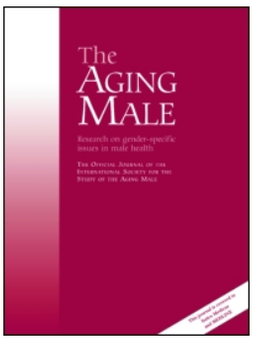

The Aging Male

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ORIGINAL ARTICLE

Fatal renal mucormycosis with *Apophysomyces elegans* in an apparently healthy male

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ABSTRACT

Mucor is an angioinvasive fungus that was reported mainly in immunocompromised patients. It usually presents as rhino-orbital, pulmonary, gastrointestinal, and disseminated disease. Isolated renal mucormycosis is an extremely rare infection in immunocompetent patients and is associated with high fatality rate. Early diagnosis, prompt antifungal treatment, and surgery give the patient the best chance for cure and survival. We describe herein a case of renal zygomycosis caused by *Apophysomyces elegans (A. elegans*) in an immunocompetent host. To the best of our knowledge, this is the first case of renal *A. elegans* to be reported from Qatar and the Middle East.

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Fungi; renal infections; immunocompetent; antifungals; mucormycosis

Introduction

Mucormycosis is a rare fungal infection caused by a group of molds called mucormycetes. These molds are ubiquitous in the environment and mainly affect people with weakened immune systems. For instance, in the United States the annual incidence of mucormycosis has been estimated around 1.7 infections per million populations; approximately 500 cases per year [1]. The most common predisposing factors for mucormycosis are HIV/AIDS, uncontrolled diabetes mellitus, cancers, chronic kidney disease, malnutrition, organ transplant, long term corticosteroid, and immunosuppressive therapy [2]. However, there have been cases of mucormycosis reported in healthy individuals with no apparent predisposing factors. *Apophysomyces elegans* is a subspecies of zygomycetes *mostly r*eported in immunocompetent patients with skin trauma [2,3]. We report a case of a healthy Indian male who developed an invasive mucormycosis of the left kidney and died with disseminated fungal infection.

Case presentation

A 35-year-old apparently healthy Indian male presented with four days history of severe left flank pain, hematuria, and fever followed by nausea, vomiting, and constipation. On examination the patient looked in pain grade 6/10, temperature 39 °C, BP 110/70 mm/Hg and had tenderness over the left flank area. Investigations revealed hemoglobin 14.4 g/dL, leukocyte blood count (CBC) 34.8×10^9/L, neutrophils 29.2×10^9/L, platelet count 241×10^3/μL, C-reactive protein 209 mg/L, procalcitonin 3.97 ng/mL, bilirubin 26 μmol/L, blood urea nitrogen 7.50 mmol/L, creatinine 128 μmol/L, LDH 1.011 μ/L, and HBA1C 5.8%. All autoimmune workup and HIV test were negative. Urine and blood cultures were sterile. His initial computerized tomography (CT) of abdomen followed by MRI (Figure 1) showed left kidney upper and mid pole lobar nephronia complicated by infarction.

Provisional clinical diagnosis of left lobar nephronia was made and the patient was started empirically on piperacillin tazobactam. The patient continued to be in severe pain with persistent fever, gradual rise in his WBC and creatinine reaching 86×10^9/L and 298 μmol/L, respectively. A CT abdomen repeated at day 7 of admission revealed progression of the bulky left kidney with heterogeneous attenuation and interval increase in the left perinephric fat stranding, with extension of the fat stranding to the peripancreatic

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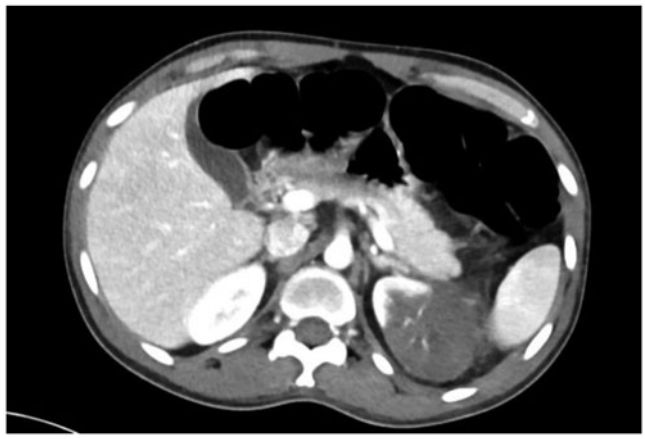

Figure 1. CT of abdomen (day2 of admission): showing left kidney with large well-defined wedge-shaped mildly swollen poorly perfused area with significant perinephric and retroperitoneal fat stranding. Delayed scan shows minimal contrast excretion from the perfused lower pole of left kidney.

