Urogenital Melioidosis: A Review of Clinical Presentations, Characteristic and Outcomes

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SUMMARY

Introduction: Melioidosis is endemic to the tropical regions, in particular Thailand and Northern Australia. Any organ can be affected by melioidosis. Involvement of the urogenital system is common in Northern Australia, but is less common in other regions. This study assesses the characteristics of melioidosis affecting the urogenital system treated in a tertiary referral centre in Brunei Darussalam.

Material and Methods: All patients treated for melioidosis of the urogenital system were identified and retrospectively reviewed.

Results: There were 9 patients with 11 episodes of urogenital infections treated over 13 years. The median age at diagnosis was 38 years old (range 29 - 63) with men predominantly affected. The major risk factor was underlying diabetes mellitus (n=9), including three patients diagnosed at the time of diagnosis of melioidosis. The median glycosylated haemoglobin (HbA1c) was 12.8% (range 6.4 to 16.6%). One patient's risk factor was only moderate alcohol consumption. Common symptoms included; fever, lethargy, rigor and anorexia. Dysuria was reported by two patients. The median duration of symptoms before presentation was 7 days (range 2 to 21 days) and the median number of sites involved were 3 (range of 2 to 6). Urogenital involvement included prostate (n=6), kidney (n=8), seminal vesicles (n=1) and testis (n=1). Radiological imaging showed that large prostate abscesses (>4.5cm) were common, and in some patients, the kidney abscess had the 'honeycomb' previously described as typical for melioidosis liver abscess. All patients were successfully treated for melioidosis and at a median follow up of 34 months (range 1 - 97), there was one death from complications of diabetes mellitus.

Conclusion: Urogenital melioidosis only accounted for a small proportion of all melioidosis involvement, with prostate and kidney most commonly affected. Concomitant involvement of other sites were common. The major risk factor was poorly controlled diabetes mellitus.

KEY WORDS:
Burkholderia pseudomallei, urological sepsis, abscesses, presentations, melioidosis

INTRODUCTION

Melioidosis is caused by *Burkholderia pseudomallei (B. pseudomallei)*, a gram negative bacillus and refers to a spectrum of infections that is endemic to the tropical regions, in particular Northern Australia and Southeast Asia.[1-2] However, this infection is also reported in other tropical and non-tropical regions as imported cases.[1-6] Almost any organ system can be affected by melioidosis. Compared to other systems, urogenital involvement is generally less common with the prostate and kidney the most commonly involved. Between regions, there are differences in frequencies of system involvement. A study from Taiwan reported urogenital involvement to account for 13.3% of all melioidosis treated [7]. Higher rates have been reported in Northern Australia, in particular prostate involvement.[8, 9] The rates are lower in the other melioidosis endemic (Southeast Asia) and non-endemic regions.[6, 10-13] To date, apart from reports from Northern Australia, there have only been several reports on prostate melioidosis in the form of single case reports or small case series.[10-13] None of these studies have reported involvement of the other parts of the urogenital system. This study assesses the clinical, laboratory and radiological characteristics of melioidosis affecting the urogenital system experienced in a tertiary referral centre in Southeast Asia.

MATERIALS AND METHODS

Patients diagnosed and treated for urogenital melioidosis (culture proven) were identified and retrospectively reviewed. Data on the patients' demographic, clinical presentations, risk factors for melioidosis, investigations and radiological investigations and follow up information were retrieved. The radiological imaging was retrieved and reviewed in detail for confirmation of urogenital involvement and also to assess the radiological characteristics. The sites and imaging characteristics were reviewed and carefully noted by two experienced consultant radiologists (ICB and FS).

