

Post Covid-19 Invasive Renal Mucor mycosis with acute renal failure; a case report and review of literature

Farzana Rasheed Narejo, Asma Nasim, Nazrul Islam Jafiri, Shaheera shakeel, Syed Fazal Akhter

Sindh institute of Urology and Transplantation (SIUT), Karachi. Pakistan

Abstract: The worst nightmare of twenty first century has been discovered, The Coronavirus, has been risen the incidence of Mucor mycosis during the (COVID-19) pandemic. There are many case reports of rhino-orbito-cerebral and pulmonary Mucor mycosis. Hypertension, COVID, and Mucor mycosis are lethal combination associated with high mortality. This is the first case of Covid-19 associated Mucor mycosis (CAM) in the kidneys from Pakistan. We report the case of a 68-years old woman who presented with fever, abdominal pain and renal failure. Mucor mycosis was diagnosed on renal biopsy. She was managed with Amphotericin- B and hemodialysis via tunneled vascular catheter. She refused nephrectomy. The case highlighted CAM can present as localized renal Mucor mycosis. In this era of Covid pandemic CAM should be in the differential diagnosis.

Key Words: Acute kidney injury, Mucor mycosis, Covid-19, infarct, amphotericin.

Corresponding Author:

Dr. Farzana Rasheed Narejo

Dept of Nephrology,
SIUT, Karachi. Pakistan

Email: farzanarasheednarejo@gmail.com

DOI: 10.53778/pjkd82255

Received 24 April, 2024 and accepted 21 June, 2024

PJKD 2024;8(2):31-36

Introduction:

Corona virus disease-2019 (Covid-19) pandemic played havoc worldwide. Covid-19 infection ranges from mild to life threatening infection usually presenting as fever, cough, and dyspnea and may lead to acute respiratory distress syndrome.¹ Covid-19 associated Mucor mycosis (CAM) is a rare fatal coinfection usually mainly affects rhino cerebral, orbital, and pulmonary and central nervous system. Risk factors are diabetes mellitus (DM), hypertension (HTN), steroid use, solid organ transplant, end stage renal disease (ESRD) and acquired immunodeficiency syndrome.² Overall, the global incidence of Mucor mycosis is between 0.2 -14 per 100,000 population. During Covid-19 there was a surge of mucor infection. The most highly affected country was India where there was a 2.1 fold increase in CAM cases.³

To the best of our knowledge, our case is the first Post-Covid isolated renal Mucor mycosis with renal failure from Pakistan.

Case:

A 68-year-old female presented in May 2021 with fever, shortness of breath on minimal exertion, nausea, vomiting, decrease urine output and abdominal pain for 4-5 days. The preliminary investigation showed acute kidney injury and renal replacement therapy was initiated, where 3 sessions of hemodialysis performed. Later patient self-referred to our center for further management of renal failure. She was diagnosed as Covid-19 pneumonia by nasopharyngeal swab in April 2021 and treated with injection dexamethasone 6 mg intravenous for 5 days and never required oxygen. She had well

Renal Mucor Mycosis

controlled HTN for 15 years and generalized urticaria for 12 years which was being treated with some unknown intramuscular injections.

