CASE REPORT

Disseminated *Klebsiella Pneumoniae* infection: prostate, an easily overlooked source of infection

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SUMMARY

Intraabdominal and prostatic abscesses are usually caused by floras, which dominate the gastrointestinal (GI) and genitourinary (GU) tract. *Escherichia coli* and *Klebsiella spp* are some of the most commonly isolated organisms worldwide. In the context of tropical diseases in Southeast Asia, they are also caused by *Burkholderia pseudomallei*, known as melioidosis, occurring rather frequently among immunocompromised individuals especially diabetics. Interestingly, the scarcity of clinical signs and symptoms in these infections often leads to misdiagnosis and patients presenting late to hospitals with severe sepsis. This case came about when a gentleman in his 50s came to our healthcare facility with complaints of an unabating high fever for 1 -month, involuntary weight loss and 2 weeks of dysuria. His prostate was examined and was found to be unusually enlarged and boggy. Ultrasound (USG) abdomen and prostate revealed disseminated abscesses involving the liver and bilateral kidneys with prostatomegaly. The left renal abscess was drained, and a positive growth for *Klebsiella pneumoniae* was noted. In this case, the prostate was believed to be the likely source of disseminated *Klebsiella pneumoniae* infection based on his symptoms. He was treated with 6 weeks of antibiotics and had achieved good recovery with no ultrasonographic evidence of the progression of prostatomegaly to prostatic abscess.

INTRODUCTION

Pyogenic intraabdominal abscess occurs following a breach in the mucosal lining of a particular abdominal organ due to infection or inflammation leading to a sealed collection of cellular debris, enzymes and remains of an infectious source. Abscesses may be liquefied or partially liquefied, and its morphology determines feasibility for drainage to achieve proper source control. Isolated organisms from these abscesses comprise largely of intestinal floras including coliforms bacteria such as *Escherichia coli, Klebsiella spp., Proteus spp., Enterobacter spp., Streptococci spp., Enterococci spp.* and certain anaerobes.[1] On the other hand, based on meta-analysis, prostatic abscesses are largely caused by *Escherichia coli,* followed by *Klebsiella spp., Pseudomonas spp., Proteus spp., Enterobacter spp., Serratia spp.,* and *Enterococcus spp.* A large proportion of patients with prostatic abscess were found to be diabetic.[2-4] It is postulated that prostatic abscess is a sequel of refluxed infected urine causing acute prostatitis, which is not properly treated. Risk factors for development of prostatic abscess include poorly controlled diabetes, benign prostate hyperplasia, non-sterile urinary catheterization, prostate biopsy and other urological instrumentation procedures.[5] In Malaysia, *Escherichia coli, Klebsiella spp.* and *Burkholderia pseudomallei* remain the most commonly isolated pathogens in both intraabdominal and prostate abscesses.[6] The same organism can result in abscesses in both the intraabdominal organs and the prostate.

The prevalence of *Klebsiella pneumoniae* (KP) prostatic abscess varies geographically. Studies have shown that there is a higher incidence rate of prostatic abscess caused by the organism in Asian countries.[3-4] This is evidenced by a recent study in Taiwan which showed an astounding 58% of prostatic abscess cases related to Disseminated KP infection.[3] Likewise, in Korea, KP was the second most commonly isolated organism (17.3%) after *Escherichia coli* (40.4%) based on a 10-year retrospective study amongst fifty two (52) patients with prostatic abscess.[4] However, in the Western set-up, *Staphylococcus aureus* was noted to be the most common causative organism (56%), followed by *Klebsiella pneumoniae* (13%) and *Escherichia coli* (9%).[7] Untreated prostatic abscess can lead to severe urosepsis and septic shock and has been reported to cause metastatic endophthalmitis, septic arthritis and osteomyelitis.

While *Klebsiella pneumoniae* (KP) primarily affects those who are immunocompromised, the Malaysian populace, who generally have a high prevalence of diabetes, is at an alarming risk of acquiring such a disease and complications. As KP infection frequently presents with slow progression of fever and other non-specific clinical symptoms, the patient often presents late with disseminated infection involving multiple organs requiring surgical intervention, prolonged hospital stay and antibiotics treatment. Clinicians should thus be made aware of the nature of KP infection in order to identify the disease in its early phase for timely antibiotic treatment and prevention of disease-related complications mentioned above.

