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BCDEF 1,2 Sujal I. Shah

BCDE 1,3 Nelson Velasco

AE 1,2 Shilpa Rungta

None declared

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

DE 1,2 Hai Bui

Biopsy for Prostate Adenocarcinoma Following Cardiac Transplant: Case Report and Review of the Literature

Incidental Finding of Cryptococcus on Prostate

1 Department of Pathology, University of Cincinnati Medical Center, Cincinnati, OH, U.S.A.

 Department of Pathology, Cincinnati VA Medical Center, Cincinnati, OH, U.S.A.
 Department of Primary Care, Veterans Affairs, Southern Oregon Rehabilitation Center and Clinics, White City, OR, U.S.A.

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 sixcore 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 diame-

ter 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

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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



Figure 1. Photomicrograph of the histopathology of the prostate biopsy. Histology (light microscopy) of the prostate biopsy shows adenocarcinoma (top) and adjacent areas containing 'foamy' cells that were suspicious for atypical infection. Hematoxylin and eosin (H&E) (Magnification ×10).



Figure 2. Photomicrograph of the histopathology of the prostate biopsy. Histology (light microscopy) of the prostate biopsy shows prostatic parenchyma with a fibrotic and histiocytic background, with pleomorphic, round-tooval, encapsulated structures that have the appearance of a round nucleus surrounded by a clear zone. Hematoxylin and eosin (H&E). (Magnification ×40).

(tissue macrophages) associated with areas of fibrosis. The foamy cells contained round and oval encapsulated structures, suggestive of fungal elements (Figure 2). The differential



Figure 3. Photomicrograph of the histopathology of the prostate biopsy: identification of budding fungal organisms. Histology (light microscopy) of the prostate biopsy stained histochemically with Grocott methenamine silver (GMS) stain shows round and oval fungal organisms (black) with narrow-based buds, diffusely present in the prostatic parenchyma. Grocott methenamine silver (GMS). (Magnification ×60).



Figure 4. Photomicrograph of the histopathology of the prostate biopsy: identification of *Cryptococcus*. The inner layer of the *Cryptococcus* capsule stains red with mucicarmine. Mucicarmine. (Magnification ×60).

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].

 Table 1. 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
1946	Voyles, et al. [15]	None	Prostatism	Autopsy	Prostatism	Autopsy	Disseminated	Prostatectomy \rightarrow 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	Meningo- encephalitis	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? <i>Not specified</i>	(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	<u>Re-examine</u> <u>prostate</u> 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; 2 nd biopsy of prostate	Prostatism	<u>2nd biopsy</u> of prostate	Bone, pulmonary	1st biopsy \rightarrow Granulomatous prostatitis; Urine culture concurrent with 2 nd 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 pneumonitis; 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)® granulo- matous prostatitis	r 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 prostate on physical exam; (5) None	(6) Autopsy	CNS (6/6), renal (3/6)	(1/2) Urine culture (+)
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, CHF	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 \rightarrow subsequent urine culture (+)
1981	Plunkett, et al. [14]	Renal transplant	Prostatism → post-TURP septicemia	Blood culture (+) ×3 (first 2 = thought to be contami- nation)	Prostatism (BPH on urologic evaluation)	TURP, (-) for fungus [suggests prostate = primary focus]	CNS, skin	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 (<u>re-</u> examination)	Disseminated (post TURP)	Sputum, CSF (+) \rightarrow 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 predisposingfactors, presenting symptoms, prostatic symptoms at presentation, mode of prostatic involvement diagnosis, other organsinvolved, 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	Post-treatment
1989	Larsen, et al. [38] (7 cases)	AIDS, cryptococcal meningitis	(+) urine culture s/p Amphotericin therapy for CNS crypto	Urine culture	None (+) urine cultures	(3) prostaticsecretions;(4) urineculture s/pprostatemassage	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	Seminal fluid (+) supports prostate as reservoir
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/ seminal fluid cultures	(+) urine culture	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	Prostate biopsy culture	Prostatism	Prostate biopsy culture	None	Needle core biopsy \rightarrow 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	Prostate biopsy	Prostatism	Prostate biopsy	None	Subsequent (+) urine culture
1992	Mamo, et al. [46]	HIV, history of PCP and cryptococcal PNA; persistent fungemia	Prostatism	Urine culture	Prostatism	Prostate biopsy	None	(+) tissue cultures

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
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) <i>tissue culture (–</i>)
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]	Immunosup- pressive 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	Lymphadeno- pathy	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 \rightarrow 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 posttransplant *Cryptococcus* infection. This case may help to raise awareness of the possibility of latent infection combined with

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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

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