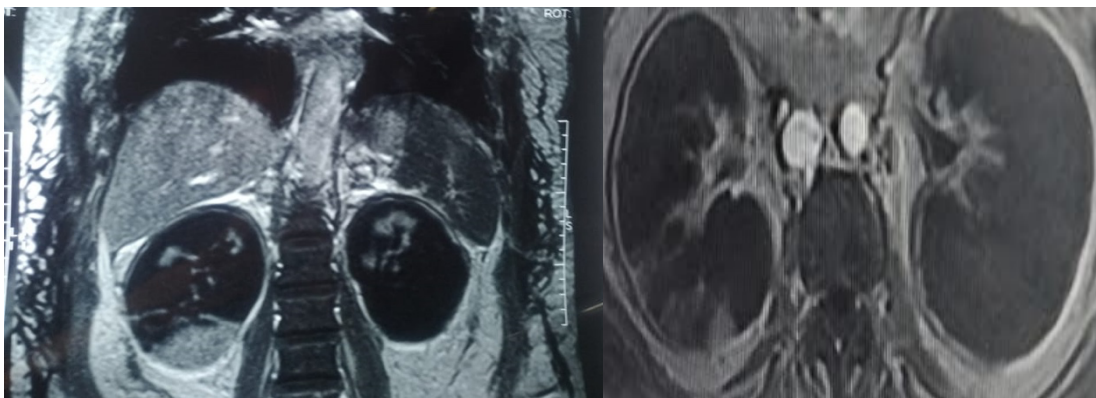
On admission she was found to be confused, pulse 120 b/min, blood pressure 156/95mmHg, respiratory rate 20 breaths/min, temperature 98°F, anemic, JVP was 10 cm, bilateral pedal edema up to mid-thigh. On systemic examination, crepitation at both sides of bases in respiratory system, audible S3, mild tenderness at left lumbar region and no focal neurological deficit.

Laboratory investigation on admission were serum urea 204 mg/dl, creatinine 4.73mg/dl, sodium 136 meq/l, potassium 7.0meq/l, chloride 107meq/l, bicarbonate 14meq/l, calcium 9.88mg/dl/l, phosphorus 9.40mg/dl, alkaline phosphate 298u/l, Hb 8.8g/l, MCV 88, TLC 26.21(4000-10,00), neutrophils count 78% Plt 92000, HbsAg, anti-HCV antibodies were non-reactive, total bilirubin 1.69mg, direct bilirubin 0.68mg, SGOT 95u/l, SGPT 46u/l, GGT 342u/l, serum total protein 5.54g, albumin 1.7g, globulin 3.63g, LDH 334u/l, PT 11(10.5), APTT 24.2(25.5), INR 1.05(1.0). Urine analysis showed albumin+, numerous RBC. ANA negative, C3 0.52g/l(0.79-1.59g/l), C4 0.07g/l(0.16-0.38g/l), IgM 0.78g/l(0.46-3.04g/l), IgG 5.55g/l(7.51-15.60g/l), IgA 2.39g/l(0.83-3.04g/l), ASOT 64.50iu/ml(166-250). HIV serology negative. ANCA and Anti GBM negative, HCV (RNA - negative) are also negative.

Urine cultures and blood cultures were no growth. In ECG her heart rate was 100 with normal rhythm and axis. 2D echocardiography did not reveal any vegetations. Chest X ray found interstitial edema with cardiomegaly.

MRI abdomen with contrast showed, there was an hypodense sharply demarcated wedge shape area 2.5 x 6.3cm in the inferior pole of the right kidney extending to renal capsule and adjacent perinephric fat and another hypodense area in middle region of left kidney with the likely possibility of an abscess or infarct (Figure -1).

Figure: 1 MRI abdomen with contrast showing wedge shaped inferior pole area involved with an infarct or abscess.



A differential diagnosis of acute pyelonephritis with abscess in the beginning was made and Meropenem was started empirically. Unfortunately, patient still required hemofiltration after 4 weeks of renal failure

Renal Mucor Mycosis

and febrile with spikes of 101°F despite 14 days of broad spectrum antibiotics. So it was decided to perform renal biopsy from left kidney to find out the cause of unexplained acute kidney injury of 4 weeks duration. Histopathological examination revealed on hematoxylin and eosin (H&E) stain, broad, aseptate, fungal hyphae with wide right angle branching in a necrotic mixed inflammatory background along with infiltration and disruption of the vessel wall leading to extensive cortical infraction. (figure2). The diagnosis of isolated renal Mucor mycosis was made. Amphotericin B was started at 1.5mg/kg and advised for nephrectomy. After multiple counseling the patient and the family refused for nephrectomy. She remained admitted and received amphotericin B for 4 weeks. Due to non-availability of new azoles like Posaconazole or isavuconazole in our country, we switched her to oral itraconazole. She was alive after 8 weeks of therapy but on maintenance hemodialysis.

