Clinical Case Reports International

Case Presentation
Published: 03 May, 2023

Disseminated Coccidioidomycosis Presenting as Prostatic Abscess in Poorly Controlled Diabetes

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Abstract

Background: Coccidioidomycosis infection classically presents as a pulmonary illness. Disseminated coccidiomycosis affects approximately 1% of patients. Most common extrapulmonary sites are skin, bones, central nervous system, and soft tissue. Even more rare is the presentation of symptomatic genital tract infections and prostatitis. We present a rare case of disseminated coccidioidomycosis in a 60-year-old male with poorly controlled diabetes and Polycythemia Vera (PV) who presented with dysuria and suprapubic tenderness found to have a prostate abscess, splenic lesions and cavitary pneumonia.

Case Report: A 60-year-old man with a history of uncontrolled type 2 diabetes mellitus (hemoglobin A1c 12.5%) and myocardial ischemia, presented with a three-week history of suprapubic abdominal pain, dysuria, unintentional 25-lb weight loss, and left lower leg numbness and weakness. He is a truck driver in Southern California delivering goods to construction sites. Computed Tomography (CT) scan of the chest, abdomen and pelvis revealed prostatic abscess, splenic abscess, cavitary right upper lobe opacities. Cultures of his prostatic and bronchoalveolar lavage fluid grew *Coccidioides immitis*, and serum *Coccidioides* serology by immunodiffusion were positive for IgM and IgG, confirming disseminated coccidioidomycosis.

Conclusion: Disseminated Coccidioidomycosis should be on the differentials on patients who presents with dysuria in endemic area.

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Received Date: *18 Apr 2023*
Accepted Date: *29 Apr 2023*
Published Date: *03 May 2023*

Citation:
Shah VD, Gao Y, Lim L, Chatta P, Rogstad D, Kazbour H. Disseminated Coccidioidomycosis Presenting as Prostatic Abscess in Poorly Controlled Diabetes. Clin Case Rep Int. 2023; 7: 1538.

Introduction

Coccidioidomycosis, a dimorphic fungal infection that presents classically as a pulmonary illness, is caused by either *Coccidioides immitis* or *Coccidioides posadasii*, and is endemic to areas particularly in the southwestern United States. The organism's spores are typically transmitted via inhalation and have shown an increase in the annual rate of infection, from a rate of 5.3 per 100,000 in 1998 to a rate of 42.6 per 100,000 in 2011, in endemic areas [1]. Approximately 1% of patients who are infected, develop disseminated coccidioidomycosis, with the most common extrapulmonary sites being skin, bones, central nervous system, and soft tissue [2-4]. Even more rare is the presentation of symptomatic genital tract infections and prostatitis as a manifestation of disseminated coccidioidomycosis. In fact, there have only been 18 confirmed cases and 6 suspected cases, but only one known recorded case of prostate abscess due to disseminated coccidioidomycosis [5,6]. We present a rare case of disseminated coccidioidomycosis in a 60-year-old male with poorly controlled diabetes and Polycythemia Vera (PV) who presented with dysuria and suprapubic tenderness found to have a prostate abscess, splenic lesions and cavitary pneumonia.

Case Presentation

A 60-year-old man with a history of uncontrolled type 2 diabetes mellitus (hemoglobin A1c 12.5%) and myocardial ischemia, presented with a three-week history of suprapubic abdominal pain, dysuria, unintentional 25-lb weight loss, and left lower leg numbness and weakness. He is a truck driver in Southern California delivering goods to construction sites. On admission, he was tachycardic with heart rate of 108 beats per minute and physical exam was notable for suprapubic tenderness. Laboratory workup was significant for leukocytosis of 16.44 bil/L (normal range 4.80 bil/L to 11.80 bil/L), urinalysis positive for pyuria with moderate bacteriuria and glucose >500 mg/dL, and final cultures grew only mixed flora. Computed Tomography (CT) scan of the abdomen and pelvis with and without contrast showed a complex multiloculated 7.9 cm × 8.1 cm × 10.4