In the case report presented below, we detailed how our findings of an unusually enlarged and non-tender prostate in a diabetic patient with unexplained fever through clinical examination led to successful identification of disseminated KP infection involving the liver, bilateral kidneys and the prostate.

CASE PRESENTATION

A gentleman in his 50s with a background history of insulin-dependent type 2 diabetes mellitus and dyslipidaemia was readmitted from our specialist clinic for unresolved fever and new onset of dysuria. On admission, his fever had already

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Table I: Blood test results showed raised total white counts predominantly neutrophils suggestive of an on-going infection, further substantiated by an increment in C-reactive protein (an important infective marker). The unusual presentation of urinary leukocytes narrowed down urinary tract as the most possible site of infection.

Parameters	Result	Units	Reference Range
Full blood count			
Total White Count	21.2	10^9/L	4.0–11.0
Haemoglobin	11.6	g/dL	13.0–18.0
Platelet count	306	10^9/L	150–400
Haematocrit	32.3	%	40–52
MCV	83.9	FL	76.0–96.0
MCH	30.1	PG	27.0–32.0
Neutrophils	17.79	10^9/L	
Neutrophils %	83.8	%	40–75
Lymphocytes	1.69	10^9/L	
Lymphocytes %	8.00	%	20–45
Eosinophils	0.04	10^9/L	
Eosinophils %	0.20	%	1–6
Basophils	0.04	10^9/L	
Basophils %	0.20	%	0–1
Renal profiles			
Urea	3.2	mmol/L	1.7–8.3
Sodium	118	mmol/L	135–145
Potassium	4.2	mmol/L	3.5–5.5
Chloride	88	mmol/L	98–107
Creatinine	72	umol/L	62–106
eGFR	>90	ml/min/1.73m^2	
Liver function test			
Total protein	70	g/L	64–83
Albumin	22	g/L	35–50
Globulin	48	g/L	20–39
Alkaline Phosphatase	148	u/L	40–150
Aspartate Aminotransferase (AST)	36	u/L	5–34
Alanine Transaminase (ALT)	10.7	u/L	<56
Total bilirubin	8.4	umol/L	5.1–20.5
Full and microscopic examination of urine (Urine FEME)			
Glucose	3+		Negative
Ketone	Negative		Negative
Nitrite	Negative		Negative
Leukocytes	3+		Negative
Blood	Trace		Negative
Bilirubin	Negative		Negative
Protein	1+		Negative
Urobilinogen	Normal		Negative
Colour	Amber		
Clarity	Turbid		
PH	6.0		5–8
Specific gravity	1.009		1.003-1.030
Infective marker			
C- reactive protein	88	mg/L	<5.0
Other infective workup			
Leptospirosis IgM	Negative		
Dengue serology	Negative		
Blood film for malaria parasite	Negative		

lasted 1 month with significant loss of weight and appetite. He experienced dysuria for 2 weeks but had denied other urinary symptoms, including urinary frequency/urgency, poor stream or incomplete bladder emptying. He denied having prolonged cough, gastrointestinal losses, abdominal/perineal pain, sexual promiscuity or contacts with other sick persons. He works as a security guard and had also denied contact with rodents, sewage or contaminated soil. He is a married man with one child.

Two weeks earlier, this gentleman was admitted to the general medical ward for unexplained fever which lasted for 1 week. He was treated empirically for occult sepsis with IV Ceftriaxone 2g OD (Duopharma®) for 5 days. None of his blood and urine cultures demonstrated positive growth. He was discharged 5 days later and was given a date to follow-up in our specialist clinic.

On admission, his vitals were stable. Lungs and cardiovascular examinations were non-remarkable. The abdomen was soft and non-tender. His liver and spleen were not palpable. Prostate examination revealed a painless enlarged prostate measuring 4 finger-breadth, boggy with complete obliteration of the median sulcus.

