

Persistent sterile pyuria in children? Don't forget tuberculosis!

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ABSTRACT

Genitourinary tuberculosis (GUTB) is exceptionally uncommon among the local paediatric population. A 10-year-old Chinese girl with no risk factors for tuberculosis presented with recurrent sterile pyuria. Despite extensive renal investigations, no apparent cause could be ascertained for her obstructed left drainage system. The diagnosis was eventually confirmed with urine acid-fast bacilli culture, after a computed tomography scan suggested possible renal tuberculosis. A left nephroureterectomy had to be performed owing to deteriorating left kidney function. This report discusses the importance of considering tuberculosis when assessing a local paediatric patient with an atypical urinary tract infection. Early diagnosis of renal tuberculosis can prevent the sequelae of GUTB, including renal impairment.

Keywords: genitourinary tuberculosis, nephroureterectomy, sterile pyuria, tuberculosis pyelonephritis, urinary tract infection

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INTRODUCTION

Genitourinary tuberculosis (GUTB) is a relatively uncommon and under-recognised disease in Singapore. It occurs more commonly in the fourth decade of life. Both genders are equally affected and present with haematuria and pyuria.⁽¹⁾ Identifying the disease early in a low-risk paediatric patient requires alertness on the part of the clinician. Many local tuberculosis patients have a background of immunodeficiency disorders such as human immunodeficiency virus (HIV). However, it is possible for immunocompetent patients to be infected by tuberculosis. This case report highlights the importance of considering a diagnosis of tuberculosis in a young adolescent girl who presented with recurrent sterile pyuria.

CASE REPORT

A ten-year-old Chinese girl was referred to the paediatric surgery clinic with recurrent urinary tract infection

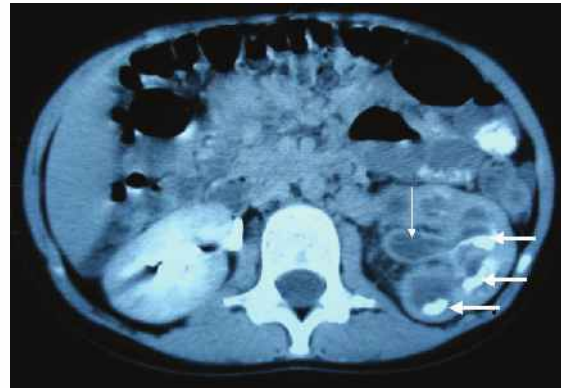


Fig. 1 CT image shows a normal excretion of contrast in the right pelvicalyceal system and a thickening (thin arrow) of the uroepithelial lining of the renal pelvis. Pooling of contrast (thick arrows) was noted in the dilated calyces in this delayed phase.

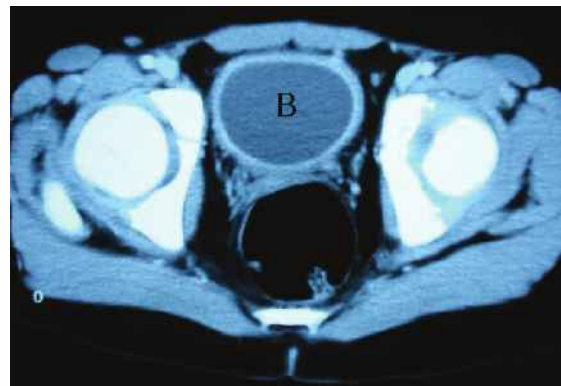


Fig. 2 CT image shows the urinary bladder (B) with a thickened and enhanced wall.

(UTI) of recent onset. She was otherwise healthy, with good height and weight development. She was born and brought up in Singapore, and had no recent travel history. Bacillus Calmette-Guerin (BCG) had been administered at the time of birth, and there was no contact history or systemic symptoms of tuberculosis. The patient's clinical examination was unremarkable with normal blood pressure. The serial urine microscopy showed more than 200 leucocytes/ul and more than 300 red blood cells/ul. No cast or crystal was detected. Four urine cultures were collected over a period of four weeks, but they failed to grow any pathogen. The patient's urinary pH was consistently acidic, as observed on follow-up. Serum investigation indicated a slightly elevated creatinine

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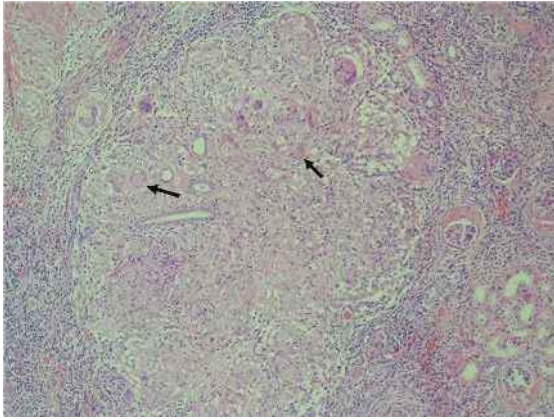


Fig. 3 Photomicrograph of the kidney specimen shows granuloma with Langerhans multinucleated giant cells (arrows) (Haematoxylin & eosin, $\times 200$).

level of 81 $\mu\text{mol/L}$ (normal range 27–80 $\mu\text{mol/L}$). Renal ultrasonography showed left hydronephrosis and hydroureter with a mildly thickened left ureter and bladder wall. Debris was observed in the bladder and left collecting system. Micturating cystourogram showed a normal bladder with no vesicoureteric reflux. Bladder volume was normal on urodynamic study. Mercapto Acetyl Tri-Glycine functional scan suggested impaired excretion by the left kidney. The left renal system was dilated with an incomplete obstruction.

