Case - Penile mycobacterium avium complex infection

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INTRODUCTION

Nontuberculous mycobacteria (NTM), including those in the Mycobacterium avium complex (MAC), are a common environmental microorganism that can be found in soil, water sources, household plumbing and various moist environments, including the oral cavity[1]. MAC are increasingly recognized as opportunistic pathogens[2]. Although MAC are associated with pulmonary disease, and disseminated infection in immunocompromised patients, the incidence of isolated extrapulmonary manifestations is rising[3]. We present a rare case of penile infection caused by MAC to contribute to the understanding of its clinical presentation and management. Because penile involvement is exceptionally uncommon, we performed a literature review to contextualize this case and to illustrate the broader spectrum of genitourinary NTM infections. In doing so, we highlight the diagnostic challenges that such unusual presentations pose and offer insights to help clinicians recognize and treat similar rare infections.

KEY MESSAGES

- Mycobacterium avium complex (MAC) is a nontuberculous mycobacterium typically associated with pulmonary disease or disseminated infection in the immunocompromised. Isolated genitourinary involvement is rare.
- We report a unique case of penile MAC infection in a 59-year-old man with a history of urethral reconstruction. The patient developed progressive penile lesions, ultimately confirmed as MAC. He was treated with prolonged multidrug therapy achieving clinical improvement.
- Given the rarity of penile involvement, we review the literature to highlight diagnostic challenges, therapeutic considerations, and the need for awareness of atypical penile MAC infection.

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CASE REPORT

A 59-year-old male with a history of suspected iatrogenic urethral injury during catheter placement at the age of 10 and Peyronie's disease presented with worsening voiding urinary tract symptoms. The patient was diagnosed with significant stricture disease from the mid penile to the distal bulbar urethra measuring 4 cm in length, and 12-French in diameter. Subsequently, the patient underwent one-stage dorsal onlay anterior urethral reconstruction with bilateral buccal mucosa grafting.

Eight months after the urethral reconstruction, the patient developed distal penile pain and an erythematous plaque on the dorsum of his penis. Biopsy of the lesion showed features of lichen planus and he received treatment with betamethasone dipropionate. The patient did not report improvement of his symptoms after steroid cream. Six months later, meatal stenosis and hardness within his corporal bodies and the glans were found on the patient's physical exam. MRI of the penis showed lesions in the glans extending to the urethra (Figure 1A). Excisional biopsy and 4 core needle biopsies of the glans lesion showed a suppurative granulomatous process with excessive epithelial reactions. The urology team referred the patient to the infectious diseases and dermatology services. Stains and culture for bacteria, fungi, and acid-fast bacilli (AFB) were negative. Initially, the patient received treatment for pyogenic superinfection with ciprofloxacin for 2 weeks, and then, amoxicillin-clavulanate for 2 weeks to cover for the remote possibility of Actinomycosis.

No improvement was seen, and further studies were performed. Blastomyces and Histoplasma serology, urine Histoplasma Ag and urine Blastomyces Ag were negative. C-reactive protein, anti-neutrophil cytoplasmic antibody, HIV and syphilis serology were negative. The patient's urine culture for AFB showed ⅓ positive for MAC. Repeated MRI, three months after initial MRI, showed a 3.2 x 2.2 cm enlarging heterogenous T2 signal-enhancing lesion almost replacing the penile glans (Figure 1B). The lesion involved the most distal portion of both cavernosa. Additionally, along the ventral aspect of the spongiosum, there was a new 0.8 cm enhancing soft tissue nodule. The lesion progressed leading to splitting of the glans (Figure 2A). Therefore, the patient underwent a repeat biopsy which showed necrotizing granulomatous inflammation. GMS and AFB stains were negative as was PCR for both M. tuberculosis complex and MAC. Urine AFB culture showed 4/4 positive results for MAC and the isolate was sent for antimicrobial susceptibility testing to the National Microbiology Lab of Canada by broth microdilution Minimum Inhibitory Concentration MIC panel (ug/mL): Amikacin 256, Ciprofloxacin 4, Clarithomycin 4, Clofazamine 0.25, Doxycycline >8, Linezolid 32, Miinocycline >8, Rifabutin 0.5, Rifampin >4, Streptomycin >32, Trimethoprim-slfamethoxazole 4/76. With negative fungal cultures and without an alternative diagnosis, in the context of a recent reconstruction procedure, the patient was therefore treated empirically for penile MAC and started on rifabutin (due to drug interactions with rifampin), azithromycin and ethambutol.