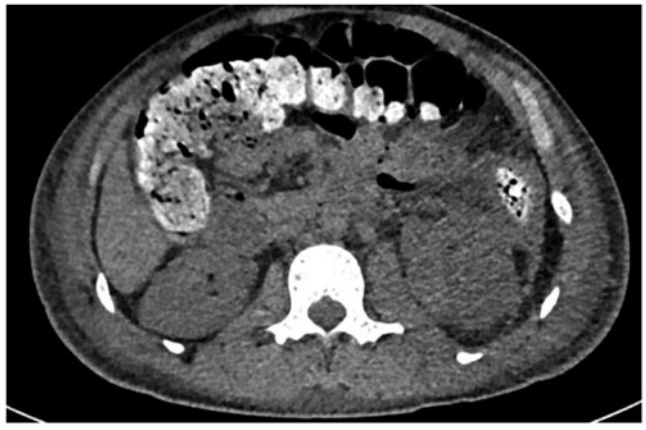

Figure 2. CT of abdomen (day 7 of admission) showing left kidney with heterogeneous attenuation and interval increase in the left perinephric fat stranding, with extension of the fat stranding to the peripancreatic region and in the pericolonic region adjacent to the splenic flexure, which appears thickened. Tiny hyperdense focus is noted in the anterior pole of the spleen, concerning for tiny hemorrhagic focus.

region and in the peri colonic region adjacent to the splenic flexure. A small hyperdense focus was noted in the anterior pole of the spleen (Figure 2). A left nephrectomy was performed on 10th day of admission.

Left nephrectomy revealed a distorted and hemorrhagic kidney (Figure 3), which on microscopic examination showed completely necrotic renal parenchyma with marked acute inflammation and abscess formation. Within many of the necrotic areas aseptate fungal hyphae, suggestive of mucormycosis were noted (Figure 4). Some of the blood vessels were thrombosed and contained aggregates of the fungal hyphae within the lumina and invading vessel walls (Figure 4).

Liposomal amphotericin B was started along with supportive measures. Patient's condition, however, continued to deteriorate. On day 4 post-surgery the patient was intubated and started on intermittent hemodialysis. A follow-up CT scan showed multiple levels of vascular occlusion, involving the superior and inferior mesenteric veins, inferior mesenteric artery, splenic artery, and vein as well as partial right renal artery occlusion. It also showed contralateral renal infarction, diffuse small bowel ischemic changes, and bilateral lung nodules. These findings were suggestive of dissemination of the fungal infection. The patient developed generalized edema, renal and respiratory failure and died on 20th day of hospitalization. Fungal culture was not done as the kidney tissue was received in formalin. We sent the formalin fixed tissue block for PCR sequencing abroad to Microbiology Laboratory at the University Medical Center, Hamburg, Eppendorf, Germany. The sequencing results showed *A. elegans* [4].

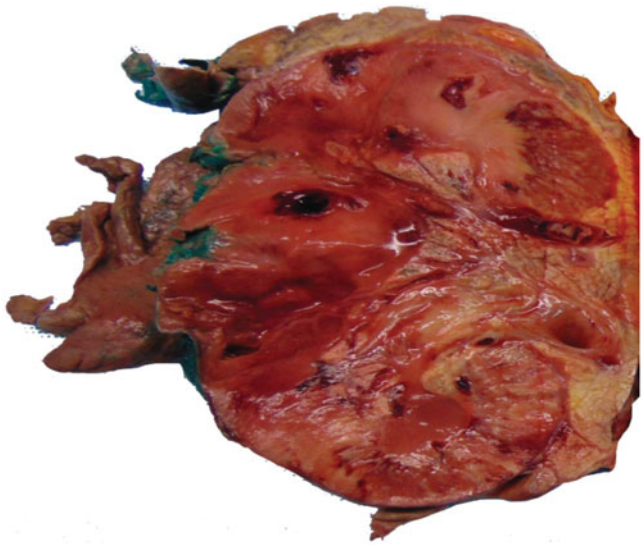

Figure 3. Left nephrectomy specimen showing diffuse inflammation and necrosis.

