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Disseminated mucormycosis with tubercular lymphadenopathy in a post covid diabetic patient: A case report

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Abstract
The additive immunosuppression in uncontrolled diabetic patients who have been infected with covid-19 increases the chance of severe opportunistic fungal and bacterial co-infections. Our patient is an uncontrolled diabetic with a history of covid-19 who had developed disseminated mucormycosis and tubercular lymphadenopathy for which appropriate interventions were carried out accordingly. Our patient was discharged in a stable condition upon symptomatically feeling better. Mucormycosis has been rampant in the second wave of covid-19 in India due to its high population of diabetics and other immuno compromised people. Literature regarding the disseminated form of mucormycosis in patients who have recovered from covid-19 is limited. Information regarding mucormycosis-extrapulmonary TB co-infections in post-covid patients is scarce. Our report hopes to shed light on such co-infections among the healthcare professionals and the general public alike.

Keywords: anti-ovulatory, infertile women, PCOS, n-acetyl cysteine, metformin, etc

Introduction

The Covid-19 pandemic is rapidly evolving with a new set of complications emerging with each wave. Studies have identified thatSARS-CoV-2 causes a deranged inflammatory and cell- mediated immune response by markedly increasing inflammatory cytokines and reducing the number of CD4+ and CD8+ T cells, respectively [1]. The ill effects of ahyperglycemic environment and immune dysfunction such as neutrophil damage in uncontrolled diabetes can produce immunosuppression. Coupled with covid-19 infection, it is theperfect synergistic combination that promotes secondary opportunistic infections. Mucormycosis, caused by organisms of Mucorales, is an uncommon, life-threatening fungal infection. It is present as a commensal in nasal flora and manifests in immunocompromised patients. The infection results in host tissue necrosis and thrombosis due to vascular invasion by hyphae. Covid-19 induces endothelialitis and microvascular thrombosis in the pulmonary and extra-pulmonary vascular beds further augmenting the angioinvasive impact of mucormycosis [2]. Covid-19 patients with diabetes mellitus and previous glucocorticoid use are susceptible todeveloping mucormycosis. The prevalence of mucormycosis in India is approximately 0.14 cases per 1000 population, about 80 times the prevalence in developed countries [3]. as of June 11, 2021, the number of mucormycosis cases have grown to 31,216 with 2,109 deaths in India [4]. Tuberculosisco-infection with covid-19 is concerning due to non-specific symptoms of both diseases and lack of specific radiological features pertaining to TB. Covid-19 or its treatment can reactivate latent tuberculosis due to immune-modulation and existing TB may worsen covid-19 infections [5]. In patients with atypical presentation, testing for both diseases is crucial. Diabetes further worsens the condition due to additive immunosuppression. Therefore, proper screening for all 3 diseases is crucial to prevent mortality.
We present a case of disseminated mucormycosis with cervical tubercular lymphadenopathy in a diabetic patient recovered from covid-19 infection.

Case Report

A 59-year old male patient with DM, hypertension and CKD presented with a history of covid-19 infection and subsequent corticosteroid use. Mucormycosis was diagnosed after FESS and wound debridement was done elsewhere. The patient was prescribed posaconazole as anti-fungal treatment. Post-surgery, the patient developed right eye swelling and pain for which he was referred to our hospital for further management. On examination, the patient was afebrile, PR was 116bpm and BP around 140/70mmHg.

Table 1

Investigations (Day 2)	
CT	Post FESS changes Residual mucosal thickening in right maxillary, frontal, ethmoid and sphenoid sinuses Minimal soft tissue seen in right orbit in medial aspect abutting medial and inferior rectus
Nasal endoscopy	Wide MMA Dried crust with clots lining sinus wall Healing mucosa
Blood Analysis	

Investigations	Results	Reference range
BUN	62 (Peak: 68)	13-43mg/dL
Sr. Creatinine	2.7	0.9-1.3mg/dL
Sodium	131	136-145mmol/L
HbA1C	8.7	<5.7%
Uric acid	8.7	3.5-7.2mg/dL
Microalbumin	1461	<20mg/dL
Spot Creatinine	83	40-278mg/dL
Microalbumin/Creatinine ratio	1760	<30mg/g

The abnormal blood values suggest acute kidney injury (non-oliguria). Anemia and Hypo magnesaemia were also observed. During hospital stay, the patient developed upper and lower limb swelling along with elbow and B/L knee joint pain. Doppler study and synovial fluid analysis indicated right leg DVT and pan- fungal growth, respectively. Due to persistent joint pain, PET-CT was performed.

Table 2

PET-CT (Day 8)
Mucosal thickening involving right sphenoid sinus, right ethmoid, right maxillary, and right frontal sinuses with patchy metabolic activity-s/o sinusitis Ill define dhypermetabolic soft tissue thickening adjacent to medial wall of orbit abutting medial rectus and inferior rectus muscles. Minimal right proptosis noted Low grade hypermetabolic bilateral level II, III, left IV cervical and left supraclavicular lymph nodes noted with few showing calcifications-likely infective/inflammatory Bronchiectatic changes with calcifications seen in left lung lower lobe. Interiobar smooth septal thickening with adjacent ground glass opacities noted predominantly in bilateral lung upper lobes B/L mild pleural effusions Low grade hypermetabolic symmetrical periarticular soft tissue thickening involving aforementioned joints-s/o inflammatory polyarthritis

Cervical lymph node biopsy on day 9 detected Myco bacterium tuberculosisat exceptionally low concentrations confirming tubercular lymphadenopathy.