After the patient was started on the therapy, urine cultures for AFB repeated at 3 and 5 months continued to be positive for MAC. He also had bronchoalveolar lavage (BAL) for an

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asymptomatic 8 mm pulmonary nodule found on chest CT that was culture positive for MAC. He continued to have distal penile pain and urethral discharge. During this time he had a supra-pubic tube (SPT) for urinary drainage. Moxifloxacin was added to his therapy. Repeated MRIs showed a progressive decrease in the size of the lesion without fistulous tracts. Physical exam continued to slowly improve at 6 and 16 months as demonstrated in Figure 2B and 2C. The patient received a total of 20 months of antibiotic therapy. Afterwards, the patient was found to have meatal stenosis and underwent a distal first-stage anterior urethroplasty up to the fossa navicularis, and his SPT was removed. After this procedure and to date, the patient remains asymptomatic and voiding without difficulty. His MAC cultures continue to be negative now 25 months out.

DISCUSSION

Penile lesions may result from a wide variety of etiologies, including inflammatory, infectious, trauma, or malignancy, making them a significant diagnostic challenge. Given this broad differential, careful clinical assessment supported by histopathological and microbiological testing is essential to establish an accurate diagnosis and to guide treatment. This is particularly important in infections caused by rare pathogens, such as nontuberculous mycobacteria, which can mimic more prevalent conditions. Infectious causes of penile lesions often include sexually transmitted infections, such as syphilis, herpes simplex virus, and human papillomavirus. Other common culprits are bacterial infections such as cellulitis or folliculitis, and fungal infections like candidiasis. Failure to correctly identify the etiology can lead to misdiagnosis, which can result in ineffective treatment, increased morbidity, or disease progression and dissemination[4]. Penile infections caused by MAC are rare and may present with nonspecific symptoms, including chronic inflammation, nodules, ulcerations, or abscess formation. These clinical manifestations can easily be mistaken for other infectious or neoplastic conditions. Because of this diagnostic overlap, a high degree of clinical suspicion and advanced diagnostic methods are often necessary to distinguish MAC from more common causes[5]. The exact incidence of MAC disease remains uncertain but is rarely described, and its pathway of dissemination is not yet fully understood. In this case, is possible that the patient was colonized with MAC, as is commonly found in the human oral cavity[1], and that the infection may have been introduced to the genital region during placement of the buccal graft at the time of urethroplasty. Table 1 describes the different reports published to date on the different presentations of penile MAC infection. Other reported genitourinary presentations include asymptomatic sterile pyuria[6], hematuria[7], granulomatous prostatitis[7,8], or symptoms of urinary infection and sepsis[9].

Table 1. Publications of penile MAC infection

The diagnosis can involve a combination of culture, molecular testing, and histopathological examination to confirm the microorganism and exclude other granulomatous diseases or malignancies. Confirmation of MAC infection in genitourinary specimens usually requires acid-fast bacillus staining, urine culture on specialized mycobacterial media, and molecular methods such as polymerase chain reaction or gene sequencing to achieve definitive identification[6,13]. An important caveat is that the clinical significance of MAC isolation from

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urine must be interpreted with caution, as it is most often due to contamination from environmental sources rather than true urinary tract infection, especially in nonsterile specimens such as midstream urine samples. Molecular characterization has shown that environmental strains of MAC can be found in hospital water systems and may contaminate urine samples, leading to false-positive results for infection[14]. Distinguishing between colonization, contamination, and true infection requires correlation with clinical findings and, ideally, molecular typing to differentiate environmental from pathogenic strains. Urine cultures for atypical organisms, including nontuberculous mycobacteria, should be performed only when there is a strong clinical suspicion, such as in this case where there was pathological findings of granulomatous disease.

Managing penile MAC infections is often challenging. To our knowledge, a specific protocol for its management has not been established. There was a wide variety of treatments used in the reported cases (Table 1). Medical treatment requires prolonged multidrug therapy tailored to the antimicrobial susceptibility results based on our experience. In some cases, particularly with localized disease or abscess formation, surgical intervention may be necessary. Standard regimens generally include at least three drugs (including ethambutol and a macrolide)[15]. However, treatment outcomes can be variable, highlighting the importance of individualized management based on the microorganism's susceptibility to medical treatment[16]. The emergence of drug resistance and patient intolerance to standard regimens further complicate care, underscoring the need for novel treatment options and personalized approaches[17].

CONCLUSIONS

This review highlights the diagnostic difficulties and treatment challenges posed by penile MAC infections, with particular attention to its nonspecific clinical presentation. Ongoing research is needed to improve diagnostic approaches and develop more effective treatment strategies for these rare cases.

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FIGURES AND TABLES

Figure 1. Magnetic resonance imaging of the penis results.

