Zygomycosis Presenting as Acute Bilateral Renal Artery Thrombosis in a Healthy Young Male

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Abstract
We present a case of acute renal artery thrombosis due to disseminated zygomycosis in a healthy young adult male. The diagnosis of renal artery occlusion was made on contrast-enhanced CT (CECT) and confirmation of etiology was made only on post mortem biopsy. We suggest that the presence of vascular thrombosis on CECT in a patient presenting with febrile illness should be regarded as an indicator of possible infection by angiotropic fungi, such as zygomycosis, which could help clinician to pursue histological diagnosis aggressively.

Introduction
Acute renal artery thrombosis is an uncommon condition. It is most often caused by hematological prothrombotic conditions such as antiphospholipid antibody syndrome, lupus anticoagulant in systemic lupus erythematosis, protein S and C deficiency, thrombosis associated with invasive malignancies, trauma, cocaine abuse and thromboembolism from cardiac source. Acute renal artery thrombosis due to disseminated invasive zygomycosis is very rare and few cases have been reported in the literature.¹ We report a case of acute bilateral renal artery thrombosis due to zygomycosis in a healthy young male, which was diagnosed on contrast enhanced CT (CECT) angiography, but the etiology was confirmed only by post-mortem biopsy.

Case Presentation
A 21-year male was admitted with complaints of abdominal pain and fever for 10 days and intermittent vomiting for 5 days, hematuria for 3 days and anuria for one day. Abdominal pain was diffuse, accompanied by tenderness. Fever was high grade and intermittent. Prior to admission to our unit, he was admitted elsewhere for 5 days with the above complaints and was treated with intravenous fluids and antibiotics. He was apparently healthy a month previously and the illness was not preceded by trauma. He complained of chest pain and epigastric pain 28 days prior to admission and was admitted in a nursing home for one day, where he received intravenous fluids and intravenous medications, the details of which were not available.

On examination he appeared toxic, temperature was 100° F, pulse 94 per minute, blood pressure 120/80 mmHg and respiratory rate was 24 per minute. He had mild icterus and pallor; and he had no edema or dehydration. Abdominal examination revealed scaphoid abdomen, diffuse tenderness, guarding and rigidity. The bowel sounds were sluggish. Cardiac examination was normal, respiratory examination showed diminished breath sounds in posterior basal region bilaterally and no adventitial sounds were audible. He was conscious, alert and there was no neurological deficit or meningeal signs.

Investigations done during hospitalization were as follows: Urine analysis could not be done since he was anuric. Blood urea 147 mg/dl, serum creatinine 5.5 mg/dl, serum electrolytes: sodium 142 mEq/L, chloride 105 mEq/L, potassium 4.5 mEq/L, bicarbonate 20 mEq/L, blood glucose 119 mg/dl, arterial blood gas: pH 7.33, PO₂ 60 mmHg, PCO₂ 31 mmHg, HCO₃⁻ 16.4 mEq/L, O₂ saturation 89%, serum protein 6.0 gm/dl, serum albumin 3.0 gm/dl, serum bilirubin 2.3 mg/dl (direct 1.9 mg/dl), serum ALT 139 IU/L, serum alkaline phosphatase 132 IU/L, serum uric acid 8.9 mg/dl, serum cholesterol 69 mg/dl, serum triglycerides 70 mg/dl, serum calcium 8.7 mg/dl, serum phosphorus 5.3 mg/dl, serum GGTP, serum CPK 3180 U/L, serum LDH 2750 IU/L, serum amylase 13 U/L and serum lipase 15 U/L. Hemoglobin 11.6 gm/dl, WBC count 18,400/cmm (neutrophil 93%, lymphocyte 2%, eosinophil 2%, monocyte 2%, myelocyte 1%), platelet count 100,000/cmm, peripheral smear showed neutrophilic leucocytosis with toxic granulations and malaria parasite negative, PT 21/13 (INR 1.9), PTT 38/35.

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(211/100), lupus anticoagulant negative, anti-cardiolipin IgG and IgM antibodies negative. Serology for ANA, anti-ds DNA and ANCA were negative. Leptospira IgM antibody was equivocal, Dengue serology, HIV and HBsAg were negative and blood cultures yielded no growth. Serum protein C and S assays were done later and were within normal limits.

Peritoneal fluid aspiration was done and showed RBC150/cmm, WBC 70/cmm, (Neutrophils: 75%, Lymphocytes: 25%); sugar 173 mg/dl, protein 2.7 gm/dl and LDH 1144 IU/L. Peritoneal fluid cultures were sterile and cytology was negative for malignant cells. Stool examination showed pus cells 4-6/hpf, presence of yeast cells and no ova and cysts. Echocardiography showed mild global hypokinesia of left ventricle (LV), no vegetations and LV ejection fraction of 50%. X-ray of chest was normal. Plain CT scan of abdomen showed enlarged kidneys bilaterally, which appeared edematous and showed ill-defined hypodense areas. Mild perinephric stranding was seen. There was evidence of hepatosplenomegaly, ascitis and bilateral pleural effusion with passive consolidation of both lower lobes. CT scan was repeated with contrast. It showed hypodense lesions in the right lobe of liver and posterior aspect of body and tail of pancreas and a large one in spleen, which was suggestive of infarcts. Both renal arteries showed abrupt cut-off beyond proximal portion (Figure 1), indicating occlusion with distal renal infarction. There was 80-90% occlusion at origin of coeliac artery. Lymph nodes were seen in left peri-aortic and aortocaval region.

