Incidental Finding of Cryptococcus on Prostate Biopsy for Prostate Adenocarcinoma Following Cardiac Transplant: Case Report and Review of the Literature

Sujal I. Shah, Hai Bui, Nelson Velasco, Shilpa Rungta

Patient: Male, 62
Final Diagnosis: Prostatic cryptococcosis
Symptoms: Elevated PSA
Medication: —
Clinical Procedure: —
Specialty: Urology

Objective: Unusual clinical course
Background: Cryptococcus is the third most common invasive fungal organism in immunocompromised patients, including transplant patients, and usually involves the central nervous system and lungs, with a median time to infection of 25 months. We report a case of Cryptococcus of the prostate gland, found as an incidental finding on prostate biopsy for prostate adenocarcinoma, four months following cardiac transplantation.

Case Report: A 62-year-old male African-American who had a cardiac transplant four months previously, underwent a six-core prostate biopsy for a two-year history of increasing prostate-specific antigen (PSA) levels, and a recent history of non-specific urinary tract symptoms. A prostatic adenocarcinoma, Gleason grade 4+4=8, was diagnosed on histopathology, and ‘foamy’ cells were seen in the biopsies. Histochemical stains, including Grocott methenamine silver (GMS), and periodic acid-Schiff (PAS) showed abundant round and oval 5–7 µm diameter fungal elements; mucicarmine highlighted the fungal polysaccharide capsule, diagnostic for Cryptococcus. Cryptococcal antigen detection was made by the latex agglutination test and cultures. We reviewed the literature and found 70 published cases (from 1946–2008) of Cryptococcus of the prostate gland, with only one previous case presenting five years following cardiac transplantation.

Conclusions: Fungal infections of the prostate are rare, and occur mainly in immunocompromised patients. We present a unique case of prostatic Cryptococcus found incidentally at four months following cardiac transplantation. This case report highlights the need to consider atypical fungal infection as a differential diagnosis for prostatitis in immunosuppressed patients, including transplant patients.

MeSH Keywords: Biopsy, Large-Core Needle • Cryptococcus • Heart Transplantation • Prostate-Specific Antigen

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/905528

Corresponding Author: Sujal I. Shah, e-mail: shah2si@ucmail.uc.edu

Conflict of interest: None declared
Background

Atypical invasive fungal infections in patients following transplantation have been found to vary depending on multiple factors, including the type of organ transplanted, the degree of immunosuppression, and the post-transplant period [1].

_Cryptococcus_ has been found to be one of the more common causative organisms of fungal infections in immunosuppressed patients [1]. The median time to the presentation is approximately 18-months post-transplant [2]. In the cardiac transplant population specifically, the median time to atypical fungal infection is 25 months post-transplant [3].

_Cryptococcal_ fungal infection most commonly involves the central nervous system and respiratory system [1–3]. The prostate gland has been found to act as a possible reservoir for systemic infections and has rarely been found to be the primary site of infection [4]. Prostatic involvement by _Cryptococcus_ infection post-transplant is very rare. We report the case of a 62-year-old man with an incidental finding of _Cryptococcus_ on prostate biopsy for prostate adenocarcinoma, four months following cardiac transplant, and review the published literature of similar cases.

Case Report

A 62-year-old male African-American underwent prostate biopsy, four months following cardiac transplant. He had a history of transthyretin-related amyloidosis presenting as restrictive cardiomyopathy with subsequent congestive heart failure and cardiogenic shock, requiring cardiac transplantation. There was no history of meningitis or pneumonia.

The patient had initially been found to have slightly elevated prostate-specific antigen (PSA) level two years prior to cardiac transplant, with the PSA increasing from 4.95 ng/mL in October 2014, to 5.64 ng/mL in October 2015. In April 2015, a pelvic computed tomography (CT) scan was performed, which showed two nodules in the prostate gland that were highly suspicious for malignancy.

Cardiac transplant occurred in May 2016. In July and August 2016, PSA levels were found to be above 12.0 ng/mL. Furthermore, he complained of recent non-specific urinary symptoms. These PSA results, symptoms, imaging findings, and an abnormal finding on digital rectal examination prompted a prostate biopsy.

A six-core prostate biopsy showed prostate adenocarcinoma, Gleason grade 4+4=8, with areas containing foamy cells (Figure 1). These foamy cells had the appearance of histiocytes (tissue macrophages) associated with areas of fibrosis. The foamy cells contained round and oval encapsulated structures, suggestive of fungal elements (Figure 2). The differential
diagnoses at this time included the following fungal organisms: *Histoplasma capsulatum*, *Pneumocystis jirovecii*, *Cryptococcus neoformans*, *Coccidioides immitis*, and *Blastomyces dermatitidis*, among others.

