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A Case Report of Coccidioidomycosis in the Renal Parenchyma of Unusual Severity

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Abstract

Coccidioidomycosis (CM) is an endemic fungal infection that is found in the Southwestern United States and adjacent areas of Mexico as well as Central and South America. In the United States, 150 000 to 300 000 infections occur annually. The majority are asymptomatic. Of the symptomatic cases, the majority are primary pneumonic disease that varies from mild to very severe. A minority of persons develop disseminated disease (extrapulmonary disease). These typically manifest as meningitis, osteomyelitis, synovitis, and integumentary. CM has been described in virtually every part of the body, including the genitourinary system. Disseminated CM to the genitourinary tract is well known to occur but is rarely documented. It is believed this is the first case to report disseminated CM to the renal parenchyma. Diagnosis and treatment are described in a 56-year-old Hispanic male.

Keywords

coccidioidomycosis, genitourinary coccidioidomycosis, renal coccidioidomycosis, renal parenchymal coccidioidomycosis

Introduction

Coccidioides immitis and *Coccidioides posadasii* are dimorphic fungi known to cause coccidioidomycosis (CM). These are endemic to the arid desert Southwestern United States, parts of Mexico, and Central and South America. CM is typically acquired via inhalation of infectious arthroconidia that become airborne due to the disruption of fungal-bearing soil[1] (see Figure 1).

Sixty percent of patients are asymptomatic. Forty percent may demonstrate mild to moderate pulmonary disease. Approximately 1% of infections eventuate in extrapulmonary dissemination.[1,2]

In patients who develop extrapulmonary disease, the predominant route of coccidioidal dissemination to any site is by lymphohematogenous spread. Common sites of disseminated disease include skin, subcutaneous soft tissue, joints, bone, and the meninges of the brain and spinal cord. Lesser known sites of dissemination are endocrine glands, liver, adrenal glands, and genitourinary (GU) tract. In GU CM, the kidneys are most commonly affected.[3-5] Male reproductive organs such as the prostate, testes, and the epididymis, are less commonly involved.[5]

Recognized at-risk groups for complicated and/or extrapulmonary CM include expectant mothers (typically in the third trimester), patients with uncontrolled diabetes or HIV disease, patients taking tumor necrosis factor-α inhibitors, and those with African American or Filipino ancestry. For GU CM, renal transplant recipients incur an additional 5% risk of disseminated coccidioidal renal disease. Renal transplant candidates should be evaluated for active mycotic disease prior to undergoing transplantation.[1,4,6] All aforementioned risk groups influence disease management decisions, regarding need for treatment, antifungal dosing, and duration.[1]

Clinical presentation of renal parenchymal CM largely depends on the location affected and the amount of tissue destruction. Some patients may demonstrate progressive features that wax and wane over many months to years. Others may be asymptomatic. Rarely, there is a complete resolution without medical intervention.[1] Renal dissemination is probably asymptomatic in many cases or results in vague symptoms. These include costovertebral angle (CVA) pain, fatigue, and urinary complaints with or without fever.[3-6]

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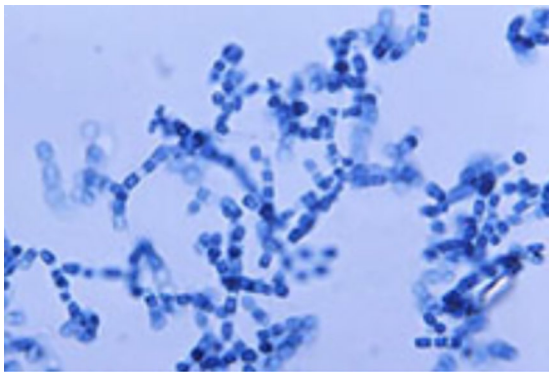

Figure 1. Photomicrograph of coccidioides arthroconidia.[2]

Genitourinary granulomas and abscesses may present rarely. Histopathology of abscess or urine fluid specimens that reveal mature spherules of *C immitis* with endospores are diagnostic for CM disease.[3,4] Urine specimens do not always yield positive immunodiffusion or complement fixation results, despite positive GU infection with CM.[3-7]

Elevated serum coccidioidal titers are both sensitive and specific for CM.[1] Other characteristic features on blood analyses may demonstrate an elevated absolute eosinophil count (≥350 cells/μL) and elevated inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate.[1,8]

Less commonly, urine specimens are examined for coccidioidouria.[3,4] In a patient without upper or lower urinary tract complaints, it is not typical to obtain fungal urine cultures for routine screenings. Reference guidelines do not comment either way on performing fungal urine culture screenings in primary and/or disseminated CM in the absence of GU symptoms. Positive urine cultures that demonstrate evidence of CM require follow-up imaging of the upper and lower GU tract.[1,2,4,5,7]