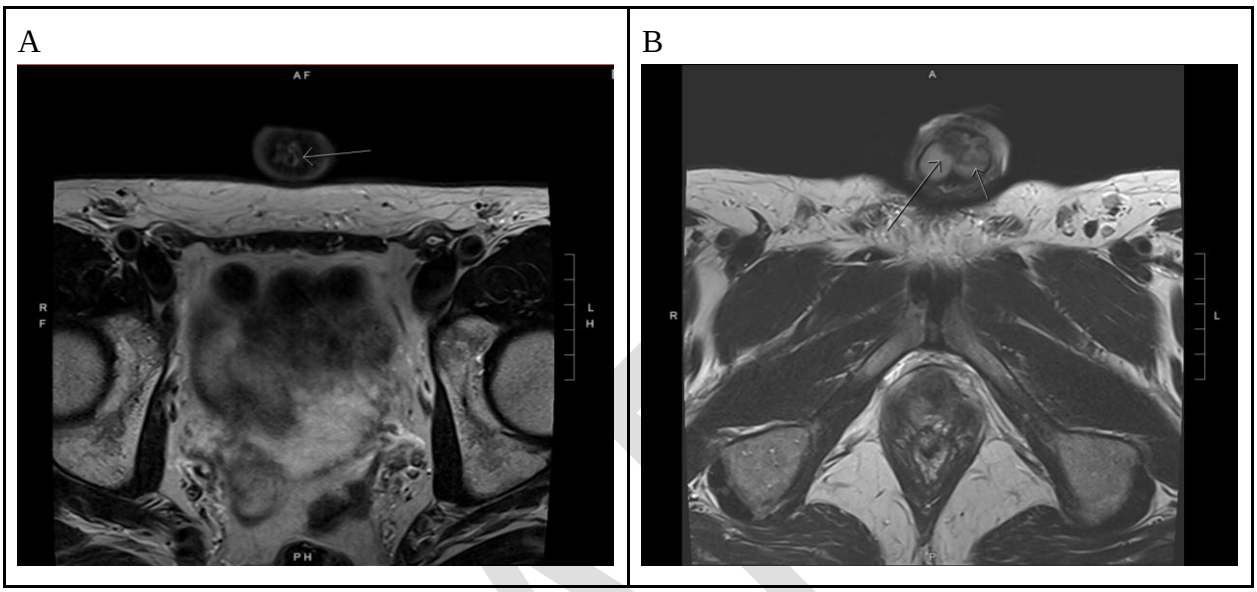

Figure 2. Clinical findings of patient's physical exam.

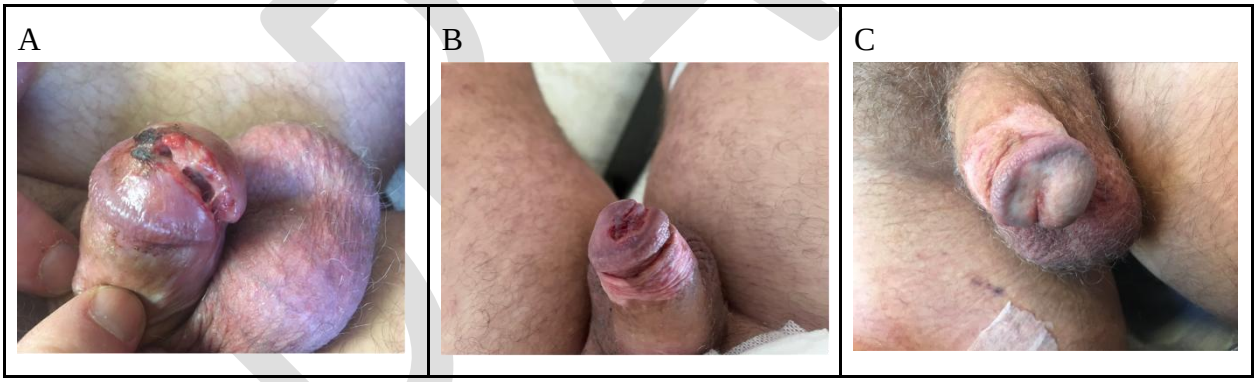

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Table 1. Publications of penile MAC infection				
Publication	**Clinical presentation**	**Diagnosis**	**Treatment**	**Clinical progress**
Niedrach et al, 1989[10]	Painful abscess	MAC, Streptococcus haemolyticus, and Clostridium perfringens	Surgical drainage and cefoxitin for 4 days followed by penicillin V potassium	No recurrence 4 months post-intervention
Ralph et al, 1998[11]	Penile ulcer infiltrating the corpus cavernosum	Cutaneous MAC	8 months of: - Rifabutin 300 mg/d - Clarithromycin 500 mg BID - Ethambutol 400 mg TID	Resolution of the ulcer at the end of the 8 months
Fonda-Pascual et al, 2018[12]	- Several yellowish firm papules on the penile shaft and foreskin - Indurated ulcer with mamelonated borders and a fibrinous base on the foreskin	MAC cutaneous involvement with fusocellular pseudotumoral pattern	Not reported	Not reported

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