CASE REPORT

Tuberculosis epididymitis complicated by a cutaneous fistula

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SUMMARY

A 63-year-old man developed scrotal swelling that became bilateral over 2 months. His symptoms persisted after treatment for epididymitis, and he developed a scrotal fistula with drainage. *Mycobacterium tuberculosis* grew from the urine and fistula. His symptoms resolved and fistula closed with medical therapy. His case highlights the importance of early recognition, diagnosis and treatment of this form of extrapulmonary tuberculosis.

BACKGROUND

Mycobacterium tuberculosis causes both pulmonary and extrapulmonary disease in humans. Genitourinary disease is a form of extrapulmonary tuberculosis (TB) and may include or be limited to infection of the epididymis. Symptoms of infection may include persistent swelling of the epididymis, sometimes resulting in a scrotal fistula. We present a case of a man from a TB endemic country who developed epididymal TB complicated by a fistula. We hope to increase awareness and recognition of this syndrome.

CASE PRESENTATION

A 63-year-old man developed scrotal swelling in December 2014. It was originally left sided, but became bilateral after 2 months. He was treated as an outpatient for presumed epididymitis and prostatitis with ciprofloxacin, but worsened. He was admitted to the hospital in early March 2015, where he partially improved on 5 days of ceftriaxone and doxycycline. Urinalysis on admission showed pyuria, and urine culture was negative. He did not have proteinuria or haematuria. He received an additional week of amoxicillin-clavulanate and doxycycline at discharge.

After hospital discharge, he continued to have scrotal swelling with epididymitis. He then developed a fistula which resulted in a cutaneous scrotal ulcer with drainage (figure 1). The ulcer expanded to a diameter of 1 cm.

He did not have fever, chills, sweats, cough, weight loss or other systemic symptoms.

He was from the Philippines and received BCG vaccine as a child. He had moved to the USA over 20 years before presentation. He had been on a visit to the Philippines in December 2014 when his scrotal swelling started.

He had a positive Mantoux tuberculin skin test (purified protein derivative or PPD) in 1996. He was never treated for latent or active TB.

His medical history was otherwise remarkable for hepatitis B. Liver function tests were normal, and he had no history of cirrhosis or hepatocellular carcinoma.

By late April 2014, his examination showed bilateral scrotal masses with epididymal swelling. There was a draining ulcer on his right scrotum. The remainder of his examination was unremarkable.

INVESTIGATIONS

Urine mycobacterial culture sent during the March hospitalisation grew *M. tuberculosis*. Subsequent sensitivity testing revealed no resistance to first-line drugs. No molecular markers of quinolone resistance were noted, though culture-based quinolone susceptibility testing was not performed.

Mycobacterial culture from the draining wound also grew *M. tuberculosis*.

Chest imaging showed no pulmonary infiltrates. Mycobacteria cultures from three induced sputums were negative.

Scrotal ultrasound (figure 2) showed marked enlargement of the left epididymis, with lesser enlargement of the right epididymis. A new

Figure 1 Scrotal fistula at time of diagnosis with drainage.

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Figure 2 Scrotal ultrasound showing an enlarged, swollen, heterogeneous and hyperaemic left epididymis (the epididymis is the area between the two '+' marks).

complex hydrocele developed on repeat ultrasound in early March (compared with a week previous) while on ceftriaxone and doxycycline.

DIFFERENTIAL DIAGNOSIS

Enteric Gram-negative bacteria are the most common cause of epididymitis in men over age 35. *Neisseria gonorrhoeae* and *Chlamydia trachomatis* are most common in younger men,¹ but can occur at any age with exposure. Other pathogens associated with cases of epididymitis include *Mycoplasma* sp, adenoviruses, enteroviruses and mumps.² He did not have risk factors for Brucellosis, though this pathogen can cause epididymitis. Chronic cases of epididymitis may be caused by a variety of agents including mycobacteria, fungi and the agents of filariasis, as well as non-infectious entities including vasculitis, Behçets and sarcoidosis.³ While his scrotal ulcer was the result of a fistula from epididymitis, scrotal ulcers in isolation may be caused by *Treponema pallidum* and other sexually transmitted pathogens, as well as non-sexually transmitted pathogens including Gram-negative bacteria.⁴ All of these were considered in his differential diagnosis.

TREATMENT

He was treated with four drug *M. tuberculosis* therapy (isoniazid, rifampin, pyrazinamide and ethambutol). Ethambutol was stopped after sensitivities returned. Pyrazinamide was stopped after 8 weeks per protocol. His planned therapy of 6 months was extended to 9 months since the ulcer had just closed (figure 3) by the 6-month mark (and after informed patient discussion of the uncertain necessity for the additional 3 months).