Computed tomography (CT) of the abdomen and pelvis with intravenous contrast or retroperitoneal ultrasound is recommended.[1] Renal CM radiographic findings have a broad range of presentations. They are relatively indistinguishable from other renal parenchymal diseases, although some reports have noted radiographic similarities between renal CM and renal tuberculosis.[1] The noted features in common include, but are not limited to, feathery, moth-eaten calices, infundibular constriction, and caliceal ballooning with eventual calcification of granulomas.[6] Imaging with CT or magnetic resonance imaging may reveal abscess formation. Follow-up with aspiration and/or biopsy with cultures of fluid/tissue samples is required.[1,7]

Treatment is necessarily protracted. A 3-year minimum is recommended. Azoles, typically fluconazole, are the first line of therapy. Serologic response may be slow.[1,5] Posttreatment follow-up is recommended every 2 years.[1]

Methods

Approval was obtained from the Institutional Review Board of Kern Medical. A retrospective review of the patient's record was performed. A literature search was conducted on PubMed, Research Gate, Google Scholar, Centers for Disease Control and Prevention, Infectious Diseases Society of America's *Clinical Infectious Diseases Journal* database, and American Urologic Association's *The Journal of Urology* database. The following search terms were applied: coccidioidomycosis, genitourinary coccidioidomycosis, renal coccidioidomycosis, renal parenchymal coccidioidomycosis, and disseminated GU coccidioidomycosis.

Case Report

A 52-year-old Hispanic man with diabetes mellitus was diagnosed with primary cavitary CM at another institution. He was an oil field worker in the San Joaquin Valley of California. Four years after his initial diagnosis, he was hospitalized at an outside institution for CM exacerbation with a ruptured cavitary lesion (coccidioidal empyema). He underwent video-assisted thoracoscopic surgery. His hemoglobin A1c at that time was 15%. He presented to our institution 1 month later with severe lower back pain. He had fatigue and unintentional weight loss of 20 pounds.

On physical examination, his vital signs were 36.4 °C temperature, heart rate 76 beats per minute, respiratory rate 24 breaths per minute, and blood pressure 153/98 mm Hg. His oxygen saturation was 99% on room air. The physical examination only was positive for left CVA tenderness.

Laboratory examination revealed mild eosinophilia (absolute eosinophil count 383 cells/μL) without lymphocytopenia, anemia, or thrombocytopenia. Chemistry was normal except for an elevated hemoglobin A1c 11% and hyperglycemia (fasting glucose 166 mg/dL).

Inflammatory markers erythrocyte sedimentation rate 25 mm/h and C-reactive protein 3.5 mg/L (≤0.3 mg/L) were elevated.[8] Coccidioidal serologic tests revealed elevated complement fixing antibodies (≥1:512). Initial urinalysis was positive for leukocyturia 5 to 10 cells and negative for proteinuria and glycosuria.

CT of the abdomen and pelvis imaging demonstrated a 15 × 11 × 16 cm left renal mass with cystic and solid components within the nephric and perinephric space (see Figure 2). Fluoroscopic-guided drainage of 800 cc of purulent fluid surrounding the left kidney was performed by interventional radiology as an outpatient procedure. Aspirate grew *C immitis*.

CM dissemination to the left kidney was diagnosed based on histopathologic evidence of CM. Antifungal therapy was initiated with 800 mg of oral fluconazole once daily. A nephrectomy was initially considered. The decision was deferred to allow time for observation of the patient's clinical response to antifungal therapy. A pigtail catheter and nephrostomy were inserted. The patient reported relief of his CVA pain.

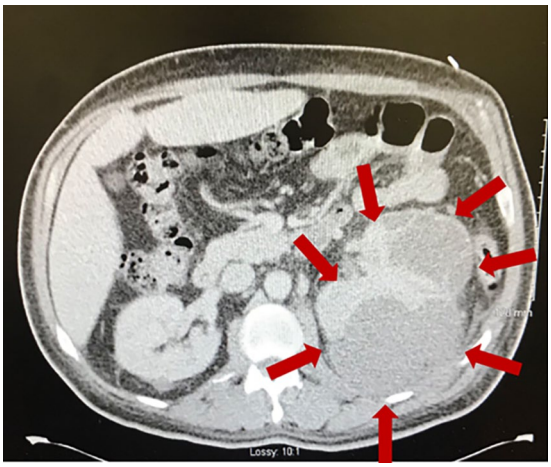

Figure 2. Computed tomography of the abdomen and pelvis with intravenous contrast of the actual patient showing heterogeneous left-sided renal abscess (15 × 11 × 16 cm) with nephric and perinephric fluid accumulation indicated by red arrows.