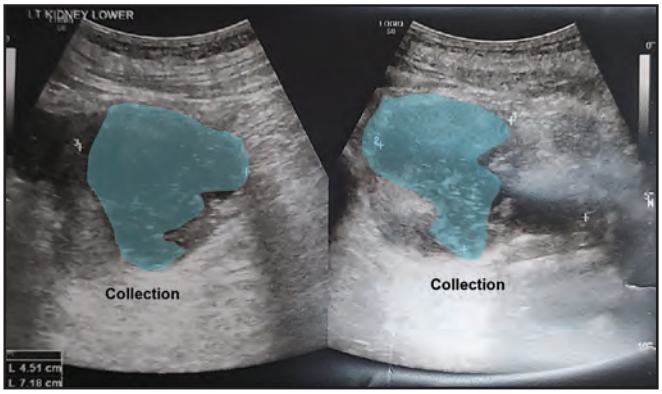

Fig. 1: Left kidney lower pole demonstrating heterogenous collection (Highlighted in Blue)

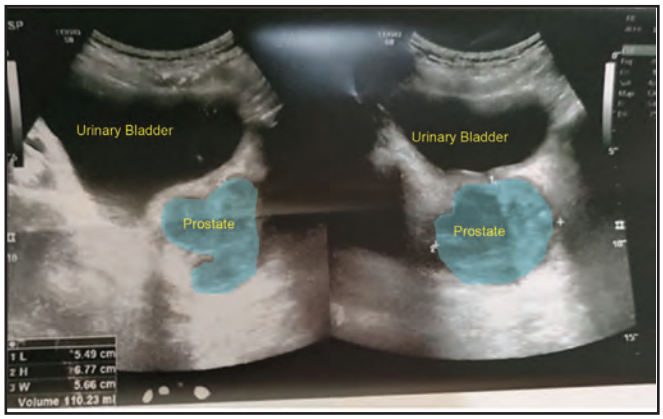

Fig. 2: An enlarged lobulated prostate (Highlighted in Blue)

His blood test results detailed in Table I showed raised total white counts, predominantly neutrophils suggestive of an active infection. Other important findings were the presence of leucocytes in his urine and a significantly raised C-reactive protein. Chest X-ray was grossly normal. Echocardiogram demonstrated no vegetation with a normal ejection fraction.

USG abdomen and prostate scans reported hypoechoic lesion in segment VI of the liver measuring 2.4cm x 1.8cm x 2.2cm, a small hypoechoic lesion with septation in the right upper pole kidney measuring 1.1cm x 1.4cm and heterogenous collection left lower pole kidney measuring 4.9cm x 5.7cm x 5.9 cm (Figure 1). The prostate was enlarged and lobulated, measuring 5.5cm x 6.8cm x 5.7cm (Volume 110cc) (Figure 2) Overall impression was consistent with focal abscesses involving the left kidney lower pole, right kidney upper pole and liver. (Note: Echogenicity of the prostate was inconclusive to be commented as an abscess)

Preliminary diagnosis of melioidosis was made in view of high prevalence of melioidosis in the country, and patient was started on IV Ceftazidime 2g TDS (Duopharma®) pending confirmation of organism from blood and urine culture. Urology opinion was sought, and an agreement was made to reassess the intraabdominal collection and prostate 2 weeks post antibiotics.

Five days after the commencement of IV Ceftazidime 2g TDS (Duopharma®), the patient developed a spiking fever up to 39^0C. We escalated antibiotics to IV Meropenem 1g TDS (Fresenius Kabi®). Following a joint discussion with urology and radiology teams, a decision for USG guided drainage of the left lower pole kidney abscess was made in order to achieve proper source control and to identify the organism for antibiotics selection. Approximately 50ml of purulent collection was drained and sent for culture and gram stain. Collection at segment VI of the liver and the right lower pole kidney was deemed too small for drainage.

Aspirate culture grew mucoid lactose fermenter colonies on MacConkey agar, which was later confirmed by our microbiologist to be *Klebsiella pneumoniae*. Kirby-Bauer testing confirmed sensitivity to Amoxicillin/Clavulanate, cefuroxime and Ampicillin/Sulbactam. The other blood and urine cultures were concluded as no growth.

Final diagnosis was concluded as disseminated *Klebsiella pneumoniae* infection confirmed radiologically and microbiological testing. Infectious disease team opinion was sought. Antibiotics were deescalated to IV Amoxicillin/Clavulanate 1.2g TDS (Mylan®)

Following the identification of Klebsiella pneumoniae, slit lamp assessment was carried out by our ophthalmology team to rule out endophthalmitis. It was confirmed that our patient did not have the condition.