In our centre, all patients diagnosed with melioidosis are usually treated with our standard regimes; a) intravenous ceftazidime (2gm,8hrly) and amoxicillin-clavulanic acid (1.2gm 8hrly) or b) intravenous meropenem (1-2gm, 8hrly) for a duration of two to four weeks during the initial intensive phase before being converted to oral antibiotic with either co-trimoxazole (Septrin, 1,290mg 12hrly) or combination of amoxicillin-clavulanic acid (675mg,12hrly) with doxycycline

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Table I: Clinical symptoms at presentations

Symptoms	n (%)
Fever	11 (100)
Lethargy	11 (100)
Rigor	10 (90.1)
Anorexia	10 (90.1)
Weight loss	9 (81.8)
Vomiting	3 (27.3)
Dysuria	2 (18.2)
Lower abdominal pain	2 (18.2)
Diarrhoea	1 (9.1)

Other symptoms included strangury (1), testicular swelling (1), night sweat (1), cough (2) and urinary retention (1)

Table II: The breakdown of the sites involved

Sites	n (%)
Haematological	11 (100)
Spleen	9 (81.8)
Kidney	8 (72.3)
Prostate *	6 (60)
Liver	3 (27.3)
Joints	2 (18.2)
Lung	2 (18.2)
Adrenal	1 (9.1)
Testis *	1 (10)
Seminal vesicles *	1 (10)

*Out of 10 episodes of infections in male patients

Table III: Laboratory investigations of patients at admissions

Parameters	Value (Reference range)
White cell count (/109)	12.4 (3.7 to 19.2)
Haemoglobin (gm/dL)	11.3 (6.7 to 15.9)
Platelets (/109)	148 (85 to 286)
C-reactive protein (mg/ml)	15.4 (10.37 to 22.3)
Erythrocyte sedimentation rate (mm/hr)	79 (44 to 124)
Random blood sugar (mmol/L)	9.2 (5.7 to 66.6)
Serum Albumin (gm/L)	19 (17 to 26)
Serum Urea (mmol/L)	7.7 (2.2 to 37.2)
Serum Creatinine (mmol/L)	145 (85 to 434)
HbA1C (%)	12.8 (6.4 to 16.6)

(200mg,daily) for a duration of five to six months (eradication phase). Patients are usually followed up with laboratory evaluation to monitor for decline of the inflammatory markers (serum C-reactive protein and erythrocyte sedimentation rate), and imaging at least once before discontinuation of oral antibiotic therapy. Post treatment of the melioidosis, all patients remain under follow up with their respective clinics; diabetic clinic (as most have underlying diabetes mellitus), physician or outpatient health clinics.

RESULTS

Over a 13 year period since 2000, there were a total 11 cases of urogenital melioidosis in nine patients.

The median age at diagnosis was 38 years old (29 - 63) and all except one were men. Most were Malay (n=7) including the two patients with relapse of the disease, while the remaining two were a Chinese and an Indian.

The major risk factor was underlying diabetes mellitus (n=9) including three patients who were newly diagnosed (two men; both 31 year old and one 63-year-old woman) at the time of presentations. Another patient's risk factor was only moderate alcohol consumption and evaluation for underlying diabetes was negative. Six patients were current or ex-smokers.

All patients had clinical symptoms with median symptom durations of seven days (2 - 21) before presentations. The most common symptoms were fever, lethargy, rigor, anorexia and weight loss. Urinary symptoms were only reported by two patients (dysuria in one and another with dysuria and strangury). The clinical presentations are shown in Table I.

The median number of sites involved was three (2-6). The breakdown of sites involved is shown in Table II. The most common site involved was the haematological system, prostate and the spleen. There was no involvement of the genital system of the only female patient.

Prostate involvement was seen in six patients and in most cases, both lobes were affected (large abscesses in five and small in one, Figures 1a and b). The size of the abscesses ranged from less than 3cm to 8cm.

Kidneys were affected in 7 patients; right in six and left in one (figures 2a-b). Ultrasound scan was done in 7 and was abnormal in 5. All abnormalities were identified on CT scan. One patient developed a right kidney abscess after admission with the initial CT scan not showing any kidney involvement. On computed tomography imaging, two large kidney abscesses had the 'honeycomb' appearance that is reported in melioidosis liver abscess.

The laboratory investigations are summarised in Table III. The majority of the patients had deranged laboratory tests including one patient with random glucose of 66.6 mmol/L. Inflammatory markers (ESR and CRP) were elevated in all patients. All had low serum albumin and the median HbA1c was 12.8%. One patient had HbA1C within normal limit.