Histochemical special stains were performed on the prostate biopsy tissue sections. Grocott methenamine silver (GMS), and periodic acid-Schiff (PAS) staining showed abundant round and oval 5–7 µm diameter intracellular fungal elements (Figure 3). On GMS staining, the fungal structures were of various sizes with narrow-based buds, and no spherules with smaller endospores (suggestive of *Coccidiomycosis*), or broad-based budding (suggestive of *Blastomycosis*), or characteristic ‘crushed ping-pong ball’-like structures (suggestive of *Pneumocystis*) were seen. Mucicarmine staining highlighted the fungal polysaccharide capsule, diagnostic for *Cryptococcus* (Figure 4). Cryptococcal antigen detection was made by the latex agglutination test and cultures, confirming the diagnosis.

The patient was treated with fluconazole (Diflucan) 400 mg daily following the prostate biopsy results. Subsequent prostatectomy showed diffuse infiltration by *Cryptococcus* with Gleason grade 4+3=7 adenocarcinoma. Patient urological follow-up has shown PSA levels of <0.01 ng/mL since prostatectomy.

Imaging performed one-month following surgery revealed new bilateral pulmonary nodules, and lung biopsy showed *Cryptococcal* organisms and an absence of malignant cells. Fluconazole treatment was extended for a total duration of one year. The patient continues to have urological, infectious disease, and cardiac transplant follow-up.

**Discussion**

Fungal infections occur in immunocompromised patients, including patients who have had solid organ transplants [1]. The risks of atypical infection have been found to vary, depending on the organ transplanted, which may be a factor that is secondary to the level of immunosuppression used post-surgery [1]. Also, the causative organism has been found to vary based on both the original organ transplanted and the period from transplantation to infection [1].

*Cryptococcus neoformans* is a small encapsulated yeast that causes infection secondary to inhalation [5]. *Cryptococcus* infection results is a mild, non-specific pulmonary tract infection that, depending on the host immune system and the infective dose and virulence of the organism, causes a latent infection or disseminated infection [6]. Occasionally, patients can have asymptomatic *Cryptococcus* infection and/or incidental discovery of a lung nodule on X-ray [5,6]. While respiratory tract infection is common, due to an inhalational spread of the organism, the most common site of disease in transplant recipients is the central nervous system, with resultant meningitis. Skin is another commonly affected organ [5,6].
Infection with *Cryptococcus* is relatively common [7]. *Cryptococcus* infection leads to a latent stage in most patients who have inhaled cryptococcal spores, which usually reside in granulomas, with no clinical evidence of disease [7]. In patients with underlying immunosuppression, an increase in the fungal burden leads to the transition from latency to disease [8]. Reactivation is also a major cause of *Cryptococcus* infection, especially in the immunosuppressed host; however, a primary disease can also be seen [1,6,7].

*Cryptococcus* infection was previously found to predominate in HIV-infected patients. However, the patient population now thought to be at greatest risk of *Cryptococcus* infection are organ transplant recipients [3]. *Cryptococcus* is the third most common invasive fungal organism in solid organ transplant recipients, responsible for approximately 8% of invasive fungal infections [2]. *Cryptococcus* infection occurs relatively late in the post-transplant period, with the literature suggesting a median time to development of 1.6 years [2,3]. This pattern of infection differs from other post-transplant fungal infections, which predominantly occur within 90 days of transplantation [2].

When looking specifically at heart transplant recipients, invasive fungal infections have been found to occur in less than 10% of recipients, with *Candida* and *Aspergillus* most commonly implicated [3]. In this patient population, 15% of cases had an onset of *Cryptococcus* infection within three months of transplantation and the median time to onset was found to be 25 months [3]. Additionally, prostate cancer was found to be the most common urologic malignancy associated with cardiac transplant patients [9].

Given the rapidly increasing PSA level following cardiac transplant that was seen in this case, a literature search was performed. However, no studies or reports were found to report accelerated cancer growth following induction of immunosuppression treatment. Of interest is the possible etiological link between prostate cancer and fungal infections. From this case report, it cannot be determined with certainty whether the rapidly increasing PSA was due to a new, incidental fungal infection occurring concurrently with a pre-existing high-grade cancer, or accelerated growth of a previously indolent cancer, following high-level immunosuppression, with incidental fungal infection, or a new-onset post-transplant cancer occurring in the presence of previous fungal infection.