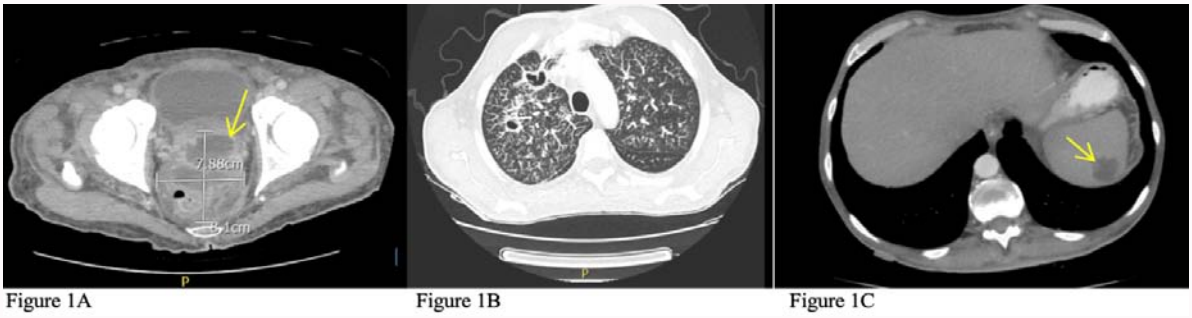

Figure 1: (A) CT abdomen and pelvis with/without contrast revealed complex multiloculated 7.9 cm × 8.1 cm × 10.4 cm prostatic abscess with likely regional colitis and cystitis. (B) Cavitary right upper lobe opacities on a background of extensive micronodularity most pronounced in the right upper lobe (miliary pattern), measuring 2.5 cm × 2.3 cm and 1.5 cm. (C) Peripheral ill-defined splenic lesions concerning for splenic abscess from hematogenous spread.

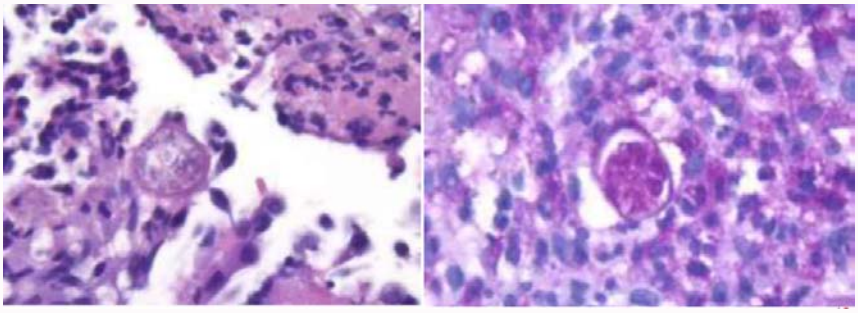

Figure 2: Coccidioides spherules seen on pulmonary biopsies obtained *via* Bronchoalveolar Lavage (BAL).

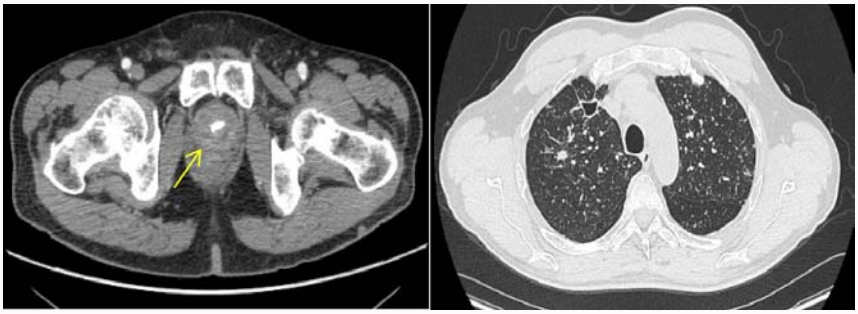

Figure 3: (A) CT pelvis at follow up showing resolution of prostatic abscess. (B) Chest CT at follow up, which revealed reduced sizes of pulmonary nodules, right upper lobe now 1.8 cm × 1.6 cm and 1.4 cm.