USG abdomen, after 20 days of antibiotics, reported hypoechoic lesion in segment VI of the liver measuring 2.6cm x 1.5cm x 2.1cm, small hypoechoic lesion with septation in upper pole right kidney measuring 1.1cm x 1.8cm, and heterogenous hypoechoic collection lower pole left kidney measuring 3.3 cm x 3.7cm x 4.3cm. Prostate size 2.8cm x 3.6cm x 2.8cm (Volume 15ml). There was no splenic lesion. In all, repeated scan showed unchanged focal abscesses of the right kidney and liver; residual focal abscess of the left kidney and complete resolution of the prostate lesion.

Our patient was allowed to be discharged with another three more weeks of oral Amoxicillin/Clavulanate 625mg TDS (Pharmaniaga ®). Followed-up USG abdomen 1 month after completion of antibiotics showed residual multiple sub-centimeter hypoechoic nodules scattered throughout the liver measuring 0.5cm each (Differential diagnoses include liver micro abscesses or liver cirrhosis with nodular appearance). Previously seen hypoechoic lesion at segment VI of the liver and bilateral kidneys were no longer apparent in this study. At the point of writing this case report, our patient remains well and is still under-going follow-up in our specialist clinic.

DISCUSSION

Untreated *Klebsiella pneumoniae* (KP) prostatic infection risks dissemination to distant organs, causing abscesses. The initial signs and symptoms of KP prostatitis and prostatic abscess are usually non-specific and misleading and thus

have resulted in delayed identification of the disease and administration of treatment. To complicate the matter further, diabetic polyneuropathy involving the genital nerves may even mask the symptoms of prostatic abscess or prostatitis at its early phase of the disease. Routine practices initiating broad-spectrum antibiotics for patients with occult sepsis have also lowered bacterial density, resulting in poor yield and negative cultures. It is uncertain whether our patient was prescribed antibiotics prior to culture sampling during the first admission, which had led to a falsely negative blood and urinary culture results.

Contrary to popular belief that KP grows readily in routine culture bottles and agar media, an observational study led by Ter et al. also reported significant false negative results after 5 days of incubation. Amongst the 195 day-5 negative blood culture samples tested, 8 of them were positive for *Klebsiella Pneumoniae* using PCR technique. It is postulated that organism death, inappropriate sampling technique and long storage time in culture bottle prior to sampling invariably led to false negative results. In our healthcare setting where PCR testing remains largely limited to tertiary hospitals, the timely identification of KP may be hampered by this factor.[8]

It is important to take note that several published case reports on *Klebsiella pneumoniae* related prostatic abscess were largely incidental findings by imaging, leading to clinical suspicion and successful diagnosis of the disease.[9] Such sophisticated imaging modalities may not be available in resource-stricken countries; thus, clinical assessment and high clinical suspicion serve as the only way to hasten referral to appropriate tertiary healthcare centres. In our patient, the finding of an enlarged prostate was not identified during his first admission. It should be an invaluable learning point to all clinicians to consider a prostate examination in patients with prolonged fever to exclude a potential pathology of the prostate.

If an enlarged prostate is identified, USG and/or CT abdomen should be utilised to visualise the presence of prostatic abscess and to identify other location of intraabdominal abscesses. Serial imaging should be done to track evolution into prostatic abscess so that urological intervention can be undertaken earlier. As the Latin medical term "Ubi pus, ibi evacua" which translates directly to "where [there is] pus, evacuate [it]". All prostatic abscesses should be considered for drainage where feasible for proper source control.

Another important point in the context of tropical diseases in Southeast-Asia (SEA), symptomatology and complications for both *Burkholderia pseudomallei* and *Klebsiella pneumoniae* are surprisingly similar. They affect primarily the immunocompromised patients particularly diabetics, and result in disseminated abscess formations. In 2009, Ng et al. reported 5 cases of prostatic abscesses caused by *Burkholderia pseudomallei* in Pahang, Malaysia, among which four of five patients were asymptomatic, and 60% of them were noted to have an enlarged and non-tender prostate during examinations.[6] Gold standard for diagnosis of *Burkholderia pseudomallei* remains routine blood culture. Serologic testing is not reliable.

In conclusion, the authors recommend that for all male patients with unknown sources of fever, a prostate examination should be considered in the clinical process after thorough exclusion of other common sites of infection. An enlarged prostate which is tender or boggy especially in younger males should raise suspicion of an early infection caused by *Escherichia coli, Burkholderia pseudomallei* or *Klebsiella pneumoniae*.

CONFLICT OF INTEREST

None.

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