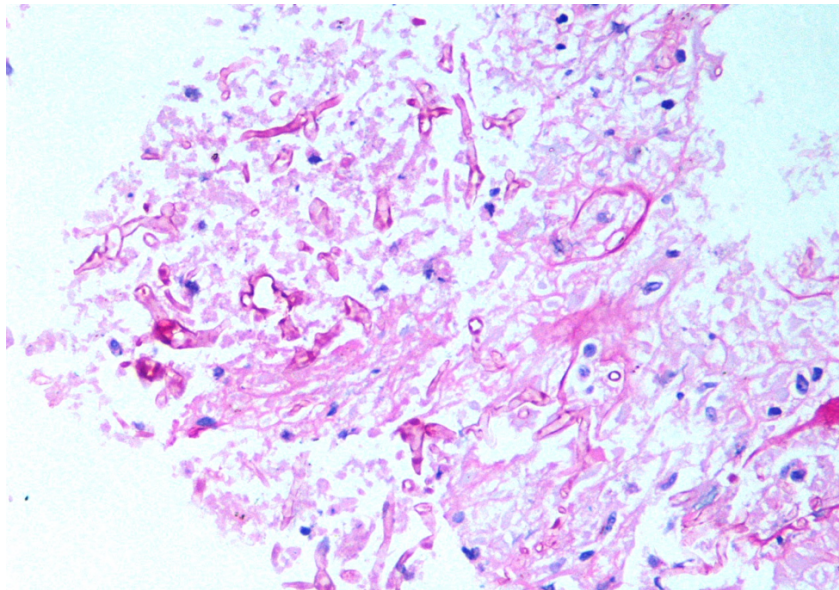


Figure 2: Histopathology of renal biopsy showing fungal Hyphae

Discussion

Covid associated Mucor mycosis is a well-known complication post-Covid-19 infection worldwide.⁴ Majority of cases are reported from low and middle income countries particularly from India.⁵ The most common manifestation is rhino-cerebral Mucor mycosis with mortality as high as 40%.³ Mucor is a mold which could infect humans. The most commonly genera infecting humans are Rhizopus, Mucor, and Rhizomucor. It is found on decomposed vegetables and in soil.⁶ The infection occurred through inhalation of spores in the environment which mainly affect rhinocerebral area, orbit and pulmonary system etc.² Mucor is an angio-invasive mold causing infarction and necrosis. The main pathogenesis of mucor infection is its ability to acquire iron from the host and multiply. Hence presence of free iron in the host secondary to acidosis is the main pathogenesis of Mucor mycosis. Diseases that can cause increase acidosis like uncontrolled diabetes mellitus and renal failure increase the risk of Mucor mycosis.⁷ The use of steroids in Covid-19 increase blood sugars which can act similar to patients with diabetes.⁸ Furthermore Covid-19 causes excessive production of hepcidin which increases intracellular iron production causing increase susceptibility to mucorale infections.⁹

Renal Mucor Mycosis

Clinically isolated renal Mucor mycosis can present in two different ways. Acute state, which can present as fever, acute kidney injury and features of sepsis where the histopathological lesions show hemorrhagic infarcts, coagulation necrosis, angio-invasion and infiltration by neutrophils. The chronic presentation can be nonspecific vague illness with presence of a mass in the abdomen and histopathologically characterized by granulomatous inflammation with presence of giant cells.¹⁰ Definitive diagnosis can be made by either culture or polymerase chain reaction of the tissue specimen.¹¹ The standard treatment of isolated renal Mucor mycosis is debridement or nephrectomy with intravenous amphotericin followed by prolonged treatment with posaconazole or newer isavuconazole. However the mainstay of successful treatment is early recognition and treatment.¹²

Table 1: The clinical characteristics and outcome of reported cases of post-Covid renal Mucor mycosis including this case.