Table 3

CT-PNS (Day 13)	Post FESS changes seen Marked mucosal thickening seen in right maxillary, frontal, ethmoid and sphenoid sinuses Hyperdensities seen in sphenoid sinus Sheet like irregular soft tissue in medial and inferior aspect of right orbit with fat stranding

The patientwas treated with IV antibiotics (cefoperazone+sulbactam, meropenem, teicoplanin). Posaconazole was continued but later switched to isavuconazole (200mg). Retrobulbar Amphotericin B was given from day 3-6. The patient was also started on standard anti-tubercular therapy. Electrolyte, renal, and hematological abnormalities were treated accordingly. Sugars were treated and kept under control. The patient was discharged after becoming symptomatically better and was advised to follow a diabetic diet with protein supplementation.

Table 4

Discharge Medications	
T. Isavuconazole(200mg)	T. Febuxostat(40mg)
T. Nefrosave(Taurine+Acetylcysteine)	T. Magnesium oxide(400mg)
T. Furosemide(20mg)	T. Axoden Plus(Multivitamin)
T. Fexofenadine(180mg)	Glutarise sachet
T. Shelcal (Calcium+Cholecalciferol):500mg	
T. Acetaminophen(325mg)+Tramadol(37.5mg)	
Syr.Lactulose:0-0-15mL	
Anti-tubercular drugs (morning before food)	T.Isoniazid300mg+T.Rifampicin600mg+T. Pyrazinamide1500mg+T. Ethambutol1000mg T.Pyridoxine40mg
Diabetic medications	Inj.Actrapid12U-14U-12U Inj.Insulin degludec0-0-10U

Discussion

Severe opportunistic infections occur in patients with compromised immunity. A 2003 study involving the SARS-CoV infection identified a high incidence of fungal co-infection (14.8- 27%) [6]. Since SARS-CoV and SARS-CoV-2 belong to the same species, an increased incidence of fungal infections is expected. Mucormycosis presents itself based on the anatomical sites involved: rhino-orbital-cerebral, pulmonary, cutaneous, and less often GI, renal, and disseminated syndromes [7]. Isolated case reports and case series have reported mucormycosis co-infections with covid-19 [8, 9]. Post-covid mucormycosis is less common. It can occur as late as 42 days and 90 days following covid- 19 [10, 11]. Sharma *et al*., report in their study that among 23 patients, 19 had recovered from covid-19 before being infected with mucormycosis [12]. Tomar *et al*., report a case of sino-orbital mucormycosis in a post-covid patient [13]. From a meta-analysis of 600 series and 851 cases, diabetes was established as an independent risk factor for rhino-orbital□cerebral mucormycosis [14]. The prevalence of diabetes in India is quite high with 77 million patients (8.9% of adult populations) [15]. Saldanha *et al*., report a case of paranasal mucormycosis in a patient with uncontrolled diabetes [16]. Sana *et al*., and Ravani *et al*., report two studies involving mucormycosis co-infection where 100% and 96.7% of patients were found to be diabetic [17, 18].

Our patient is a known uncontrolled diabetic with a history of corticosteroid use and covid-19 infection which is the ideal triad for mucormycosis. He has been identified to have disseminated mucormycosis based on synovial fluid analysis. Only one case of disseminated mucormycosis in post-covid patient has been reported [19]. Treatment involves surgical intervention with systemic antifungal therapy. Our patient underwent FESS and was treated with amphotericin B and posaconazole which was switched to is avuconazole due to its broad spectrum of activity.

Tuberculosis covid-19 co-infections should be taken seriously in India due to the former□s high disease burden. According to the WHO 2019 Global Tuberculosis Report, the incidence of TB was 193 individuals per 100,000 people in India [20]. There is few literature regarding covid-19 and extra-pulmonary TB co-infection. Gerstein *et al*., report a case of covid-19 and peritoneal tuberculosis co-infection [21]. The first cohort of 49 cases of the co-infection reported by Tadolini *et al*., had 2 cases of lymphadenitis alone [22]. Gupta *et al*., in their cohort of 22 cases of co-infections reported only 1 case of cervical lymphadenopathy [23]. At present, there is no reported case of a post-coviddiabetic patient with a diagnosis of mucormycosis with cervical tubercular lymphadenopathy co-infection.

Conclusion

The covid-19 pandemic has increased the incidence of opportunistic infections in immune- deficient patients. Fungal infections such as mucormycosis and latent infections such as tuberculosis manifesting in patients with a history of covid-19 is a cause of concern due to unpredictability in the treatment response owing to factors such as altered physiology, comorbid conditions and multiple drug interactions. Therefore, adequate information needs to be promulgated regarding such co-infections among healthcare professionals as well as the general public.

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