

*Teaching Point*  
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## Emerging role of radiological criteria for antemortem diagnosis of renal zygomycosis: an uncommon cause of acute renal failure

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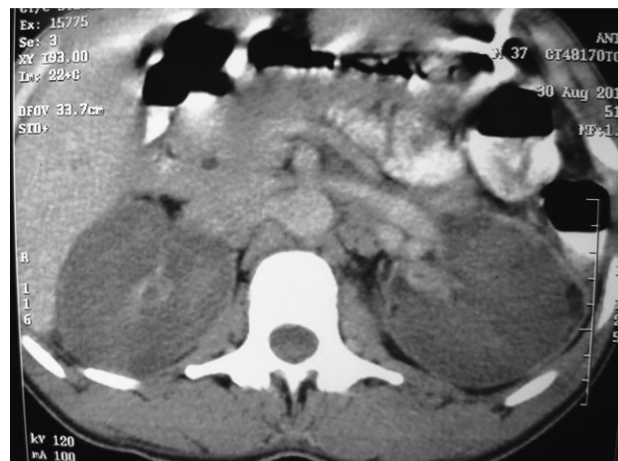
### Introduction

Renal zygomycosis is a lethal disease with a high mortality rate mainly because it is difficult to diagnose antemortem and mostly is detected after autopsy [1]. It requires the patient to have an immediate life saving nephrectomy in case of severe disease from fungal sepsis. With the advancement in modern imaging techniques, characteristic computed tomography (CT)/Doppler and magnetic resonance imaging (MRI) findings along with a strong clinical suspicion resulting in a quick urine smear for fungus can confirm the diagnosis and help in effective and more importantly early management of this grave disease. Renal biopsy reports with special stains for fungus takes hours to process, time which the treating clinician cannot afford.

### Case history

The patient was a 35-year-old young man, who presented to the emergency department with complaints of a high grade fever for 20 days, diffuse abdominal pain and altered sensorium along with passage of a very small amount of hemorrhagic urine (~100 mL in the past 24 h). He was not seropositive for HIV and did not have any history of diabetes, drug abuse, prolonged treatment with steroids or any other form of immunosuppression. He was variously treated outside for complaints of diffuse abdominal pain and fever by numerous antibiotics and had interspersed afebrile periods before he presented to us. At presentation, he was in sepsis with a total leukocyte count of  $>50\,000/\text{mm}^3$ . He was

pale and his serum creatinine was  $>10\text{ mg}\%$  and had deranged coagulation parameters. Blood gases revealed low oxygen saturation and severe metabolic acidosis, with a base deficit of  $>10$ . His abdomen was silent and before coming to us, he was being treated at a peripheral hospital on lines of acute pancreatitis. An abdominal ultrasound revealed bilateral enlarged kidneys consistent with a diagnosis of acute severe pyelonephritis. The urine culture was sterile but urine routine microscopy was full of pus cells. He received emergent dialysis in view of worsening hyperkalemia and acidosis. A CT scan was done outside (which indeed had aggravated his renal failure) which revealed bilateral globular renal enlargement and completely hypodense nonenhancing kidneys (Figure 1). The main renal artery and vein were patent on either side. There was a small part of



**Fig. 1.** A CT scan showing bilateral globular renal enlargement along with hypodense, non enhancing kidneys indicating no blood flow within them. This pattern is highly suggestive of intrarenal vascular thrombosis due to angioinvasive renal Zygomycosis. The main renal vessels are spared.

upper polar parenchyma which was being lit up by contrast (~10% of the total renal mass) and only the apical branch of the left renal artery was visualized supplying that area (Figure 2). There were pockets of subcapsular fluid collections as well. An immediate suspicion of intrarenal vascular thrombosis leading to renal infarction was raised. Our probable diagnosis included angioinvasive fungal infection of the kidneys or a systemic vasculitis affecting the intrarenal vessels. A color Doppler revealed no flow on either side in the intrarenal segmental branches, except in the left superior pole. Urine and blood cultures were sent immediately. An immediate ultrasound-guided biopsy was done and simultaneously a urine smear was sent for microscopy for fungus. We also did an MRI to characterize the renal lesion which

revealed bilateral avascular infarcted kidneys with a characteristic restriction in the T2-weighted image (Figures 3 and 4). This diffusion restriction could possibly be explained by the high iron content in the tissue which is very important for the growth of the zygomycosis fungi. The microscopy revealed aseptate right-angle branching hyphae, consistent with renal zygomycosis. The renal biopsy tissue histopathology also revealed hyphae in the glomeruli causing glomerular degeneration and disruption along with hyphae and thrombus seen in the vessel walls. The patient was dialyzed daily, stabilized and was started on intravenous Amphotericin B. He was then taken up for emergency bilateral nephrectomy via a midline abdominal incision. Intraoperatively, the ascending and descending colons along with their