There has been growing evidence suggesting an association between prostate carcinogenesis and intra-prostatic inflammation [10–12]. A literature search showed limited information regarding a possible link between prostate cancer and fungal infection, possibly due to the low prevalence of prostatitis cases caused by these organisms. Further studies need to be performed to determine the impact of fungal infections, and corresponding intra-prostatic inflammation, on carcinogenesis.

While fungal organisms are not a common cause of prostatitis in the immunocompetent population, prostatic involvement by *Cryptococcus* is a not-uncommon finding in the immunosuppressed population [10–15]. The prostate gland is thought to be a possible sanctuary for the organism in patients receiving systemic treatment for cryptococcal meningitis, allowing the organism to be cultured in the urine or even causing reinfection at a later period of immunosuppression. However, prostatic involvement by *Cryptococcus* in post-transplant patients has rarely been reported, with such presentation in post-cardiac transplant patients being even rarer [10–15].

Review of the literature has shown 70 reported cases of *Cryptococcus* infection in the prostate gland (Table 1) [13–57]. Of these reported cases, only one case (1.4%) was seen in a cardiac transplant recipient, with onset occurring five years post-transplant [13]. An additional case (1.4%) was reported in a patient who had previously had a renal transplant [14]. Commonly seen immunosuppressive factors include steroid therapy, HIV/AIDS, leukemia/lymphoma, and diabetes; rare reports present patients listed as having no significant predisposing factors or immunosuppression (Table 1).

Among the 44 patients (63%) presenting without definite symptoms suggestive of *Cryptococcus* infection involving the prostate gland, 16 cases (36%) were patients with incidental findings of prostatic involvement found on autopsy; one patient (2%) was found to have *Cryptococcus* on a biopsy done for a prostatic nodule noted on physical examination. The remaining cases were diagnosed predominantly by urine or semen cultures; 27 (61%) of these 44 cases were in patients that had a previous diagnosis of *Cryptococcus* infection, 25 (93%) of which had previous diagnoses of cryptococcal meningitis. Only 10 of the 70 cases (14%) were diagnosed by prostate biopsy, with one biopsy performed secondary to the presence of a prostatic nodule, and the remaining nine biopsies (90%) done secondary to presenting symptoms of prostatism (Table 1).

A case of *Cryptococcus* infection of the prostate, diagnosed on prostate biopsy, in the setting of prior renal transplant was the sole case (1%) where prostatic adenocarcinoma was concurrently diagnosed [14]. One additional case involved a patient initially diagnosed with prostate cancer on biopsy, with the examination of the prostate gland at autopsy showing *Cryptococcus* infection with no identifiable prostatic adenocarcinoma [15].
| Year | Author                  | Predisposing condition | Presentation        | Initial Diagnosis on | Prostatic symptoms | Prostate Diagnosis | Other organs                  | Notes                                                                 |
|------|-------------------------|------------------------|---------------------|----------------------|--------------------|--------------------|-------------------------------|----------------------------------------------------------------------|
| 1946 | Voyles, et al. [15]      | None                   | Prostatism          | Autopsy              | Prostatism         | Autopsy            | Disseminated                  | Prostatectomy → called prostate cancer                               |
| 1951 | Zelman, et al. [16]      | Chronic granulocytic leukemia | Fever, fatigue, weakness | Autopsy              | None               | Autopsy            | Disseminated                  |                                                                      |
| 1952 | Cohen, et al. [17]       | None                   | Meningitis          | CSF culture           | None               | autopsy            | CNS, pulmonary                |                                                                      |
| 1954 | Bowman, et al. [18]      | DIABETES               | Meningoencephalitis | Urine culture         | None               | Autopsy            | CNS, adrenal                  | (2; Cryptococcus in urine culture, prostate at autopsy)               |
| 1955 | Baker, et al. [19] (2 cases) | (1) None (2) Hodgkin’s lymphoma | (1) Meningitis (2) ??? Not specified | (1) Autopsy? (2) Autopsy? | (1) None (2) None | (1) Autopsy (2) Autopsy | (1) CNS, disseminated (2) Adrenals, spleen | (2) No mention of presenting symptoms                               |
| 1961 | Dreyfuss, et al. [20]    | None                   | Prostatism          | CSF culture           | Prostatism         | Re-examine prostate s/p CSF culture | disseminated (post-surgery) | Urine culture → yeast, no further identification; Initially called “granulomatous” |
| 1962 | Huter, et al. [21]       |                        |                      |                      |                    |                    |                               | (1 case, no further discussion)                                      |
| 1965 | Tillotson, et al. [22]   | None                   | Prostatism, UTI     | Urine culture; 2nd biopsy of prostate | Prostatism         | 2nd biopsy of prostate | Bone, pulmonary | 1st biopsy → Granulomatous prostatitis; Urine culture concurrent with 2nd biopsy |
| 1965 | O’Connor, et al. [23]    | Chronic lymphocytic leukemia | Prostatism          | Post-op urine culture and prostatectomy | Prostatism         | Perineal prostatectomy | None | Post-op perineal fistula developed; Initially thought to be BPH |
| 1965 | Randall Jr, et al. [24]  | On steroid therapy for RA | Pyelonephritis, meningitis | Urine culture         | None               | Autopsy            | CNS, renal                    |                                                                      |
| 1965 | Brooks, et al. [25]      | Hodgkin’s disease, steroid therapy for spherocytic hemolytic anemia | Pneumococcal pneumonia; incidentally felt enlarged prostate | Prostatic fluid culture | None (enlarged prostate on physical) | Prostatic fluid culture | CNS, renal | CSF culture and autopsy; both found before symptoms of involvement; prostate biopsy done after diagnosis made |
| 1966 | Rubiao, et al. [26]      | None                   | Prostatism          | Prostate biopsy (?)   |                    |                    | Pulmonary                     |                                                                      |
Table 1 continued. Previously reported cases of prostatic involvement by Cryptococcus neoformans from 1946-2008, with predisposing factors, presenting symptoms, prostatic symptoms at presentation, mode of prostatic involvement diagnosis, other organs involved, and case notes.