Case and year reported	Age/ Sex/ comorbids	Time since Covid	Signs and symptoms	Imaging	Diagnosis	Treatment	Outcome
Kumar et al ¹⁷ India (2022)	31/M/no	21 days	Hematuria, oliguria, hemodialysis	CT: bilateral renal infarcts	Histopathology, urine culture	Nephrectomy Histopathology	Alive
Chau et al, ¹⁶ Australia (2023)	51/M/no	5wks to 2 mths	rhino-orbital-cerebral and renal	CT: renal abscess	Histopathology, PCR	Amphotericin, posaconazole, orbital exenteration, nephrectomy	Alive
Sethia et al ¹³ India (2022)	46/M/DM	2 months	Fever, flank pain, hemodialysis	CT: emphysematous pyelonephritis	Histopathology	Amphotericin B	Died
Madhumitha et al ¹⁹ India (2022)	64/M/DM	1 month	abdominal pain, dysuria, hematuria, and decreased urine output	CT: left kidney air specks and renal vein thrombosis	Histopathology	Amphotericin B	Died
Vaddi et al ¹⁴ India (2022)	62/ F/non-DM	1 week	Hematuria, anuria	CT: bilateral hydronephrosis	Tissue aspirate culture	Percutaneous nephrostomy, Liposomal amphotericin, posaconazole	Died
Nepali et al ¹⁵ Nepal (2022)	38/M/no	5 month	Dysuria, Oliguria,	CT: mass right vesicoureteric junction and distal ureter, hypodensities in renal cortex	Histopathology of necrotic mass	Nephroureterectomy, liposomal amphotericin, posaconazole	Alive
Singh et al India ²⁰ (2021)	32/M/no	1 month	Abdominal pain, constipation, vomiting	CT: Right renal infarction and artery thrombosis	Histopathology	Nephrectomy	Died
Choudhary et al ²¹ India (2021)	32/M/ Non-DM	45 days	Fever and flank pain	CT: left pyelonephritis	Histopathology	Nephrectomy and bowel gangrene, liposomal amphotericin	Died
Narejo et al Pakistan (2023)	68/F/HTN	1month	Shortness of breath, abdominal pain, oliguria	CT KUB: bilateral renal infarcts	Renal biopsy	Amphotericin B, itraconazole	Alive

Renal Mucor mycosis post Covid-19 is extremely rare. To the best of our knowledge so far 8 cases of post-Covid renal Mucor mycosis post has been reported in the literature.¹³⁻¹⁸ Table 1 shows reported cases in the literature. Majority were male, average age was 44.5 years, average time since Covid infection was 16 weeks. Almost all needed nephrectomy and the diagnosis was made on histopathology of renal tissue. Three out of 8 cases were successfully treated and the mortality was very high around 60%. Our patient was a middle-aged female presented 4 weeks post-covid with bilateral renal infarcts which was found to be Mucor mycosis on biopsy. She refused further treatment and left against medical advice.

In conclusion, post-Covid localized renal Mucor mycosis is an uncommon infection with fatal outcomes. This case demonstrates the emphasis on earlier histological diagnosis in non-resolving pyelonephritis.

References:

1. Baqi S, Naz A, Sayeed MA, et al. Clinical Characteristics and Outcome of Patients With Severe COVID-19 Pneumonia at a Public Sector Hospital in Karachi, Pakistan. *Cureus*. 2021;13(2):e13107.
2. Rudramurthy SM, Hoenigl M, Meis JF, et al. ECM/ISHAM recommendations for clinical management of COVID-19 associated Mucor mycosis in low- and middle-income countries. *Mycoses*. 2021;64(9):1028-1037.
3. Tayabali K, Pothiwalla H, Narayanan S. Epidemiology of COVID-19-Associated Mucor mycosis. *Curr Fungal Infect Rep*. 2023;1-20.
4. Hoenigl M, Seidel D, Carvalho A, et al. The emergence of COVID-19 associated Mucor mycosis: a review of cases from 18 countries. *Lancet Microbe*. 2022;3(7):e543-e552.
5. Ozbek L, Topcu U, Manay M, et al. COVID-19-associated Mucor mycosis: a systematic review and meta-analysis of 958 cases. *Clin Microbiol Infect*. 2023;29(6):722-731.
6. Walther G, Wagner L, Kurzai O. Updates on the Taxonomy of Mucorales with an Emphasis on Clinically Important Taxa. *J Fungi (Basel)*. 2019;5(4).
7. Ibrahim AS, Spellberg B, Walsh TJ, Kontoyiannis DP. Pathogenesis of Mucor mycosis. *Clin Infect Dis*. 2012;54 Suppl 1(Suppl 1):S16-22.
8. Tamez-Perez HE, Quintanilla-Flores DL, Rodriguez-Gutierrez R, Gonzalez-Gonzalez JG, Tamez-Pena AL. Steroid hyperglycemia: Prevalence, early detection and therapeutic recommendations: A narrative review. *World J Diabetes*. 2015;6(8):1073-1081.
9. Perricone C, Bartoloni E, Bursi R, et al. COVID-19 as part of the hyperferritinemic syndromes: the role of iron depletion therapy. *Immunol Res*. 2020;68(4):213-224.
10. Cornely OA, Alastruey-Izquierdo A, Arenz D, et al. Global guideline for the diagnosis and management of Mucor mycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium. *Lancet Infect Dis*. 2019;19(12):e405-e421.
11. Hammond SP, Bialek R, Milner DA, Petschnigg EM, Baden LR, Marty FM. Molecular methods to improve diagnosis and identification of Mucor mycosis. *J Clin Microbiol*. 2011;49(6):2151-2153.
12. Singh SK, Wadhwa P, Sakhuja V. Isolated bilateral renal Mucor mycosis. *Urology*. 2004;63(5):979-980.
13. Sethia RK, Charag AH. A case of isolated unilateral renal Mucor mycosis post COVID-19 pneumonia with fatal outcome. *Urol Case Rep*. 2022;43:102061.
14. Vaddi SP, Khetavath SM, Babu DM, et al. Bilateral Renal Mucor Mycosis Presenting as Anuria in a Covid 19 Recovered Patient: A Case Report and Review of Literature. *Urology*. 2022;161:12-14.
15. Nepali R, Shrivastav S, Singh Shah D. Renal Mucor mycosis: Post-COVID-19 Infection Presenting as Unilateral Hydronephrosis in a Young Immunocompetent Male. *Case Rep Nephrol*. 2022;2022:3488031.
16. Chau M, Swarbrick N, Kong J. Renal Mucor mycosis in post-COVID patients in Australia. *Urol Case Rep*. 2023;47:102353.
17. Kumar RK, Annigeri RA, Gopalakrishnan R, Kaveripattu SS, Jain N. Bilateral renal Mucor mycosis following COVID-19 infection: A therapeutic challenge. *Clin Nephrol Case Stud*. 2022;10:76-81.
18. Madduri VKS, Jena R, Baid G, Choudhary GR, Sandhu AS. Renal Mucor mycosis presenting during the COVID-19 pandemic: A series of 11 cases from a tertiary care center in India. *Indian J Urol*. 2022;38(2):115-120.

Renal Mucor Mycosis

19. Mukuntharajan BMGRNKT. Post-Covid Renal Mucor mycosis: A Case Report. *Journal of Gastrointestinal and Abdominal Radiology* 2022;5(1).
20. Singh T, Chaudhari R, Gupta A. Renal artery thrombosis and Mucor mycosis in a COVID-19 patient. *Indian J Urol.* 2021;37(3):267-269.
21. Choudhary GR, Aggarwal A, Jain V, Jena R. COVID-19 and fatal renal Mucor mycosis: Contributory or coincidental? *Indian J Urol.* 2021;37(3):270-273.