One month later, the patient was admitted due to decreased urinary stream from the nephrostomy and recurrent lower back pain. CT of the abdomen and pelvis revealed displacement of his pigtail catheter and nephrostomy. The nephrostomy conduit and pigtail catheter were repositioned by interventional radiology, and proper drainage was confirmed. The patient's lower back pain improved. He was discharged home and monitored closely in the clinic. His pigtail catheter was removed at 6 months of therapy. Nephrostomy tube was removed at 7 months of therapy.

Renal function throughout his entire course of CM before (glomerular filtration rate [GFR] = 70 mL/min), during (GFR = 58 mL/min), and after (GFR = 77 mL/min) antifungal therapy was preserved most of the time.

He remained adherent to antifungal therapy (oral fluconazole 800 mg daily) for 36 months. His coccidioidal complement fixation (CF) serum titers improved from 1:>512 to <1:2. Fluconazole levels were monitored regularly. His coccidioidal left renal abscess completely resolved as demonstrated by clinical improvement and radiographic evidence. Antifungal therapy was discontinued as planned at the end of the 36th month.

The patient was instructed to maintain sequential follow-up visits for routine evaluation of serum coccidioidal CF titers. His last 2 years of follow-up visits revealed CF titers <1:2. He was later lost to follow-up.

Discussion

This is the first reported case of renal parenchymal abscess as a disseminated coccidioidal disease in a living patient. Based on our extensive literature review prior cases were noted at autopsy. He is an at-risk patient with uncontrolled diabetes. Symptoms were vague; his physical examination revealed CVA tenderness. His routine laboratory test was unremarkable except for borderline eosinophilia. Imaging was nonspecific. The elevated coccidioidal serologies could be easily attributed to his pulmonary coccidioidomycosis. The aspirate and the identification of *C immitis* by stain and culture made the diagnosis. The management plan was developed from experience with the treatment of other disseminated disease.

An autopsy series from 1975 stated dissemination to the kidney was the sixth most common site for extrapulmonary coccidioidomycosis. Autopsy analysis of 50 subjects with coccidioidal-related deaths were studied in this report.[6] Two autopsy series from the 1980s described renal coccidioidal involvement in 35% to 60% of patients with fatal disease. The renal parenchyma, prostate, epididymis, and the urinary bladder have been described as known sites of involvement in chronic CM and fatal-disseminated disease.[3]

The Centers for Disease Control and Prevention acknowledges that the total number of CM cases reported are likely underestimated.[2] Tens of thousands of cases are probably missed each year due to misdiagnosis. In highly endemic areas such as the San Joaquin Valley of California and southwestern Arizona, CM is a rising cause of community-acquired pneumonias, but low testing rates suggest that CM is probably underrecognized. The true incidence of CM involvement with the GU system is largely unknown.[1,2,4]

Weinberg et al,[3] in 1984, reported that coccidioidouria occurs in patients with disseminated disease and rarely in primary pulmonary disease. The authors reported that urine specimens are seldom examined, and for this reason, GU CM has possibly been underestimated.[3]

Due to the paucity of cases, specific strategies for the treatment of disseminated CM to the renal parenchyma does not exist. Although recommendations cannot address every individual variation among patients in CM, this case demonstrates that oral azole antifungals may provide an adjunctive or alternative to surgical intervention for CM of the GU tract. Nephrectomy was considered but not required. Management was followed for soft tissue dissemination to a solid organ. See guidelines by the Infectious Diseases Society of America.[1]

The success in this case of renal CM with 36 months of oral azole therapy and renal abscess drainage may not be applicable to all cases.

Prospective trials for soft tissue coccidioidomycosis reported response rates to azole therapy ranging from 25% to 91% for disseminated disease. Of these, 60% relapsed within 45 days after cessation of therapy. Eleven percent relapsed 12 months after cessation of therapy.[1] There are no trials comparing AmB with oral azole therapy.[1]

The actual incidence of renal CM is currently unknown. It may be an asymptomatic manifestation or with vague upper and/or lower GU symptoms. The disease may not be revealed by blood or urine analysis. Anatomical seeding and subsequent local destruction affect disease presentation clinically and radiographically.[3-5]

Expert opinion may be the only resource available for treatment recommendations as in this case. It was decided at the Valley Fever Institute to administer antifungal therapy with fluconazole for a duration of 36 months in which a salutary result was achieved.

Authors' Note

This case has been proudly presented at the American Federation of Medical Research's Western Conference, January 2018, as well as the Coccidioidomycoses Study Group conference of 2018.

Declaration of Conflicting Interests

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Ethics Approval

Ethical approval to report this case was obtained from the Kern Medical Institutional Review Board (Approval ID: 17076).

Informed Consent

Informed consent for patient information to be published in this article was not obtained because he was lost to follow-up.

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