| Year | Author | Predisposing condition | Presentation | Initial Diagnosis on | Prostatic symptoms | Prostate Diagnosis | Other organs | Notes |
|------|--------|------------------------|--------------|---------------------|--------------------|--------------------|--------------|-------|
| 1972 | Strom, et al. [27] | On steroid therapy for RA | Meningitis | Autopsy | None (bladder obstruction on x-ray) granulomatous prostatitis | Autopsy | CNS | Urine culture → yeast, not further identified |
| 1972 | Brock, et al. [28] | On steroid therapy for sarcoidosis | Prostatism | TURP | Prostatism | TURP | Pulmonary | Urine/sputum culture confirm |
| 1972 | Orr, et al. [29] | Polycythemia vera | Prostatic nodule on physical exam | Prostate biopsy | None (prostatic nodule on physical) | Prostate biopsy | None | Abscess fluid culture, urine culture (+); abscesses seen on open perineal biopsy |
| 1973 | Salyer, et al. [30] (6 cases) | None | Meningitis | (1) Urine culture; (5) Not specified | (1) Nodular prostatitis on physical exam; (5) None | None | | |
| 1977 | Kaplan, et al. [31] | Not definitely stated | Not definitely stated | Not definitely stated | None | Autopsy | Not definitely stated | 1/23 autopsy cases had prostate involvement |
| 1981 | Hinchey, et al. [32] | Steroid therapy for chronic active hepatitis, alcoholism, diabetes, tuberculosis | Prostatism | TURP | Prostatism | TURP | None | Urine cultures done after histologic diagnosis made |
| 1981 | Braman [33] | Steroid therapy for chronic active hepatitis/cirrhosis, tuberculosis | Prostatism | TURP | Prostatism | TURP | None | Elective prostatectomy → subsequent urine culture (+) |
| 1981 | Plunkett, et al. [14] | Renal transplant → post-TURP septicemia | Blood culture (+) × 3 (first 2 = thought to be contamination) | Prostatism (BPH on urologic evaluation) | Prostatism (re-examination) | Disseminated (post TURP) | Single focus grade I adenocarcinoma BPH; post-cath/TURP septicemia; CSF/skin biopsy (+) |
| 1982 | Allen, et al. [34] | None | Prostatism | Bronchial washings (s/p TURP) | Prostatism | TURP | Sputum, CSF (+) → re-examine TURP |
| 1982 | Huynh, et al. [35] | DIABETES, cryptococcal meningitis (2 years ago) – diagnosed by CSF culture | Prostatism | TURP | Prostatism | TURP | None CSF before; prostate again after | Recurrent in prostate at 8 years (by TURP); testing in between (–) |
Table 1 continued. Previously reported cases of prostatic involvement by *Cryptococcus neoformans* from 1946-2008, with predisposing factors, presenting symptoms, prostatic symptoms at presentation, mode of prostatic involvement diagnosis, other organs involved, and case notes.

