Genitourinary histoplasmosis in post-renal transplant patient: Diagnostic dilemma

Arun Chawla, Kiran Chawla†, Joseph Thomas
Departments of Urology and †Microbiology, Kasturba Medical College, Manipal, Karnataka, India

ABSTRACT
Genitourinary histoplasmosis is very rare and to our knowledge only four cases of epididymal histoplasmosis and nine cases of prostatic histoplasmosis have been reported in literature. We hereby report a case of a middle-aged male, who presented three years after renal transplant, with complaints of fever, pain, and swelling in the scrotum. Imaging disclosed an enlarged right epididymis with prostatic and retrotrigonal abscess, suggesting tuberculosis infection. However, histopathology of the epididymal biopsy revealed histoplasmosis, and the drained pus on culture confirmed infection with Histoplasma capsulatum.

Key words: Epididymis, histoplasmosis, prostate

INTRODUCTION
Histoplasma capsulatum, is a dimorphic fungus that commonly causes pulmonary infection. Disseminated histoplasmosis is seen in immunocompromised patients like renal transplant recipients. Genitourinary histoplasmosis is rare and its clinical presentation can mimic genitourinary tuberculosis. The diagnosis is usually made by demonstration of antigen in the urine, serum, relevant body fluids or pus and by fungal culture. Herein we are presenting a rare case of genitourinary histoplasmosis where the diagnostic dilemma was resolved by fungal culture of prostatic abscess and histopathological examination of epidydimal tissue.

CASE REPORT
A 37-year-old male, a renal transplant recipient, with the mother as donor, presented with complaints of pain and swelling in the scrotum and fever of one week duration, three years after the transplant. Post transplantation, he was on triple immunosuppressive therapy with Tacrolimus, Azathioprim, and Prednisolone, and his allograft function was stable. One-and-a-half years after his renal transplant, he had dysphagia and melena, and was diagnosed with esophageal candidiasis and colonic histoplasmosis on the basis of upper gastrointestinal endoscopy and colonoscopy, respectively. Histoplasmosis was confirmed by demonstrating Histoplasma capsulatum on histopathology of the biopsy from colonic ulcers and stool culture. He responded to Itraconazole, which was continued for nine months and was asymptomatic on follow-up.

At the time of this presentation, three years after the transplant, blood investigations revealed severe anemia, leucopenia, thrombocytopenia, and serum creatinine of 3.0 mg / dl. Urinalysis showed proteinuria (300mg / dl) with numerous red blood cells (RBCs) and pus cells. The stool was positive for occult blood and showed presence of pus cells. Local examination revealed an enlarged tender epididymis on the right side. Digital rectal findings suggested bogginess on the anterior rectal wall with prostatic landmarks not well appreciable. Systemic examination did not reveal any abnormality. The ultrasound showed enlarged, heterogenous epididymis, with fluid collection and a thick-walled collection in the prostate and retrotrigonal area. Computerized tomography of the pelvis confirmed the ultrasound findings [Figures 1a,b].

The epididymal swelling was explored and tissue biopsy was sent for polymerase chain reaction (PCR) for Mycobacterium tuberculosis and histopathology. The prostatic and retrotrigonal collection was drained via the per-rectal...
route and sent for culture studies. Histopathology diagnosed Histoplasmosis [Figure 2] and culture of the pus (obtained from the prostatic / retrotrigonal abscess) confirmed the growth of *Histoplasma capsulatum* [Figure 3]. Tissue PCR and culture for *Mycobacterium tuberculosis* were negative. A repeat colonoscopy was done, which did not reveal any ulcers or polyps or any other finding suggestive of intestinal histoplasmosis. Biopsies taken on colonoscopy did not reveal *Histoplasma* on culture or histopathology. Blood and urine cultures were also negative for *Histoplasma*. The patient was restarted on Itraconazole for nine months, to which he responded successfully. The patient was doing well on follow-up.

**DISCUSSION**

In immunosuppressed patients, like renal transplant recipients, infections are very common. The risk of genitourinary tuberculosis is increased in transplant recipients, who are either born or live in areas where tuberculosis is endemic.\(^1\)

The frequency of *Mycobacterium tuberculosis* disease among the recipients of solid organ transplants in most developed countries is 1.2 – 6.4%, but among transplant recipients living in areas of high endemicity, it can reach 15%.\(^1\) It is worth noting that diverse, unsuspected, and elusive sites of tuberculosis infection have been described.