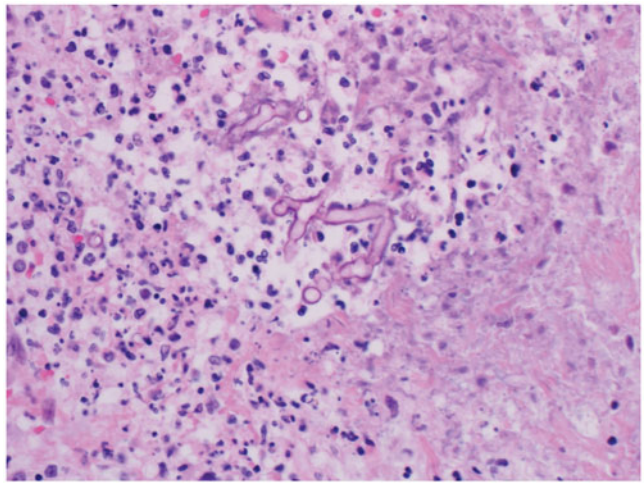

Figure 4. Left renal biopsy showing aseptate board ribbon-like hyphae in a background of inflammation and necrosis.

Discussion

Mucormycosis is an infection caused by filamentous fungi of the class Zygomycetes. They are ubiquitous in the environment and can enter the human body *via* respiratory, gastrointestinal tracts, or breached skin [5]. Once in a favorable environment, they rapidly grow and cause local and systemic disease with mortality rates reaching 100% in certain clinical scenarios [6]. Rhino-orbital-cerebral is the most common site of mucormycosis, especially in diabetic patients with mortality rate reaching above 50% [7]. Mortality is even higher for the pulmonary mucormycosis with complications including thrombosis and infraction [8,9]. Gastrointestinal mucor infection classically presents in premature and malnourished babies. The spores are ingested with contaminated food from where they can spread to other organs as well with an average mortality rate of 85%. Renal involvement by mucormycosis is extremely rare and was reported mostly in immunosuppressed patients [10–12]. Isolated renal mucormycosis is encountered in patients from certain demographic locations and risk factors. While rhino-orbital and pulmonary mucormycosis are caused by spore inhalation and skin infections are attributed to cutaneous transmission [5], isolated renal mucormycosis, is hard to explain. Its distribution restricted to a few countries shows some sort of complex transmission affected by the climate in that region.

Patients with isolated renal mucormycosis usually have predisposing risk factors like intravenous drug abuse, renal transplant history, and immunosuppression. However, isolated infection in healthy immunocompetent hosts has also been reported [13–16]. Most of the cases reported in literature were from India. For

instance, Chakrbarti et al. have described isolated renal mucormycosis as an emerging entity with around 29% of patients being healthy individuals [17]. The fungi gain entry into the skin through trauma and later disseminate to other organs. The most common clinical presentation is fever and flank pain which can be misdiagnosed as bacterial pyelonephritis. Blood, urine cultures and microscopic examination of other body fluids are usually negative as was the case in our patient. Most patients develop extensive kidney infarction leading to renal failure and subsequently nephrectomy. The diagnosis is usually histological in the cases of isolated renal mucormycosis in immunocompetent hosts [11–16]. Fungal culture and PCR are significant for determining the genus of the species. Biopsy of an infected kidney might also be helpful [17–20].

The treatment for renal mucormycosis is usually a combination of antifungal and surgery. Amphotericin B is the drug of choice for zygomycosis [21]. Itraconazole and posaconazole have also shown good *in vitro* anti-zygomatic activity [21]. Nephrectomy as treatment of isolated renal mucormycosis has been described in few cases. It is thought to limit the infection. Surgical treatment accompanied by aggressive antifungal therapy may control the spread of infection [11–16].

Conclusion

Isolated renal mucormycosis in a healthy patient is an extremely rare disease with high mortality. We should keep high index of suspicion for patients coming from endemic regions and presenting with severe flank pain, acute renal failure, sterile urine, and blood cultures. Prompt diagnosis with early surgical intervention and appropriate antifungal therapy may save the patient's life.

Disclosure statement

No potential conflict of interest was reported by the authors.

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