rather than a primary focus. Hassan *et al.* (2010) and Zueter *et al.* (2016) described only one case of primary melioidotic prostatic abscess in their series. Additionally, Kingsley *et al.* (2016) demonstrated only three cases of primary prostatic melioidosis from 56 cases. Thus, prostatic abscess as the primary focus of melioidosis is exceedingly rare.

Most prostatic abscess patients present with urinary tract symptoms that include dysuria, urgency, frequency, retention or incontinence (Kozlowska *et al.*, 2018; Tan *et al.*, 2015). Kozlowska *et al.* (2018) concluded that the absence of urinary symptoms had a negative predictive value of 96% for prostatic abscess. However, Chong *et al.* (2014) showed that only two out of their nine patients had dysuria. A digital rectal examination can be inconclusive, because a tender prostate is elicited in less than half of prostatic abscess patients (Kozlowska *et al.*, 2018). The presence of leukocyturia was perhaps the most consistent finding – all melioidosis patients with prostatic abscess had urinary leukocyte counts of at least 50 x 10^6/L, and the value of < 50 x 10^6/L correlated with a 100% negative predictive value (Kozlowska *et al.*, 2018). Echoing these findings, our patient also had a classical history of urinary symptoms, a tender enlarged prostate and significant leukocyturia.

TRUS and CT scan modalities are useful imaging investigations. In most cases, they will reveal large abscesses (> 4.5 cm) (as was seen in our patient), involvement of both lobes and multiloculated abscesses (Chong *et al.*, 2014; Tan *et al.*, 2002). Microbiological culture will help to confirm *B. pseudomallei*. A pus specimen drained from the abscess is perhaps the most useful specimen for bacterial culture (Tan *et al.*, 2015; Tan *et al.*, 2002; Chee & Chee, 2018). The bacterium can also be isolated from urine specimens and blood specimens in some patients (Tan *et al.*, 2015; Tan *et al.*, 2002). In our patient, the bacteria was isolated from both pus and blood specimens, but not from the urine.

The role of surgery for this condition remains controversial. It is suggested that a small abscess of less than 1 cm may be managed conservatively with antimicrobial therapy (Acherman *et al.*, 2018) whereas a larger abscess should be promptly drained (Tan *et al.*, 2002). Antimicrobial treatment of melioidosis can be divided into an initial intensive phase of at least two weeks on an intravenous antibiotic, followed by an eradication phase of at least 3 months on oral antibiotics (Pitman *et al.*, 2015). Ceftazidime is considered the first-line intravenous antibiotic but the switch to carbapenem can be contemplated in the event of ceftazidime failure (Limmathurotsakul & Peacock, 2011). The suggested maximum dosages for ceftazidime and meropenem are 2 g and 1 g, respectively, every 8 hours for a minimum duration of 10–14 days (Limmathurotsakul & Peacock, 2011). Coming back to our patient, he was given the maximum ceftazidime dosage but clinical improvement was not apparent and in fact was complicated by respiratory failure secondary to sepsis. Thus, the switch to a carbapenem was made, and he was successfully treated with meropenem for 12 days.

It was noted that a relapse or recurrence can occur in melioidosis. Culture-confirmed recurrences were reported in 11.4% of patients who survived their initial

hospitalisation in Singapore (Chien *et al.*, 2018). A recurrence is more likely to occur in those with multifocal disease and/or an intraabdominal abscess (Chien *et al.*, 2018). The choice of oral therapy has been shown to influence relapse rates. A study has shown that the use of amoxicillin-clavulanate as well as TMP-SMZ alone and doxycycline alone was associated with higher relapse rates (Limmathurotsakul *et al.*, 2006). In the same study, it was observed that the duration of oral therapy was negatively associated with relapse. The hazard ratio decreased by 29% for each 4-week increase in the duration of standard oral treatment (Limmathurotsakul *et al.*, 2006). Thus, it is important to give emphasis on the choice and duration of oral therapy during the maintenance phase. Our patient was appropriately prescribed with a combination of oral amoxicillin-clavulanate and doxycycline (as he was allergic to TMP-SMZ). Alas, although both the drug dosages and treatment duration were adequate, his drug compliance was poor, leading to a possible relapse and ultimately his demise.

CONCLUSION

The diagnosis of primary melioidotic prostatic abscess remains a diagnostic and therapeutic challenge. The diagnosis should be considered in diabetic patients with urinary tract symptoms. Pharmacological treatment consists of two phases, with the total treatment duration taking several months in order to prevent a relapse. Drug compliance is particularly paramount during the second (i.e. maintenance) phase.

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgement. The authors express their sincere gratitude to the Director General of Health, Ministry of Health Malaysia and Dean, Faculty of Medicine, Universiti Kebangsaan Malaysia for their permission to publish this case report.

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