All patients were successfully treated with standard intravenous antibiotic regimes without requiring drainage, even those with large prostate abscesses. At a median follow up of 34 months (1 - 97), there was one death. This was a 43-year-old man who was treated two episodes of urogenital melioidosis; the second episode 15 months after the initial episode. He died 14 months after the second episode of urogenital melioidosis of other complications of diabetes mellitus.

DISCUSSION

Our study showed that urogenital involvement in melioidosis is uncommon with only 11 cases encountered over the study period. Our finding is comparable to what have been reported elsewhere in the Southeast Asia region, [10-12] but much lower compared to what have been reported from Taiwan and Northern Australia. [7-9] In Northern Australia, prostate involvement is common with up to 20% of male patients affected. [8, 9] It is uncertain why there are such differences in the rates of urogenital involvements, in particular prostate

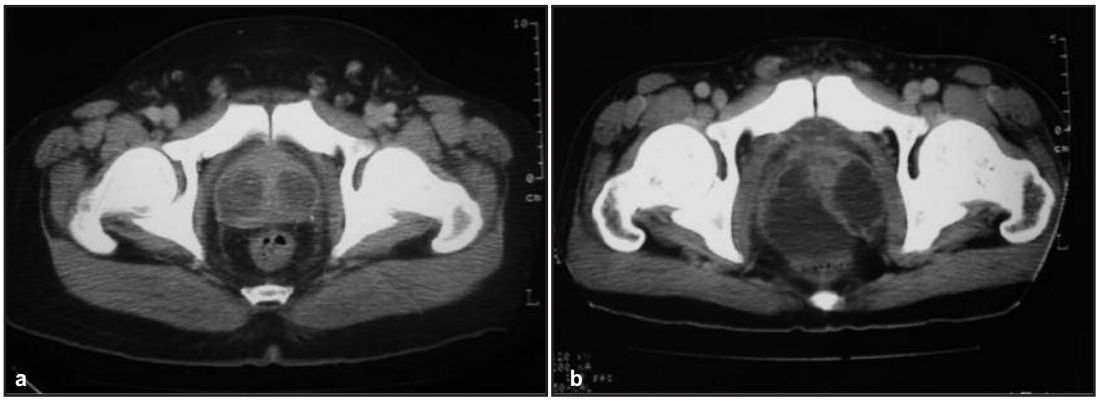

Fig. 1: Axial computed tomographic imaging showing bilobar prostate abscesses (a: moderate and b: large).

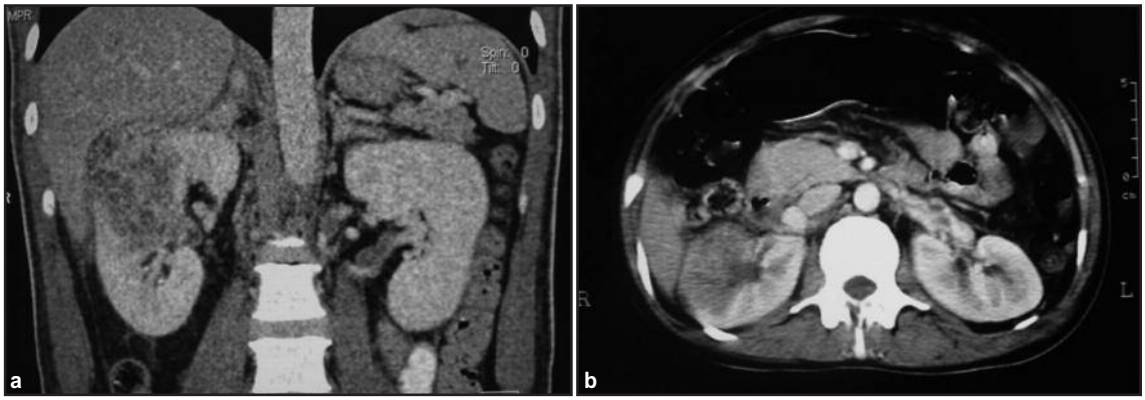

Fig. 1: a) Reconstructed sagittal CT scan showing involvement of the right kidney with cystic 'honeycomb' appearance and b) an axial CT scan showing involvement of the right kidney in another patient.

involvement. Routine practice of screening for prostate involvement in Northern Australia may be a factor. However, we believe that the difference in the incidence of prostate involvement is real, as despite the increasing and now routine use of CT imaging, the overall number of prostate abscess including those with melioidosis infections continued to be low in our setting. This is reflective of what have been reported from other Southeast Asian centres and generally centres outside of Northern Australia. This suggests that population, environmental and even genetic differences may be important in the type of manifestations of melioidosis infections.