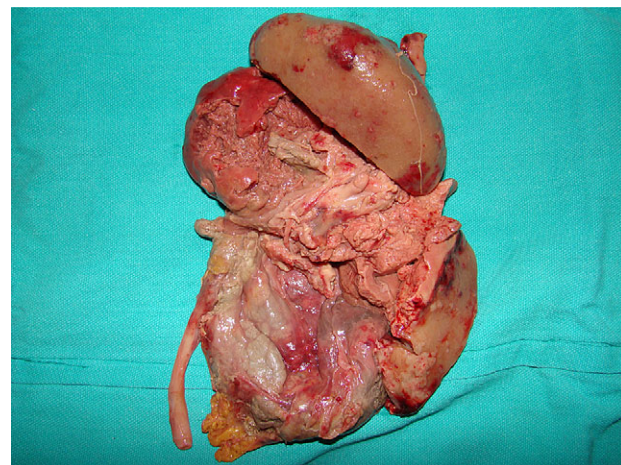
**Fig. 2.** A CT scan demonstrating bilateral hypodense kidneys with preserved blood flow at the left upper pole.



**Fig. 3.** MRI showing bilateral infarcted kidneys due to intrarenal vascular thrombosis. Only a small bit of parenchyma on the right lower pole and left upper pole is viable.



**Fig. 4.** MRI showing characteristic restriction in both the kidneys due to presence of iron, vital for the growth of fungi. This pattern is quite characteristic of invasive Renal Zygomycosis.

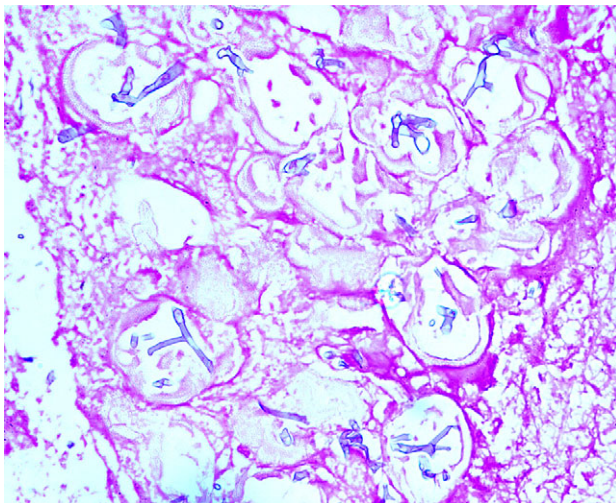


**Fig. 5.** Specimen of the left kidney demonstrating avascular kidneys with thrombosed vessels as a result of renal Zygomycosis.

respective mesocolons were diffusely inflamed and were frozen over the pararenal fat. On the left side, even the mesocolic vessels were thrombosed. We were able to do bilateral subcapsular nephrectomy and it was possible only to remove the renal tissue in piecemeal. The renal parenchyma was necrotic and foul smelling and was plastered to the posterior abdominal wall. There were satellite nodules seen on the undersurface of the liver as well which were left alone owing to the poor general condition of the patient. The specimen which was removed had hardly any viable renal parenchyma left (Figure 5). Post-operative histopathology of the tissue was consistent with renal Zygomycetes (Figure 6). The patient died in the postoperative period because of hyperkalemia, acidosis and uncontrolled sepsis. It is probable that we spent too long (around 4 days) in making a diagnosis and waiting for the histopathology report of the renal biopsy. Traditional biopsy report procedures at our institute takes ~2 days to process and the special stains for fungus took  $\geq 24$  h. Since the patient had bilateral disease and had to be made anephric by surgery, so the decision for bilateral nephrectomy was delayed till we had a histopathology report for medicolegal reasons. In the retrospect, we realized that the radiological findings of the MRI, CT Scan and Doppler were so characteristic and unmistakable that a decision to proceed to nephrectomy should have been based on them, then probably early nephrectomy could have salvaged the patient out of fungal sepsis. These modern radiological techniques are usually done within minutes on emergency basis. We also had experienced two more similar cases, one of them which was bilateral and was being managed as acute renal failure of unknown origin and the other was admitted and explored in the gastrosurgery department for intestinal obstruction. Both had similar history and radiological features as well.

