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Isolated Renal Mucormycosis Post Covid-19 Infection

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Abstract: The following case describes a 49 year old gentleman who developed COVID-19 infection and was treated with injectable steroids. Two months after the infection he developed bilateral hydroureteronephrosis and renal failure. On evaluation, it was detected that he has bilateral ureteric strictures. Despite bilateral DJ stenting his renal failure persisted and the hydroureteronephrosis recurred after removal of stents require restenting on the left and PCN placement on the right side. Since his renal failure persisted, DTPA scan done showed non functioning right kidney. Right nephrectomy was subsequently done and it showed Mucormycosis on histology. He was subsequently treated with liposomal amphotericin B, however his constitutional symptoms persisted. A FDG-PET did not show FDG uptake elsewhere except the left kidney. Subsequently he underwent left nephrectomy, which too showed mucormycosis on histopathology. Posaconazole was continued for another 3 months. Patient is doing well symptomatically, with no fever and has gained weight. He is being worked up for a renal transplant.

Keywords:. COVID-19, Renal Mucormycosis, Post Covid infection.

CASE SUMMARY

49-year-old gentleman with no prior comorbidities was admitted for COVID-19 infection in April 2021. He presented with cough, fever, and breathlessness. His HRCT lung showed a score of 11/25 and was treated with injectable steroids for duration of 1 week. He did not receive remdesivir, heparin or plasma therapy. His creatinine was 0.9 mg/dl in this admission.

In June 2021, he complained of backache and decreased urine output. He had renal dysfunction with a serum creatinine of 5.6 mg/dl, oliguria and pulmonary edema. He was initiated on hemodialysis for the same. On further evaluation he was detected to have bilateral HUN on CT KUB. He underwent a cystoscopy with bilateral retrograde pyelography and was detected to have bilateral mid-ureteric strictures. There was no history of prior tuberculosis, calculi, tumours, urinary tract infections or urinary interventions and procedures. He underwent DJ stenting for the same. Despite the above intervention his renal functions did not recover. A renal biopsy was performed which was reported to have moderate acute tubular necrosis and acute interstitial nephritis. The details of subsequent treatment were not available, however the kidney functions settled with serum creatinine of 4.6mg/dl and did not require further hemodialysis. His stents were removed in September 2021. Subsequently had a decline in his urine output. His renal functions worsened and required hemodialysis again. He underwent repeat DJ stenting of the left kidney while the right kidney could not be stented in view of the tight stricture. Eventually a percutaneous nephrostomy was done on the right side with good drain output of 1000ml per day. His per urethral output was 400ml per day. However, the renal functions did not recover and the patient required maintenance hemodialysis.

He presented to our centre with the above history. CT KUB done showed right kidney of 10 cm with mild hydronephrosis, with nephrostomy tube in situ. Left kidney measured 11.4 cm and showed moderate hydronephrosis with DJ stent in situ. Mild to moderate perinephric fat stranding was noticed. Ureters were however reported to be normal.

Urinalysis for acid fast bacilli done thrice was negative. Urine microscopy showed numerous pus cells; however, the culture was negative. In view of non-recovery of renal functions, and right kidney being non-functioning on DTPA scan; right nephrectomy was performed. The histopathology showed multiple well-formed granulomas with central necrosis and fungal hyphae suggestive of renal mucormycosis. He was treated with liposomal Amphotericin B for 3 weeks followed by Posaconazole. He did not respond, had poor appetite, weight loss, anaemia requiring packed red blood cell transfusions, malnourishment, intermittent fever with sterile cultures. PET scan did not show FDG uptake elsewhere except the left kidney. Subsequently underwent left nephrectomy, which too showed mucormycosis on histopathology. Posaconazole was continued for another 3 months. He being anephric, is on maintenance hemodialysis through a tunneled cuff catheter, with his anemia of chronic disease & mineral bone disease parameters optimised. He is

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doing well and has gained 10 kgs in the last month. He is planned for renal transplant with his wife as the prospective donor.

DISCUSSION

Mucormycosis, earlier called zygomycosis, is an infection with fungi belonging to the order Mucorales. Rhizopus species are the most causative organisms of this group. Mucormycosis causing species include Mucor, Cunninghamella, Apophysomyces, Lichtheimia, Saksenaea, Rhizomucor, and other species in descending order.(Kwon-Chung, K.J, 2012) Mucormycetes are thermotolerant molds that are found in the environment.(Richardson, M, 2009) Transmission occurs through inhalation, inoculation, or ingestion of spores from the environment. There are five major clinical forms (Rhinocerebral, Pulmonary, Cutaneous, Gastrointestinal, Disseminated) of mucormycosis. The rhinocerebral and pulmonary infections are the most common.(Petrikkos, G. *et al*., 2012- Spellberg, B. *et al*., 2005) Most mucormycosis infections are life-threatening. Risk factors such as diabetic ketoacidosis and neutropenia are present in most cases. Successful mucormycosis treatment requires correction of the underlying risk factor(s), antifungal therapy (traditionally with a polyene), and aggressive surgery. Since mucor is an angio-invasive fungus causing extensive necrosis, antifungal therapy alone fails because of poor tissue penetration. They are vasotropic and angioinvasive, usually affecting immunocompromised patients. Disseminated mucormycosis generally occurs in the immunocompromised host and has a high mortality reported up to 75–100%. Renal involvement due to mucormycosis mostly occurs concurrently with disease affecting other parts of the body or as a part of disseminated disease.(Dansky, A.S. *et al*., 1978; Ingram, C.W. *et al*., 1989) Interestingly, majority of the patients (75%) suffering from isolated renal mucormycosis in India are apparently healthy individuals.(Gupta, K.L. *et al*., 1999) The incidence of COVID-19-associated mucormycosis (CAM) has increased in India, however, presentation of mucor as isolated bilateral renal involvement is still rare.(Revannavar, S.M. *et al*., 2021-Sen, M. *et al*., 2021) Survival after isolated renal mucormycosis has been reported to be 65% with combined surgical debridement and antifungal therapy.(Verma, R. *et al*., 2011)