cm prostatic abscess (Figure 1A) with regional colitis and cystitis and heterogeneous peripheral ill-defined splenic lesions concerning for splenic abscess (Figure 1C). CT of the chest was also obtained given the patient's history of weight loss and concern for malignancy, and this revealed cavitary right upper lobe opacities on a background of extensive micronodularity, most pronounced in the right upper lobe (miliary pattern) (Figure 1B). The patient underwent radiologic-guided drainage of the prostate and splenic abscesses. Bronchoalveolar Lavage (BAL) was also performed, which showed fungal spherules consistent with *Coccidioides* organisms (Figure 2). Cultures of his prostatic and BAL fluid grew *Coccidioides immitis*, and serum *Coccidioides* serology by immunodiffusion were positive for IgM and IgG, confirming disseminated coccidioidomycosis. Antibody titers by complement fixation were negative. The patient was treated with voriconazole (4 mg/kg q12h for 9 days), micafungin (100 mg daily for 5 days), and amphotericin B (5 mg/kg for 9 days) in the acute setting and transitioned to oral fluconazole at 800 mg daily once the organism was known and infection was better controlled. Our patient reported symptomatic improvement following drainage of both the prostatic and splenic abscess along with several days of antifungal therapy. He was subsequently discharged with plans to continue fluconazole daily, for at least one year as suppressive therapy.

In addition, during the admission, our patient had persistent polycythemia with hemoglobin ranging from 17.0 g/dL to 20.2 g/dL (normal range 10.5 g/dL to 15 g/dL) and hematocrit 48.7% to 63.8% (normal range 32% to 46%). On review of his medical records, a JAK exon 12 mutation had been identified one year prior, but he was lost to follow up and was yet to initiate any medical therapy. At a one-month outpatient hematology follow-up visit, the patient was started on hydroxyurea and aspirin based on a newly established diagnosis of PV.

In regards to the response to therapy by his disseminated coccidioidomycosis infection, he underwent repeat imaging at a nine-month follow up visit, which revealed complete resolution of the prostatic abscess (Figure 3A) and significant reduction in size

of the pulmonary lesions (Figure 3B). Considering the clinical and radiographic improvement, his fluconazole dose was reduced to 400 mg daily. In addition, around the same time his hemoglobin was noted to be 13.8 g/dL and hematocrit 39.1%.

Discussion

This case represents a rare clinical entity of disseminated *Coccidioides* involving the genitourinary tract. Fewer than forty cases of *Coccidioides* involving the genitourinary tract have been identified in men, of which less than twenty involved the prostate [5]. A retrospective review of 3,676 prostate pathology reports (from biopsy and surgery), from two hospitals in areas endemic to *C. immitis*, found four cases of previously unrecognized Coccidioidal infection of the prostate, suggesting that the condition, though rare, may be underdiagnosed [5,6].

Due to its non-specific presentation, the diagnostic workup of genitourinary *Coccidioides* infection is challenging. Coccidioidal prostatitis may present with symptoms similar to that of acute bacterial prostatitis, with urinary obstruction and prostatic tenderness on exam [7,8]. Urine cultures may be helpful in diagnosing prostatic involvement especially when done after performing a prostate massage to express prostatic fluid, and the yield is improved when using a fungal culture growth medium [7,9]. However, fungal cultures of urine specimens are not routinely performed if fungal prostatitis is not suspected. In cases where clinical improvement is not seen within 48 h of medical therapy, further investigation with trans-rectal ultrasound or CT scan may be warranted [10,11].