| Year | Author | Predisposing condition | Presentation | Initial Diagnosis on Prostatic symptoms | Prostate Diagnosis | Other organs | Notes |
|------|--------|------------------------|--------------|-----------------------------------------|-------------------|--------------|-------|
| 1986 | Lief, et al. [36] | HIV | Prostatism, meningitis | CSF culture | Prostatism | Prostate biopsy | CNS |
| 1988 | Staib, et al. [37] | HIV | Not defined | (+) CSF, blood culture, stool, urine culture | None | Autopsy | Seminal vesicles, thyroid |
| 1989 | Larsen, et al. [38] (7 cases) | AIDS, cryptococcal meningitis | (+) urine culture s/p Amphotericin therapy for CNS crypto | Urine culture | None | (3) prostatic secretions; (4) urine culture s/p prostate massage | Subsequent CNS recurrence in (3) 3 with (+) secretions had abscesses at autopsy |
| 1989 | Staib, et al. [39] | HIV, cryptococcal meningitis | Teratospermia, hypospermia | Seminal fluid culture | None | Seminal fluid culture | None |
| 1990 | Staib, et al. [40] | HIV, Cryptococcus of lungs “suggested;” (+) sputum, urine, seminal fluid; Pneumocystis pneumonia | Urine, sputum, seminal fluid cultures | Urine and seminal fluid cultures | None | (+) urine/semen fluid cultures | Disseminated initially; just in urine and seminal fluid cultures after treatment 10-week follow-up on therapy after (+) sputum, urine, and seminal fluid |
| 1990 | King, et al. [41] | Hodgkin’s disease, cryptococcal meningitis (1 m ago) – diagnosed in CSF | Prostatism | Prostatism | Prostate biopsy culture | None | Needle core biopsy → yeasts |
| 1990 | Milchgrub, et al. [42] (capsule-deficient Cryptococcus) | None | Prostatism | TURP | Prostatism | TURP | None | Fungal culture of prostatic tissue (-), urine culture (-) ×3 |
| 1991 | Bailly, et al. [43] | HIV, disseminated cryptococcosis | Cryptococcus in urine, CSF, lungs | CSF/urine/lung cultures | None | Urine cultures (+) post-treatment | None | Persistence in urine post-treatment |
| 1991 | Bozzette, et al. [44] (14 cases) | HIV, cryptococcal meningitis (post-treatment) | None (sterile blood/CSF cultures) | (+) urine cultures | None | (+) urine cultures | (2) recurrent meningitis [6, 22 weeks] Persistent prostatic involvement |
| 1992 | Adams, et al. [45] | CABG w/blood transfusion (donor diagnosed w/HIV) | Prostatism | Prostatism | Prostate biopsy | None | Subsequent (+) urine culture |
| 1992 | Mamo, et al. [46] | HIV, history of PCP and cryptococcal PNA; persistent fungemia | Urine culture | Prostatism | Prostate biopsy | None | (+) tissue cultures |
Previously reported cases of prostatic involvement by *Cryptococcus neoformans* from 1946-2008, with predisposing factors, presenting symptoms, prostatic symptoms at presentation, mode of prostatic involvement diagnosis, other organs involved, and case notes.

