RHINO-ORBITAL MUCORMYCOSIS IN A COVID-19 PATIENT IN PAKISTAN : CASE REPORT

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ABSTRACT ____

Severe acute respiratory syndrome coronavirus (SARS-CoV-2) or 2019 novel coronavirus (2019-nCoV) was first reported in China, which spread all over the world causing a pandemic. Opportunistic infections are very commonly seen with Covid-19 infection. Patients with comorbidities are at higher risk. We report a case of an elderly male who was diagnosed with Covid-19 on HRCT and PCR. Non-contrast MR brain and non-contrast CT paranasal sinuses showed pansinusitis with internal differential high densities and suggestion of fungal infection was given. Functional endoscopic sinus surgery (FESS) was performed followed by amphotericin B lavage. Postoperative contrast-enhanced MRI brain showed interval reduction in the enhancing mucosal thickening with abnormal signal intensity signal extending into bilateral orbital apices. Thus, post-Covid rhino-orbital mucormycosis was timely diagnosed by radio-pathological aid. Despite appropriate intervention including antibiotics cover and surgical debridement, the disease progressed into orbits, due to multiple factors like immunocompromised status, comorbidities or use of excessive steroid therapy in treating Covid-19 infection. Post Covid-19 infection, rhino-orbital mucormycosis presentation is very rare and one of its kind case reported in Pakistan.

Keywords: Mucormycosis, Orbit, Covid-19, Fungal infections, Case report, Pakistan.

Introduction ___

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (COVID-19) infection which ranges from mild to severe disease burden. Super-infections are frequently seen with underlying comorbidities (diabetes mellitus, tuberculosis, etc).¹ Pakistan has a very high prevalence rate for type-2 diabetes mellitus (13.7% of adults), which is known to be a notorious risk factor.² Mucormycosis is seen in immunocompromised or patients with underlying chronic illnesses (steroid therapy).³ In the background of the Covid-19 pandemic, mucormycosis has been very rarely reported in Pakistan. We report a case of post-Covid-19 pneumonia associated rhino-orbital mucormycosis in Pakistan.

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Case Presentation ____

An elderly male, known diabeticfor last 7 years, and compensated chronic liver disease patient presented with fever, cough, and shortness of breath for 5 days. In consideration of the ongoing Covid-19 pandemic, a complete workup was done for Covid-19 pneumonia including RT-PCR, complete blood counts, inflammatory markers, and HRCT. The patient was vitally stable and maintaining oxygen saturation at the time of hospital presentation. SARSCOV-2 PCR was detected positive and HRCT showed multifocal, multilobar confluent and non-confluent ground-glass opacities in bilateral lower lungs, signifying mild disease burden (Fig.1).



Figure 1: HRCT Axial View

Complete blood counts, coagulation profile, liver function tests, and inflammatory markers showed no significant derangement at the time of initial presentation and short-term serial follow-up (Fig.2). Following inflammatory marker values were recorded, LDH = 227 U/L, CRP 23.1 mg/L, D-dimers 0.52 mg/L etc. The patient was advised home management for the disease, no significant severe disease complication incidence was reported by the patient during recovery of Covid-19 pneumonia. He was treated with dexamethasone, loprin, moxifloxacin and vitamin supplements, based on the local Covid-19 treatment protocol at that time. After 10 days follow up there was a significant interval decrease in CRP values, i.e 2.0 and d-dimers were consistently normal in the range at a value of 0.48. PT and INR values were 13.2 seconds and 1.2 respectively.

Parameters	Day1		Day10	Day20	Day30	Normal Values
WBC Total	8990	/µL	15710	11600	16800	(4000/µL -10500/µL)
RBC, Total	3.26	m/µL	3.40	2.98	2.64	(4.5 - 6.5)m/µL
Hemoglobin	10.2	g/dL	10.2	9.10	8.0	13.5 - 18.0)g/dL
нст	30.5	%	32.7	26.8	24.0	(42 - 52)%
MCV	93.6	fL	96.2	89.9		(78 - 100)fL
MCH	31.3	pg	30.0	30.5	30.3	(27 - 31)pg
MCHC	33.4	g/dL	31.2	34.0	33.3	(32 - 36)g/dL
Platelet Count	168000	/µL	116000	150000	162000	(150,000 - 400,000)/µL
Neutrophils	60	%	82	82	80	(54 - 62)%
Lymphocytes	30	%	08	08	10	(25 - 33)%
Monocytes	10	%	10	10	10	(1 - 4)%
Eosinophils	00	%	00	00	00	(1 - 3)%
Basophil	00	%	00	00	00	(0 - 0.75)%
RDW	18.9	%	16.8	15.2	14.5	(11.5 - 14.0)%
MPV	9.90	6	11.4	13.1	11.7	(6.8 - 10.2)fL

Figure 2: Complete Blood Count

The patient presented to us after 1 month with complaints of headache, vertigo, drooping of eyelids; followed by gradual onset altered sensorium, and vision loss. Non-contrast brain MRI was performed which showed moderately extensive mucosal disease with retention cysts is present in bilateral maxillary, ethmoid, sphenoid sinuses with relative sparing of frontal sinuses, mastoids, and skull base tissues. The findings were documented as combined chronic and superimposed acute sinusitis. After few days, patient again presented to us with worsening headache. Noncontrast CT paranasal sinuses was performed which showed pansinusitis with internal differential high densities and bilaterally ossified ostiomeatal complexes. The suggestion of fungal infection was given due to the extent and presentation of the disease. No air-fluid level, sinus walls destruction, sinus expansion, or sinonasal mass was recognized with unremarkable nasal turbinates (Fig.3).