Having made a provisional diagnosis of acute pyelonephritis at admission, he was given intravenous meropenem and vancomycin (1 gm) pending the blood and peritoneal fluid cultures. He was seen by a surgeon and he felt that there was no visceral disease which warranted surgical intervention. He also received intravenous heparin infusion after renal artery thrombosis was demonstrated on CT angiography.

However, despite these measures his condition deteriorated rapidly during the later part of 4 days of hospitalization. He developed hypotension and needed ventilator support 3 days after admission and subsequently his condition deteriorated rapidly over the next 12 hours and he died. A postmortem liver biopsy was done after obtaining the consent from the relatives, which established the diagnosis. Liver biopsy was preferred to renal biopsy for ease of performance and there was evidence of systemic involvement including liver. Post-mortem liver biopsy showed evidence of acute zygomycosis (Figure 2).

**Discussion**

Our patient had several unique features.

First, our patient was apparently healthy previously and had no risk factors for zygmocosis. Zygomycosis is a rare opportunistic infection caused by fungi of the order *Mucorales* and the genera *Rhizopus*, *Absidia* and *Mucor*. These organisms are ubiquitous saprophytes found in soil, plants and decayed food. Generally the disease is transmitted via respiratory route by inhalation of spores from environmental sources. Incidence of zygomycosis, especially due to the species *Apophysomyces elegans* is on the rise in India in the last two decades. Several factors are known to predispose to zygomycosis, such as immunocompromised state, prolonged antibiotic therapy, diabetes mellitus, administration of the contaminated intravenous drugs...

**Fig. 1**: Contrast enhanced CT angiography showing bilateral abrupt cut-off of renal arteries after origin (white broad arrows).  
**Fig. 2**: Histopathology of liver biopsy showing irregular, broad non-septate hyphae against a background of necrotic liver tissue.
and iron overload. Zygomycosis in healthy individuals is very rare, but has been reported.3

Second, he presented with febrile illness, hematuria and abrupt onset of anuria. Bilateral acute renal artery thrombosis was demonstrated pre-mortem by contrast-enhanced CT renal angiography. However, the etiology was established only post-mortem by histological demonstration of invasive fungi in the liver. Renal involvement in zygomycosis is rare, seen in 2%.4 Very few cases of acute thrombosis of renal artery are reported in the literature. In the largest series of renal zygomycosis, Gupta et al reported renal artery thrombosis in 7 out of 18 cases, all of which were diagnosed at autopsy.1 Renal zygomycosis presenting as part of disseminated disease is almost always fatal. The diagnosis is difficult since it has a rapid course and most often made post-mortem. Isolated renal zygomycosis has a better prognosis and early diagnosis is the key for a better outcome in renal zygomycosis. However, definitive pre-mortem diagnosis of zygomycosis is often difficult, due to 1) blood and tissue culture for zygomycosis are often negative and 2) a positive culture may not be sufficient to make a definitive diagnosis due to the possibility of a contamination of this ubiquitous saprophyte. Definitive diagnosis of zygomycosis is made on histological demonstration of invasion of hyphae. Recent advances in radiological imaging provide an opportunity to make provisional diagnose of zygomycosis early and pre-mortem. Several characteristic findings on contrast-enhanced CT (CECT) are described in renal zygomycosis, such as enlarged kidneys, inhomogeneous or non-enhancement of kidneys, areas of low attenuation and perinephric fluid collection.5 Vascular invasion with thrombosis and infarction of vessels at different vascular beds is a hallmark of disseminated zygomycosis and CECT renal angiography would help one to suspect the disease. Indeed, in our case a correct diagnosis was not made by initial non-contrast CT. Even though there were features to suggest possible fungal infection of kidneys such as enlarged kidneys with hypodense areas within, diagnosis of renal artery thrombosis was made only by CECT renal angiography. There is a widespread reluctance amongst clinicians to do a contrast study in a patient with renal failure and we feel that one should supersede this in certain situations, to do CECT to make an early diagnosis of renal artery thrombosis. The presence of vascular thrombosis on CECT in a patient presenting with febrile illness should be regarded as an indicator of possible infection by angiotropic fungi, such as zygomycosis, which could help clinician to pursue histological diagnosis aggressively.

Third, the possible route of inoculation remains unclear in our patient, but we speculate that intravenous route by prior administration of intravenous medications was a probable source. The pathogenesis of zygomycosis in our patients is unclear. In our patient, zygomycosis involved predominantly kidneys and liver and apparently sparing lungs. But one can speculate that he may have been predisposed to develop this infection possibly due to two reasons, 1) prior antibiotic therapy received for upper respiratory infection and 2) the administration of intravenous fluid contaminated with the fungus. Indeed, experimental intravenous inoculation of Absidia spores in mice resulted in germination and pathological changes predominantly in kidney and brain, but not lungs.6

Conclusion

We conclude that renal zygomycosis may present as acute renal artery thrombosis and should be suspected in a febrile patient with abrupt anuria. Contrast-enhanced CT would help to strengthen this diagnosis, but eventually requires histological proof to confirm zygomycosis.

References