In this patient, with enlargement of epididymis coupled with findings of an abscess in the prostatic and retrotrigonal region, tuberculosis was a strong probability. However, tissue PCR and culture for *Mycobacterium tuberculosis* was negative and findings of histopathology and culture were conclusive for Histoplasmosis. Genitourinary involvement was reported infrequently in disseminated histoplasmosis. Even as most cases of histoplasmosis were asymptomatic or self-limiting, they could rarely lead to severe and progressive disseminated infections. Diagnosis of disseminated histoplasmosis required a high index of suspicion.\(^2,4\)

Only four cases of epididymal histoplasmosis have been
reported in literature so far. Two cases were diagnosed from the United States in 1981,[5,6] one was presented by Kahn DG, et al., at a conference in the United States in 1992 (International Conference on acquired immunodeficiency syndrome (AIDS) 1992 Jul 19-24; 8: 93)[5,6] and the fourth case was reported from India in 1995.[4,5] Three cases were diagnosed by histopathological examinations and pus cultures, and the fourth case was diagnosed with the help of a seminal culture. All the cases had a similar clinical presentation: fever, weight loss, and testicular pain and/or swelling.[5,6]

Involvement of the prostate is very rare and only nine cases have been previously reported. Prostatic involvement may resemble tuberculosis, bacterial prostatitis or neoplasms.

The present infection may either be a reinfection or reactivation. Reinfection can occur in patients who have had histoplasmosis in the past, like our patient who had colonic histoplasmosis. When there is a decline in immunity in such a host, residual host defenses cannot combat invasion by *Histoplasma*. Reactivation of latent histoplasmosis can also occur in immunocompromised patients.[7] Diagnosis of histoplasmosis is made by the demonstration of antigen in the urine, serum, relevant body fluids or pus. Histopathology of the suspected lesion can reveal yeast structures of *H. capsulatum* via the hematoxylin and eosin stain; however, the organism is better visualized using methenamine silver or periodic acid Schiff stains (PAS). Confirmation can be obtained by setting up appropriate cultures, demonstrating the growth and dimorphic properties of the fungus.[8]

A high index of suspicion is needed for the diagnosis of histoplasmosis in immunosuppressed patients. The tissue, pus, and body fluid available for diagnosis must be subjected to investigations for uncommon infections, too.

REFERENCES

1. Munoz P, Rodriguez C, Bouza E. Mycobacterium tuberculosis infection in recipients of solid organ transplants. Clin Infect Dis 2005;40:581-7.
2. Sathapatayavongs B, Batteiger BE, Wheat J, Slama TG, Wass JL. Clinical and laboratory features of disseminated histoplasmosis during two large urban outbreaks. Medicine (Baltimore) 1983;62:263-70.
3. Kauffman CA. Histoplasmosis: A clinical and laboratory update. Clin Microbiol Rev 2007;20:115-32.
4. Assi MA, Sandid MS, Baddour LM, Roberts GD, Walker RC. Systemic histoplasmosis: A 15-year retrospective institutional review of 111 patients. Medicine (Baltimore) 2007;86:162-9.
5. Randhawa HS, Chaturvedi S, Khan ZU, Chaturvedi VP, Jain SK, Jain RC, et al. Epididymal histoplasmosis diagnosed by isolation of Histoplasma capsulatum from semen. Mycopathologia 1995;131:173-7.
6. Mawhorter SD, Curley GV, Kursh ED, Farver CE. Prostatic and central nervous system histoplasmosis in an immunocompetent host: Case report and review of the prostatic histoplasmosis literature. Clin Infect Dis 2000;30:595-8.
7. Wheat LJ, Connolly-Stringfield PA, Baker RL, Curfman MF, Eads ME, Israel KS, et al. Disseminated histoplasmosis in the acquired immune deficiency syndrome: Clinical findings, diagnosis and treatment, and review of the literature. Medicine (Baltimore) 1990;69:361-74.
8. Wheat LJ. Improvements in diagnosis of histoplasmosis. Expert Opin Biol Ther 2006;6:1207-21.