Chakrabarti et al. in their 10 years of experience reported two cases of isolated renal mucormycosis, who were treated with antifungal therapy alone but did not survive. (Chakrabarti, A. *et al*., 2001)

The largest series of zygomycosis from India had 129 patients; the rhino-orbito-cerebral type was most common (44.2%) and renal involvement was seen in 14.0% of patients. About 23% of patients were apparently healthy and 35% were diagnosed postmortem.(Chakrabarti, A. *et al*., 2001) The cutaneous form is most common in immunocompetent patients, followed by rhino-orbito-cerebral disease.(Petrikkos, G. *et al*., 2023; Mignogna, M.D. *et al*., 2011)

IRM (Isolated Renal Mucormycosis) has been reported in patients with acquired immune deficiency syndrome, intravenous drug abusers and those on corticosteroid therapy.(Weng, D.E. *et al*., 1998; Levy, E. *et al*., 1995) In contrast, IRM in immunocompetent individuals is extremely rare and the majority of cases have been reported from the Indian subcontinent and China.(Yu, J. *et al*., 2006; Jianhong, L. *et al*., 2004)

It is presumed to occur via seeding of kidneys during an episode of fungemia from a subclinical pulmonary focus or due to ascending infection of the urinary tract.(Stas, K.J. *et al*., 1996; Gupta, K. *et al*., 2010) Renal parenchymal necrosis results from angioinvasion of fungal hyphae, leading to vascular thrombosis and infarction. Mucor hyphae may also invade the glomeruli and tubules, sometimes with associated giant cell reaction and granuloma formation.(Sharma, R. *et al*., 2006)

As reported by Dharmendra Bhadauria et al. patients presented with oligoanuric renal failure, six were dialysis dependent and most of patients were treated initially in lines of sepsis-/pyelonephritis-induced AKI; as in our case; while specific therapy was confirmed subsequently. (Bhadauria, D. *et al*., 2018)

Gupta et al. described six patients with bilateral renal involvement and all of them presented with severe irreversible renal failure and died while one patient was successfully treated, who had unilateral disease and had undergone nephrectomy. Specific infective species were identified in 2 of the 18 patients, with Rhizopus arrhizus and A. elegans. (Gupta, K.L. *et al*., 1999)

Pahwa et al. in their single case report of IRM with no identifiable risk factors, proposed that simple nephrectomy without antifungal therapy may be sufficient in immunocompetent, afebrile, nontoxic patients with a coincidental finding of renal

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mucormycosis in a nephrectomy specimen. (Pahwa, M. *et al*., 2013)

Chugh et al. found four cases of IRM; three were immunocompetent and one had bilateral disease. All three cases underwent nephrectomy in combination with antifungal therapy and two succumbed to the illness. (Chugh, K.S. *et al*., 1993)

On contrast-enhanced CT of the abdomen, findings described as 'diffuse patchy nephrogram' may include enlargement of the kidneys, nonenhancing areas in the parenchyma, reduced or absent contrast excretion and perinephric collections. In the presence of such suspicious radiologic findings, a biopsy is indicated to confirm the diagnosis. In our case, biopsy did not reveal the diagnosis and it was histopathology of nephrectomy specimen which clinched the diagnosis. Stas, K.J. *et al*., 1996 -(Levy, E. *et al*., 1995)

Diagnosis of mucormycosis is difficult, especially antemortem, due to variable clinical presentation and limitations in achieving a tissue diagnosis. Even in immunocompetent patients, with a high index of suspicion, nonresolving pyelonephritis should prompt the possibility of a fungal infection.

Molecular diagnosis with real-time polymerase chain reaction has also been suggested for early diagnosis.(Verma, R. *et al*., 2011)

Our patient had only mild COVID-19 infection and had received short duration of steroids. He is thus presumed to be relatively immunocompetent, however we did not do a specific evaluation for other primary immunodeficiency syndromes, which could be considered as limitation of our report. However, a high index of suspicion for rapid diagnosis and early initiation of systemic antifungal therapy and surgical intervention are necessary for this life-threatening condition.

The more common causes of non-responding pyelonephritis are generally obstruction due to stone, sloughed papilla, blood clots or intraluminal tumors. In a clinical scenario of non-responding pyelonephritis who has been treated and evaluated logically, a change of management plan to push for histological diagnosis is required early on. More detailed studies though are required to evaluate for occult immunodeficiency state.

CONCLUSION

This case describes the rare incidence of renal mucormycosis requiring bilateral nephrectomy in a patient with no comorbidities except the COVID-19 infection two months prior to the development of hydronephrosis and ureteric stricture. There was no evidence of mucormycosis elsewhere in the body for the patient.

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