While guidelines are lacking regarding prostatic abscess from coccidiomycosis, Abdelmoteleb et al. suggest that in cases where prostatic abscesses are larger than 1 cm or do not quickly resolve with antimicrobial therapy, drainage of the infected site should be considered, in order to prevent formation of fistulas to surrounding structures [12]. These samples should be sent for fungal, mycobacterial, and bacterial cultures, and may assist in confirming the overarching diagnosis of disseminated coccidioidomycosis, particularly in endemic areas. Guidelines by the Infectious Disease Society of America (IDSA) for management of disseminated Coccidioidomycosis recommend treatment with amphotericin B until clinical stabilization followed by itraconazole or fluconazole, with adjunct surgical intervention in select cases—those with large abscesses, bony sequestration, instability of spine, or nerve impingement [3].

While primary pulmonary coccidioidomycosis may be asymptomatic in as many as 60% of patients, concern for disseminated coccidioidomycosis should be high in patients with certain epidemiologic factors and/or risk factors (e.g., immunocompromised state) [13]. Interestingly, both, disseminated coccidioidomycosis (~1% of coccidioidomycosis cases) and prostatic abscess (0.5% of urologic cases) are exceedingly rare [3,12]. Those with HIV/AIDS off of antiretroviral therapy are especially at risk for prostatic abscesses and disseminated coccidioidomycosis [12,14]. One study also showed patients with poorly controlled diabetes (average blood glucose >200 mg/dL) were more likely to develop disseminated *Coccidioides* infections with reduced response to treatment [15].

Moreover, a case series performed by Blair et al. showed that patients with hematologic malignancies including leukemia (27%), lymphoma (27%), multiple myeloma (13%), myelodysplastic (4%), or myeloproliferative disorders, which included agnogenic myeloid metaplasia and PV (9%) were at higher risk of dissemination. Fatality from coccidiomycosis, while being disposed to such co-morbidities, was also noted to be much higher (50% when disseminated and 27% when pulmonary alone). However, it is possible that malignancy-associated morbidity and mortality from coccidiomycosis could have been exacerbated by chemotherapy or corticosteroids with associated immunosuppression [16]. While untreated PV may progress to immunocompromising conditions such as myelofibrosis and acute leukemia, PV does not necessitate fungal prophylaxis according the NCCN guidelines, as there has not been a direct relationship with increased rates of fungal infections [17].

It is suggested that cellular immunity plays a significant role in fighting acute coccidioidal infections and therefore, patients with dampened cellular immunity are more susceptible to coccidioidal infection, particularly with risk for dissemination [15,18]. A retrospective review by Santelli et al., concluded that individuals with diabetes were more likely to have cavitary lung disease and of those with diabetes, individuals with uncontrolled serum glucose concentrations were likely to have disseminated infection [15]. Diabetes has been shown to significantly weaken cellular immunity (delayed type sensitivity) reactions [19]. Prior publications have also reported increased occurrence of relapsed infection and increased difficulty in controlling disseminated coccidioidomycosis infection, in those with uncontrolled diabetes [20,21]. While it is difficult to provide a direct correlation between uncontrolled diabetes and severity of coccidioidomycosis infection, tighter serum glucose control and frequent monitoring has been recommended to perhaps prevent complications of disseminated cocci. As for the underlying history of Polycythemia Vera, some studies have shown some correlation between myeloproliferative diseases and occurrence of *Coccidioides* infection perhaps compounded by chemotherapy, which was not yet used in our patient [16].

Conclusion

Rates of coccidiomycosis disseminating to prostate and spleen with abscess formation is extremely rare. Our patient with poorly controlled diabetes may have suffered from resultant cellular immune dysfunction, increasing propensity to disseminated coccidiomycosis. In patients with poorly controlled diabetes in an endemic area, patients (namely men) who present with signs of urinary tract infection should be evaluated for possible fungal prostatitis and prostatic abscess. Our patient responded well to source control with drainage of the prostate. He was treated with broad spectrum anti-fungal in the acute setting and transitioned to long-term fluconazole, with remission of infection at 9-month follow-up. In order to prevent relapse, however, aggressive management of diabetes may be imperative in prevention of relapse. Finally, while PV may not have contributed to the initial infection, chemotherapy that may be used for treatment could increase risk of morbidity from disseminated coccidiomycosis, highlighting the importance of sufficient therapy.

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