OUTCOME AND FOLLOW-UP

He remains without recurrence of scrotal swelling or fistula more than a year after completing treatment.

Figure 3 Scrotal fistula after 5+ months of therapy.

DISCUSSION

TB infects one-third of the world's population,⁵ causing over 10 million cases of active TB and 1.4 million deaths annually.⁶ Incidence in the USA decreased to 2.9/100 000 persons/year in 2016, though some areas and populations had significantly high incidence rates. Sixty-seven per cent of US TB cases were in foreign-born individuals, and 90% of these foreign-born cases are due to reactivation of latent infection.⁷ While pulmonary TB is the most common manifestation of disease, extrapulmonary disease can affect other organs.

Genitourinary TB, or urogenital TB,⁸ includes TB of the kidney, ureter, bladder, epididymis, prostate and testis. Most cases of genital TB also involve the kidney.⁹ Presenting symptoms may include urinary frequency, haematuria, dysuria, scrotal swelling, perineal discomfort and fever.^{9 10} Renal function is normal in most patients,¹¹ though obstruction can lead to renal insufficiency. Cases may be complicated by ureteral stricture.¹¹ A significant minority (38%) patients have pulmonary as well as extrapulmonary disease.¹¹

TB of the epididymis represents a subset of genitourinary TB.⁹ Many cases are associated with renal TB, but isolated epididymal infections are seen.¹² Patients with epididymitis may not have other urinary symptoms.¹³ Clinical symptoms include a thickened epididymis with swelling. Symptoms may be unilateral or bilateral, and may mimic acute bacterial epididymitis.¹³ A cutaneous scrotal fistula forms in some patients.⁸

Cutaneous fistulas may complicate TB of other organ systems. The presence of a draining scrotal sinus and chronic epididymitis is highly suggestive of genitourinary TB in endemic regions.^{10 13 14}

Diagnosis of genitourinary TB is challenging.¹⁰ Serial urine mycobacterial cultures will eventually yield a positive culture in around 80% of diagnosed patients.¹¹ PCR testing has higher yield.¹⁵ The presence on ultrasound of heterogeneous enlargement of the tail of the epididymis and heterogeneous echo

texture suggests TB.¹⁶ For patients who undergo biopsies for renal masses, the finding of a caseating granuloma on biopsy is suggestive of TB.¹¹ Chest imaging may show evidence of prior TB, or active TB.⁹ Coinfections with Enterobacteriaceae may complicate diagnosis.¹⁷ The delay in diagnosis in the case patient was partially due to lack of awareness of genitourinary TB by the treating clinicians at various points in his work-up. His worsening before the hospital was commented as being more consistent with a pyogenic infection than TB in the medical record. Fortunately, those clinicians still sent the mycobacterial urine culture that led to the diagnosis. This highlights the importance of investigating at-risk patients for genitourinary TB.

Six-month therapy is recommended by genitourinary TB,¹⁸ though individual patients are sometimes treated for longer periods.^{19 20} In contrast to pulmonary TB, where a cavitary disease or a positive sputum culture at 2 months are markers of relapse risk if longer therapy is not used,¹⁸ markers for relapse in genitourinary TB are less well defined. High relapse risks (19%) were reported when using a regimen of isoniazid, rifampin and ethambutol (no pyrazinamide) for 12 months.¹⁷ The authors of that study suggested that host factors, including poor nutritional status, may have contributed to high relapse rates. Surgery is needed for some patients,^{10 20} including scrotal fistulae.⁸ Our case patient responded well to medical therapy, including healing of his fistula.

Most cases of genitourinary TB represent reactivation of infection acquired decades earlier.¹¹ Identification and treatment of latent TB in high-risk populations is a public health priority.⁷ The case patient had positive PPD 20 years before this presentation. Treatment of latent TB would have likely prevented this episode. His prior BCG may have influenced his treating physicians against treatment at the time, though the subsequently available interferon gamma release assays are not affected by prior BCG.

TB should always be kept in the differential diagnosis of unexplained symptoms in patients from endemic countries. While reactivation risk is increased with conditions which suppress the immune

system,⁷ reactivation may occur in any infected patient. Epididymal TB should be considered in at-risk patients with swelling of the epididymis with or without the presence of fistula. In our case patient, medical therapy alone led to a successful outcome.

Contributors SAW and QRY were involved in the patient's care. Both authors have created and approved the manuscript.

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Learning points

- Epididymitis in at-risk patients should prompt consideration of tuberculosis.
- Lack of consideration of tuberculosis in the differential diagnosis of chronic epididymitis leads to treatment delays and increased complications such as scrotal fistulas.
- Several urine cultures for mycobacterial culture should be performed as part of diagnostic work-up.
- Medical treatment alone may be successful in tuberculosis of the epididymis complicated by fistula, though fistula resolution may take months.

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