Despite empirical antibiotic treatment with a therapeutic dosage of cephalexin and co-trimoxazole over a one-month duration, the patient had further episodes of UTI with sterile pyuria. A repeat renal ultrasonography six months later showed no improvement in the hydroureteronephrosis. In view of the presumed diagnosis of left partial vesicoureteric junction obstruction, a ureteric stent was placed in the left ureter cystoscopically. The bladder mucosa showed evidence of chronic inflammation. Computed tomography (CT) revealed abnormalities mainly in the renal system. There was a dilated left renal system with proximal left ureteric dilatation (Fig. 1 & 2). The renal pelvic uroepithelium was thickened and showed contrast enhancement. No calcifications or abscesses were observed. Although the right kidney was not dilated, focal pyelonephritis was noted. Radiological opinion suggested the possibility of renal tuberculosis. A left nephrostomy was performed for drainage. Although the urine acid-fast bacilli (AFB) smear was negative, the urine AFB culture grew *Mycobacterium tuberculosis*. Mantoux test showed a mildly positive reaction with a 15-mm induration. The patient's chest radiograph showed no lesion in the lungs. She was administered anti-tuberculosis therapy (ATT) (isoniazid, rifampicin and pyrazinamide). Dimercaptosuccinic acid (DMSA) renal scan revealed a

complete loss of left kidney function during this period. A repeat nephrostogram revealed multiple strictures over the left renal pelvis. The patient underwent left nephroureterectomy. The histology showed tuberculous pyelonephritis with multiple tuberculous granulomas (Fig. 3). Acid-fast bacilli were identified. The anti-tuberculosis medication was continued for one year.

The follow-up renal ultrasonography showed a right pelvicalyceal dilatation which had developed recently. The right ureter was also noted to be distended until the level of the vesicoureteric junction. A ureteric stent was placed into the tortuous and distended right ureter. A repeat renal ultrasonography one month later showed an improvement of the right pelvictasis. The patient was started on enalapril for proteinuria (secondary to hyperfiltration). Currently, she is being closely monitored and followed up.

DISCUSSION

Although Singapore is still an endemic area of tuberculosis, a decreasing trend in local incidence has been observed. While tuberculosis is not a common disease in the developed world, several local reports have highlighted the need for creating an awareness of this disease.⁽¹⁻³⁾

GUTB is the second most common extrapulmonary manifestation of tuberculosis after cervical lymphadenopathy.⁽⁴⁾ It is difficult to diagnose, as the presentation mimics bacterial cystitis with low-grade urological symptoms. The challenge becomes even greater in children, as it has not been reported in the local paediatric community. To the best of the authors' knowledge, only one case of a 14-year-old boy diagnosed with tuberculosis epididymitis had previously been reported.⁽¹⁾ Undiagnosed GUTB may mimic pyelonephritis, renal stones, or manifest with renal failure. Suspicion of GUTB must be considered if the patient has symptoms of recurrent UTI or haematuria associated with sterile pyuria.⁽⁵⁾ Hydroureteronephrosis, which develops newly in a grown up child with sterile pyuria, is also suggestive of GUTB. The diagnosis requires a strong clinical suspicion and can be confirmed with urinary culture for AFB and a histopathology of tissue biopsy. It is recommended that at least three first-morning void urine samples be collected for the AFB smear and culture when investigating for GUTB.⁽⁶⁾ Advanced laboratory techniques, such as polymerase chain reaction, have facilitated an early diagnosis. Among the imaging studies, a CT scan is able to provide most of the necessary information in abdominal tuberculosis.⁽²⁾ Although calcifications are

typical of renal tuberculosis, their absence does not preclude the diagnosis. As illustrated by this case, pelvicalyceal dilatation and generalised thickening of the uroepithelium demonstrated on CT scan, indicated a chronic inflammatory process. Although calcification and abscess were not seen, such features, together with the absence of a positive bacterial culture of the usual pathogen and urinary calculi, raise suspicion of tuberculosis. Renal tuberculosis usually results from haematogeneous spread of the disease in the lungs.^(4,5) Nevertheless, as demonstrated in this case, the primary lesion might have healed when GUTB presented. Concurrent *Escherichia coli* urine infection has been reported and could mislead the clinician.⁽⁴⁾

GUTB can lead to the loss of kidney function, infertility and other long-term complications. Foo et al reported in their study that 50% of the affected kidneys were non-functioning at the time of diagnosis.⁽¹⁾ Renal parenchymal infection and obstructive uropathy are believed to be the causative mechanisms. The obstruction is a result of inflammatory changes, and fibrosis can be total or segmental.⁽⁴⁾ Renal papillary and calyceal ulceration with calyceal stenosis are characteristics of renal tuberculosis. A tuberculous bladder can become contracted with an irregular shape. Cystoscopy may reveal erythematous bladder mucosa with bullous oedema.⁽⁴⁾ In addition to ATT, invasive procedures such as percutaneous nephrostomy, ureteric stenting and partial or total nephrectomy may be indicated in GUTB, as in this case. In more severe cases, reconstructive surgery of the upper and lower urinary tract may be required.

In conclusion, GUTB is a disease with preventable complications if timely diagnosis and treatment is established. In order to avoid outcomes such as renal failure, clinicians need to be aware of the signs and symptoms of GUTB when treating children with urinary problems. In Singapore, tuberculosis has become a resurgent public health problem due to the rising incidence of HIV, multidrug-resistant tuberculosis and the influx of immigrants.⁽²⁾ A diagnosis of GUTB should always be considered in a child presenting with symptomatic UTI and sterile pyuria.

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