| Year | Author | Predisposing condition | Presentation | Initial Diagnosis on | Prostatic symptoms | Prostate Diagnosis | Other organs | Notes |
|------|--------|------------------------|--------------|----------------------|--------------------|--------------------|--------------|-------|
| 1994 | Ndimbie, et al. [47] | HIV, history of PCP, Cryptococcus meningitis, etc. | Meningitis | CSF culture | None | Autopsy | None | Previous CNS Cryptococcus (2 years prior; treated) tissue culture (–) |
| 1994 | Sax, et al. [13] | Heart transplant, mild BPH | Persistent UTI | Blood culture | None (enlarged prostate on physical) | TURP | None | Prostatic abscess |
| 1995 | Fuse, et al. [48] | Immunosuppressive therapy for Behcet’s disease | Prostatism | Needle biopsy culture | Prostatism | Needle biopsy culture | None | Biopsy → PAS(+) capsules of cysts; “culture of the specimen” (+) |
| 1997 | Byrne, et al. [49] | Mild BPH, recurrent prostatitis (>20 years); Hairy cell leukemia | Fevers, chills, prostatism | Urine culture | Bacterial prostatitis; prostatism | Urine culture | None |
| 1997 | de Lima, et al. [50] | AIDS, TB Lymphadenopathy | Autopsy | None | Autopsy | None | Disseminated mycobacteriosis |
| 1998 | Yip, et al. [51] | On steroid therapy for myasthenia gravis, DIABETES | Meningitis, prostatism | Blood culture | Prostatism | TURP | CNS | (+) CSF culture; prostatic abscess |
| 1999 | Caballes, et al. [52] | T-cell deficiency, DIABETES | Prostatism | TURP (pathology consultant) | Prostatism | TURP (pathology consultant) | CNS | TURP called → granulomatous prostatitis; subsequent (+) blood and CSF culture |
| 2000 | Sharma, et al. [53] | Chronic lymphocytic leukemia | Prostatism | Prostatic nodule aspiration | Prostatism | Prostatic nodule aspiration | Disseminated |
| 2005 | Siddiqui, et al. [54] | Renal transplant, DIABETES | Prostatism, fungemia | Blood culture, urine culture | Prostatism | Prostate biopsy | None |
| 2006 | Seo, et al. [55] | Alcoholic cirrhosis | Prostatism | Prostate biopsy | Prostatism | Prostate biopsy | None |
| 2008 | Wada, et al. [56] | DIABETES | Pain on micturition | Discharge culture | None (hardened on physical; normal size) | Discharge culture | CNS, pulmonary | “Purulent discharge obtained at biopsy,” biopsy done concurrently |
| 2008 | Chang, et al. [57] | None | Prostatism | Prostatectomy | Prostatism | Prostatectomy CNS | Meningitis → urine, CSF and blood culture (+), 3 weeks after surgery |
Conclusions

Fungal infections of the prostate are rare and occur mainly in immunocompromised patients. We have reported a unique case of prostatic Cryptococcus found incidentally at four months following cardiac transplantation. This case report highlights the need to consider atypical fungal infection as a differential diagnosis for prostatitis in immunosuppressed patients, including transplant patients. A literature review has shown this case to be the second case of post-cardiac transplant prostatic Cryptococcus infection and the second case of concurrent prostatic adenocarcinoma and Cryptococcus infection, and is the first case to combine all three of these factors. Additionally, this case had an unusually rapid onset of post-transplant Cryptococcus infection. This case may help to raise awareness of the possibility of latent infection combined with carcinoma. While in our case, we cannot definitely determine whether it was the cancer or the infection that led to the recent onset of urinary symptoms or the spike in PSA levels, this case raises the necessity to rule out infectious etiologies in transplant recipients with urinary symptoms.

Conflicts of interest
None.

Statement
This material is the result of work supported with resources and the use of facilities at the Cincinnati VA Medical Center. The contents do not represent the views of the U.S. Department of Veterans Affairs or the United States Government.

References:

1. Singh N, Dromer F, Perfect JR, Lortholary O: Cryptococcosis in solid organ transplant recipients: Current state-of-the-science. Clin Infect Dis, 2008; 47(10): 1321–27
2. Pappas PG, Alexander BD, Andes DR et al: Invasive fungal infections among organ transplant recipients in the United States: Results of the Transplant-Associated Infection Surveillance Network (TRANSNET). Clin Infect Dis, 2010; 50: 1101–11
3. Husain S, Wagener MM, Singh N: Cryptococcus neoformans infection in organ transplant recipients: Variables influencing clinical characteristics and outcome. Emerg Infect Dis, 2001; 7: 1–14
4. Wise GJ, Shteynshlyuger A: How to diagnose and treat fungal infections in chronic prostatitis. Curr Urol Rep, 2006; 7(4): 320–28
5. Rohatgi S, Pirofski L: Host immunity to Cryptococcus neoformans. Future Microbiol, 2015; 10(4): 565–81
6. Lee SJ, Choi HK, Son J et al: Cryptococcal meningitis in patients with or without human immunodeficiency virus: Experience in a tertiary hospital. Yonsei Med J, 2011; 52(3): 482–87
7. Goldman DL, Khine H, Abadi J: Serologic evidence for Cryptococcus neoformans infection in early childhood. Pediatrics, 2001; 107(5): E66
8. Garcia-Hermoso D, Janson B, Dromer F: Epidemiological evidence for dormant Cryptococcus neoformans infections. J Clin Microbiol, 1999; 37(10): 3204–9
9. Goldstein SI, Williams DI, Oz MC et al: De novo solid malignancies after cardiac transplantation. Ann Thorac Surg, 1995; 60: 1783–89
10. De Marzo AM, Platz EA, Sutcliffe S et al: Inflammation in prostate carcinoma. Nat Rev Cancer, 2007; 7(4): 256–69
11. Sfanos KS, De Marzo AM: Prostate cancer and inflammation: The evidence. Histopathology, 2012; 60(1): 199–215
12. Sutcliffe S, De Marzo AM, Sfanos KS, Laurence M: MSMB variation and prostate cancer risk: Clues towards a possible fungal etiology. Prostate. 2014; 74: 569–78
13. Sax PE, Mattia AR: Case 7-1994 – A 55-year-old heart-transplant recipient with a tender, enlarged prostate gland. N Engl J Med, 1994; 330: 490–96
14. Plunkett JM, Turner BI, Tallent MB, Johnson HK: Cryptococcal septicaemia associated with urologic instrumentation in a renal allograft recipient. J Urol, 1981; 125(2): 241–42
15. Voyles GQ, Beck EM: Systemic infection due to Torula histolytica (Cryptococcus hominis). Arch Intern Med, 1946; 74: 504–15
16. Zelman S, O’Neill RH, Plaut A: Disseminated visceral torulosis without nervous system involvement with clinical appearance of granulocytic leukemia. Am J Med, 1951; 11(5): 658–64
17. Cohen JR, Kaufmann W: Systemic cryptococcosis. Am J Clin Pathol, 1952; 22(11): 1069–76
18. Bowman HE, Ritchey JO: Cryptococcosis (Torulosis) involving the brain, adrenal and prostate. J Urol, 1954; 71(3): 373–78
19. Baker RD, Haugen RK: Tissue changes and tissue diagnosis in cryptococcosis: A study of 26 cases. Am J Clin Pathol, 1955; 25(2): 14–24
20. Dreyfuss ML, Simon S, Sommer RI: Granulomatous prostatitis due to Cryptococcus Neoformans (Torula) with disseminated cryptococcosis and meningitis. NY State J Med, 1961; 61: 1589–92
21. Huter RVP, Collins HS: The occurrence of opportunistic fungus infections in a cancer hospital. Lab Invest, 1962; 11: 1035–45
22. Tillotson JR, Lerner AM: Prostatism in an eighteen-year old boy due to infection with Cryptococcus neoformans. N Engl J Med, 1965; 273(21): 1150–52
23. O’Connor FJ, Foussée JHS Jr., Cox CE: Prostatic cryptococcosis: A case report. J Urol, 1965; 94: 160–63
24. Randall RE Jr, Stacy WK, Toone EC et al: Cryptococcal pyelonephritis. N Engl J Med, 1968; 279(2): 60–65
25. Brooks MH, Scheerer PP, Linman JW: Cryptococcal prostatitis. JAMA, 1965; 192: 639–41
26. Rubiao PE, Gontijo J, Magalhaes MM: [Mycotic (cryptococcic) prostatitis simulating cancer of the prostate: report of a case.] Hospital J (Rio); 1966; 70(5): 1327–36 [Portuguese]
27. Strom RL, Payson R, Kitzmiller G: A steroid-induced infectious complication of rheumatoid arthritis. Minn Med, 1972; 55(5): 501–10
28. Brock DJ, Greico MH: Cryptococcal prostatitis in a patient with sarcoidosis: Response to 5-flucytosine. J Urol, 1972; 107(6): 1047–50
29. Salyer WR, Salyer DC: Involvement of the kidney and prostate in cryptococcosis. J Urol, 1973; 109(4): 695–98
30. Kaplan MH, Rosen PP, Armstrong D: Cryptococcosis in a cancer hospital: Clinical and pathological correlates in forty-six patients. Cancer, 1977; 39(5): 2265–74
31. Hinchee WW, Someren A: Cryptococcal prostatitis. Am J Clin Pathol, 1981; 75(2): 257–60
32. Braman RT: Cryptococcosis (torulosis) of prostate. Urology, 1981; 17(3): 284–85
33. Allen R, Barter CE, Chachoua LL et al: Disseminated cryptococcosis after transurethral resection of the prostate. Aust NZ J Med, 1982; 12(4): 296–99
34. Huynh MT, Reyes CV: Prostatic cryptococcosis. Urology, 1982; 20(6): 622–23
35. Lief M, Sarrafzai F: Prostatic cryptococcosis in acquired immune deficiency syndrome. Urology, 1986; 28(4): 318–19
36. Staib F, Seibold M: Mycological-diagnostic assessment of the efficacy of amphotericin B + flucytosine to control Cryptococcus neoformans in AIDS patients. Mycoses, 1988; 31(4): 175–86
38. Larsen RA, Bozzette S, McCutchan JA et al: Persistent Cryptococcus neoformans infection of the prostate after successful treatment of meningitis. Ann Intern Med, 1989; 111(2): 125–28