## Discussion

Systemic fungal infections are rare in the kidneys but when they occur, they are difficult to diagnose antemortem and



**Fig. 6.** Histopathology of the kidney specimen demonstrating right angle branching non septate hyphae in the tubules and glomeruli suggestive of renal Zygomycosis. The glomeruli were degenerated and disrupted along with vascular invasion in the intrarenal vessels.

mostly prove lethal. Reno-invasive fungi are associated with overt segmental vascular thrombosis due to direct hyphal invasion of the renal vessels and parenchyma [1, 2]. Rarely, *Aspergillus* infection can cause intrarenal vascular thrombosis but it is most consistently seen in infection caused by the angioinvasive fungi belonging to the class zygomycosis [3, 4]. This infection has now been reclassified as zygomycosis, whereas earlier it was called mucormycosis [5]. The most common pathogenic species are *Absidia corymbifera*, *Rhizopus oryzae* and *Rhizomucor pusillus* and usually cause disseminated disease in the immunocompromised patient [3–6], although, rarely healthy subjects may also be affected [7–9]. Isolated renal involvement is uncommon and usually the kidney is involved as a part of the disseminated disease [2, 10, 11]. The isolated renal disease has mostly been described as case reports mainly from the Indian subcontinent [12–15]. The disease has so far been a nightmare to both urologists and nephrologists but in recent times, certain radiological signs have been described and searched for aggressive antemortem diagnosis of this lethal disease. These include CT and MRI and emphasize on the dire urgent need of nephrectomy based on radiology findings before even the pathology report is validated [2, 10]. The importance of characteristic radiological findings is that a combined CT/MRI and a color Doppler need just an hour, whereas a kidney biopsy with special stains takes at least 24–48 h to be validated. As we have learnt over the years that even delay of an hour in removing the kidney directly proportionates to the mortality of the patient. In our institution, we have learned to rely on a radiological protocol for diagnosing such cases rather than waiting for the pathology report. The combined findings of CT, MRI and color Doppler are so characteristic and unmistakable that a decision to remove the kidney should be based on them. At the most, a urine smear can be prepared to stain for detecting right-angle branching hyphae under the light microscope. Until the fungus laden, kidney, which is throwing out fungemia in the blood leading to fungal sepsis, is removed, the mortality approaches 100%. In such cases, an utmost aggressive and early decision to proceed to nephrectomy should be taken even if the disease is bilateral along with Amphotericin B therapy. The wait for other evidences can be lethal for the patient. Some patients in early stages can be salvaged with medical management with liposomal Amphotericin B and Amphotericin B irrigation with the help of a percutaneous nephrostomy [16].

## Teaching points

- (1) Renal Zygomycosis can also occur in healthy immunocompetent individuals. Bilateral renal zygomycosis should be suspected in any patient who presents with hematuria, oligoanuria, flank pain and otherwise unexplained diffuse acute abdominal pain, especially if he has an epidemiological link to India.
- (2) If the sepsis and flank pain are not explained by acute pyelonephritis, immediate contrast enhanced CT scan should be done, if the patient's serum creatinine is normal or else a noncontrast CT is also supportive.

- (3) Globular renal enlargements along with hypodense nonenhancing areas are quite suggestive of renal zygomycosis. Even the entire kidney could be uniformly hypodense owing to total loss of blood flow. Renal artery and vein may also be thrombosed. Renal segmental vascular thrombosis can also be confirmed on a color Doppler.
- (4) Characteristic MRI findings include all the above along with restriction in the T2-weighted image due to presence of iron, again a confirmatory feature of renal zygomycosis.
- (5) Nephrectomy should not be delayed while awaiting the histopathology report as the specimen processing and special fungal stains take 24–48 h to get validated. Each hour is crucial in renal zygomycosis. Time to nephrectomy is a strong predictor of mortality.
- (6) Even after nephrectomy, an aggressive approach is warranted with regard to the management of acidosis, electrolyte imbalance and septicemia.
- (7) Liposomal Amphotericin B should be used instead of conventional preparation especially if the disease is bilateral and the patient has elevated serum creatinine.

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*Conflicts of interest statement:* None declared.

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