Among our patients with urogenital involvement, prostate and kidneys were the main sites affected. The kidney was the most commonly affected site with the right kidney affected in the majority of patients. All manifested with a solitary abscess. Some of these kidney abscess especially the bigger ones, had the 'honeycomb' appearance that had been reported to be typical or characteristic of melioidosis liver abscess. [14, 15] The *honeycomb* appearance consists of multiple septations within the large abscess resembling a honeycomb. In addition to this, there is also the peripheral enhancing giving the 'necklace sign' which was not observed among our patients. These will require further study. Among patients with prostate involvement, most had involvement of both lobes. Only one patient each had involvement of the seminal vesicles and testis. All but one of our patients was males. The only female patient (63-year-old) did not complain of any urogenital symptoms. Apart from the CT imaging showing left kidney involvement, there was no genital involvement. This suggests that perhaps the urogenital system in men is more prone to melioidosis.

Apart from the urogenital system, involvement of the other organ systems was also common. The median number of sites involved was three with a range of two to six. All patients had *B. pseudomallei* isolated from blood cultures; suggesting the mode of dissemination is through haematological spread. The next common sites involved were the spleen, kidney and prostate. *B. pseudomallei* is found in the environment, mainly soil and water, hence the route of entry is commonly through breaks in the skin and also through the aero-digestive tract.[1,2] Spread to the other part of the lower part of the urogenital system is likely after seeding of the kidney with resultant spread to affect the prostate, testis and seminal vesicle.

The risk factors for melioidosis in our patients were mainly diabetes mellitus which in most cases was poorly controlled.[1] In our study, three patients were diagnosed with diabetes

mellitus when they presented with melioidosis. Other reported risk factors included end stage renal failure on haemodialysis and thalasseamia major requiring chronic blood transfusion and iron overload.[16] However, among our patients with urogenital melioidosis, none had the latter risk factors. One of our patients did not have any risk factor at all apart from previous mild to moderate alcohol use.

There have been several reports of radiological features of prostate melioidosis. The most consistent manifestation is multilobe involvements.[15,18-20] Concomitant involvements of other organs have also been reported to be specific for melioidosis. Honeycomb appearance of melioidosis abscess has been previously described for melioidosis liver abscess.[14,15] This CT feature along with the lace and necklace pattern has been reported to be characteristics for melioidosis liver abscess. Our experience has also supports this description. However, honeycomb appearance of kidney abscess has not been previously reported. Among our six patients with kidney abscess, two had the honeycomb appearance. This was only seen in abscesses larger than 3 cm. This is also true for abscess involving the liver and spleen. Hence, findings of honeycomb appearance seem to be suggestive of melioidosis in aetiology.

The treatment of melioidosis is standardised with only slight variation in the regime and the duration between different centres.[1, 2, 20] In most instances, use of ceftazidime is central along with amoxicillin-clavulanic acid, carbepenem, doxycycline and co-trimoxazole. All our patients were treated with our standard regime consisting of combination of intravenous ceftazidime and amoxicillin-clavulanic acid for four to six weeks in the intensive phase followed by either combination of amoxicillin-clavulanic acid with doxycycline or ciprofloxacin or co-trimoxazole monotherapy in the eradication phase. Interestingly, none of our patients required any drainage, even those with large prostate abscesses. This is in contrast to the reports from Northern Australia where patients with prostate abscesses are subjected to drainage.

In conclusion, our experience with urogenital melioidosis showed that multi-site involvements are common. Among urogenital melioidosis, prostate and kidney involvements were common. The major risk factor was underlying diabetes mellitus either known or newly diagnosed. None of our patients even those with large abscesses required any percutaneous or surgical drainage. However, the number of cases is small, reflective of the frequency of urogenital involvement in melioidosis similar to what has been reported in Southeast Asia.

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