39. Staib F, Seibold M, L’age M et al. Cryptococcus neoformans in the seminal fluid of an AIDS patient. A contribution to the clinical course of cryptococcosis. Mycoses, 1989; 32(4): 171–80

40. Staib F, Seibold M, L’age M: Persistence of Cryptococcus neoformans in seminal fluid and urine under itraconazole treatment. The urogenital tract (prostate) as a niche for Cryptococcus neoformans. Mycoses, 1990; 33(7–8): 369–73

41. King C, Finley R, Chapman SW: Prostatic cryptococcal infection. Ann Intern Med, 1990; 113(9): 720

42. Milchgrub S, Visconti E, Avellini J: Granulomatous prostatitis induced by capsule-deficient cryptococcal infection. J Urol, 1990; 143(2): 365–66

43. Bailly MP, Boibieux A, Biron F et al: Persistence of Cryptococcus neoformans in the Prostate: Failure of Fluconazole Despite High Doses. J Infect Dis, 1991; 164(2): 435–36

44. Bozzette SA, Larsen RA, Chiu J et al: Fluconazole treatment of persistent Cryptococcus neoformans prostatic infection in AIDS. Ann Intern Med, 1991; 115(4): 285–86

45. Adams JR, Mata JA, Culkin DJ et al: Acquired immunodeficiency syndrome manifesting as prostate nodule secondary to cryptococcal infection. Urology, 1992; 39(3): 289–91

46. Mamo GI, Rivero MA, Jacobs SC: Cryptococcal prostatic abscess associated with the acquired immunodeficiency syndrome. J Urol, 1992; 148(3): 889–90

47. Ndimbie OK, Dekker A, Martinez AJ, Dixon B: Prostatic sequestration of Cryptococcus neoformans in immunocompromised persons treated for cryptococcal meningocerebritis. Histol Histopathol, 1994; 9(4): 643–48

48. Fuse H, Ohkawa M, Yamaguchi K et al: Cryptococcal prostatitis in a patient with Behçet’s disease treated with fluconazole. Mycopathologia, 1995; 130(3): 147–50

49. Byrne R, Hamill RJ, Rodriguez-Barradas MC: Cryptococcuciria: Case reports and literature review. Infect Dis Clin Pract, 1997; 6: 513–18

50. de Lima MA, dos Santos JA, Lazo J et al: [Cryptococcus infection limited to the prostate in an AIDS patient with disseminated mycobacteriosis. A necropsy report.] Rev Soc Bras Med Trop, 1997; 30(6): 501–5 [in Portuguese]

51. Yip SK, Cheng C, Wong MY et al: Cryptococcal prostatic abscess in an immunocompromised patient: A case report and review of the literature. Ann Acad Med Singapore, 1998; 27(6): 873–76

52. Caballes RL, Caballes RA Jr.: Primary cryptococcal prostatitis in an apparently uncompromised host. Prostate, 1999; 39(2): 119–22

53. Sharma N, Vama S, Varma N et al: Cryptococcal prostatitis in a patient with chronic lymphocytic leukemia. J Assoc Physicians India, 2000; 48(10): 1015–16

54. Siddiqui TJ, Zamani T, Parada JP: Primary cryptococcal prostatitis and correlation with serum prostate specific antigen in a renal transplant recipient. J Infect, 2005; 51(3): e153–57

55. Seo IY, Jeong HJ, Yung KJ, Rim JS: Granulomatous cryptococcal prostatitis diagnosed by transrectal biopsy. Int J Urol, 2006; 13(5): 638–39

56. Wada R, Nakano N, Yajima N et al: Granulomatous prostatitis due to Cryptococcus neoformans: diagnostic usefulness of special stains and molecular analysis of 18S rDNA. Prostate Cancer Prostatic Dis, 2008; 11(2): 203–6

57. Chang MR, Paniago AMM, Silva MM et al: Prostatic cryptococcosis – a case report. J Venom Anim Toxins Incl Trop Dis, 2008; 14(2): 378–85

This work is licensed under Creative Common Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)