Figure 3: CT PNS Axial View

Pre-and postcontrast enhanced MRI brain performed on same day demonstrated severe mucosal disease involving all sinuses, consistent with chronic and superimposed acute sinusitis (Fig.4) No significant postcontrast enhancement or intracranial extension of sinus mucosal infection was seen.

One month later, the patient reported malaise, proptosis, chemosis, periorbital cellulitis, and restricted medial gaze. Visual acuity was 6/6 with partial ophthalmoplegia. Surgical debridement of sinus fungal

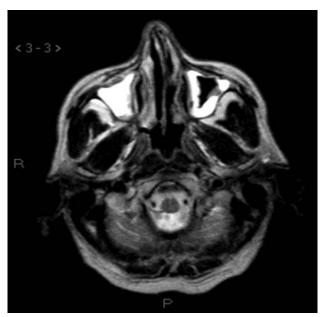


Figure 4: T2 Axial MR

infection was done by functional endoscopic sinus surgery (FESS) followed by amphotericin B lavage. Histopathological analysis was done which showed aseptate broad-based hyphae and gram-positive bacilli, which confirmed the diagnosis of paranasal mucormycosis. The patient was started on an antifungal regime including oral and injectable antifungal agents (amphotericin B). Postoperative contrastenhanced MRI brain showed interval reduction in the enhancing mucosal thickening in left maxillary and residual ethmoid air cells (Fig.5).

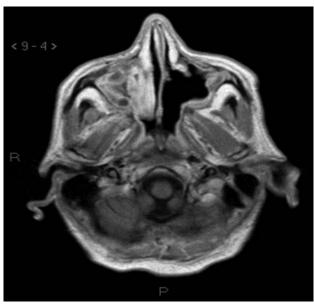


Figure 5: T2 Axial MR

There was interval increase in the enhancing mucosal thickening in bilateral sphenoid sinuses with extension of disease process in bilateral orbits showing areas of marginal enhancement suggesting abscess formation. The abnormal signal intensity was extending into bilateral orbital apices, however no definite evidence of any intracranial extension of disease process was documented (Fig.6). The flow voids of ICAs were preserved.



Figure-6: T1 Post Contrast Axial MR

Discussion

Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2). This primarily began in Wuhan, China, and now has become a worldwide pandemic. This has tendered an uncompromising threat to public health of all ages.⁴ A complex interplay of factors with underlying illnesses like diabetes mellitus, respiratory pathology, immunosuppressive therapy, neutropenias, leukemias, or systemic immune alterations of COVID-19 infection impose a threat for superinfections which can be bacterial or fungal.⁵ Drugs used most commonly in Covid-19 infections are corticosteroids, which can be dexamethasone or methylprednisolone. With their beneficial effects as an anti

-inflammatory and reducing disease progression,6 they impose certain side effects like secondary infections, manifestation of latent diabetes mellitus, insomnia, and weight gain.7 Mucormycosis is caused by Mucorales species of the phylum zygomycota8 causing fatal and deadly infections in immunocompromised patients, particularly in patients with a history of diabetes mellitus, leukemia, transplant, and lymphoma.9 The incidence rate of mucormycosis globally varies from 0.005 to 1.7 per million population while in Pakistan prevalence of 0.14/1000 population is seen.¹⁰ The mold enters the host through the respiratory tract and grows along arterial internal elastic lamina causing infarction and thrombosis. 11 Disease progression is either direct or by vascular occlusion from the nose and sinuses. Different routes are known to cause intracranial involvement like invasion through the superior orbital fissure, cribriform plate, or by perineural route.12 Early diagnosis and prompt treatment are necessary to avoid any morbidity and mortality. Disease should ideally be identified earlier by pathological means and the extent can be noted with radiology help. Diagnosis depends upon clinical picture along with radio-pathological correlation. Various radiological modalities like CT scan and MRI can aid in diagnosing these. CT scan is gold standard for diagnosing the osseous involvement while MRI delineates intracranial or intraorbital extension of disease.13 Once diagnosed, mainstay management is an early medical treatment by amphotericin B or later surgical debridement. Prognosis depends on various factors and the mostcrucial one is theearly initiation of treatment. Thus, fungal superinfection suspicion should be kept in mind in patients presenting with Covid-19 infection along with comorbidities. Furthermore, immediate imaging studies should be considered and instant medical/surgical treatment should be advised according to patient condition. Physicians should be careful while using steroids in Covid-19 infection to avoid flaring up the fungal infection.

Conclusion _

Further research work should be probed for the prevention, early detection and management of opportunistic infections in Covid-19 patients. Steroids and immuno-

supressants should be cautiously used while treating Covid-19 infection in patients with comorbidities. Use of such therapeutic agents should be carefully monitored for the maximum therapeutic effects at minimal possible dose for shortest period of time, to reduce subsequent complications, morbidity and mortality.

Conflict of Interest: All authors declare no conflict of interest.

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Author Contributions: All authors contributed equally to the drafting of study.

Ethical Statement: The patient signed an informed consent form, as per the ethical guidelines of hospital board.

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