Comparison of CT and MRI findings in orbital Mucor mycosis in COVID-19 and post COVID-19 patients and correlation with histopathological changes

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Abstract
Background: Identification of the invasive fungal infection changes in COVID-19 and post COVID-19 patients on CT and MRI can help in making an early diagnosis which will be lifesaving. These imaging changes are proportionate to the fungal invasion into the respective tissue. **Materials And Methods:** We, hereby evaluated 40 cases of clinically diagnosed orbital Mucor mycosis with concurrent COVID-19 illness at our institute over a period of three months (April 2021 to June 2021). Preoperative CT and MRI findings of each tissue, in every case, is compared with the post operative and histopathology changes. **Results:** On correlating CT with histopathology, the presence of soft tissue collections and scleral involvement and optic nerve involvement are more accurate in suggesting the presence of fungal invasion. On correlating MRI with histopathology fat stranding, scleral involvement and optic nerve involvement are more accurate in suggesting the presence of fungal invasion. **Conclusion:** Comparing MR and CT findings with histopathology, statistics revealed that MRI determines the extent of invasion very well, and demonstrates involvement of sclera and optic nerve at an earlier stage. DWI added specificity to the diagnosis by showing restricted diffusion in the path of fungal invasion. Whereas on CT, soft tissue collections earlier demonstrate fungal invasion. But CT is a widely available, fast, effective, and more feasible imaging option specially in sick and uncooperative patients. CT is useful in preoperative planning and in directing the surgical approach.
Key Words: COVID-19, Mucormycosis, CT, MRI, orbit
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Introduction: Mucormycosis is a fulminant opportunistic fungal infection caused by Mucorales, predominantly seen in the immunocompromised population. In the pre-COVID-19 era, the incidence of Mucormycosis was much more common in India as compared to the western world, SARS CoV-2 has further skewed this disease epidemiology, partly due to the irrational use of board spectrum antibiotics, steroids and also due to COVID-19 associated immunosuppression. COVID-19 related immunosuppression causes rapid progression of the invasive fungal sinusitis, with extension across tissue planes to involve orbit and cerebrum leading to high morbidity and mortality. Early suspicion, rapid diagnosis, and initiation of treatment are the most important factors that determine prognosis in the management of Mucormycosis[1]. Imaging studies are readily available and rapidly give corroborative evidence when the disease is clinically suspected, thus forming cornerstone in the management of patients with Rhino-Orbital-Cerebral Mucor mycosis (ROCM). In patients with clinical suspicion and imaging evidence of ROCM, empirical antifungal therapy can be started even before confirmation of the diagnosis by microbiology or histopathology [2]. In patients with proven ROCM, imaging plays an important role in determining the extent of disease, which is critical in deciding about further line of management. In patients where biopsy is planned, imaging can be used to help guide the site for biopsy to ensure maximum diagnostic yield. In the current communication we elaborate the role of CT and MRI in ROM.

Methods

This study is approved by institutional ethics committee. The study included 40 patients, out of which 31 were males and 9 were females, aged between 35 to 75 years, who were clinically diagnosed orbital Mucor mycosis patients with, either Nasopharyngeal RT-PCR positive for COVID-19 or patients with past history of COVID-19 infection with positive HRCT chest findings. Patients who had contraindication to MRI were excluded from our study. The study was conducted for a period of three months from April 2021 to June 2021. CT examination was done on 128 slice HITACHI CT machine, with and without the use of intravenous contrast medium, as needed. MRI was performed on 1.5 Tesla GE MRI machine. The CT and MRI findings were correlated. Depending on the severity, few of the patients underwent surgery, and the samples were sent for histopathological examination. The intraoperative findings and histopathological report of each tissue were compared with the CT and MRI findings.

Results

Out of 40 patients, 31 patients were males and 9 were females .42% of the patients belonged to 51-60 years age group. The most common symptoms with which the patients presented were pain and eye swelling, other symptoms being headache, eye redness and eye discharge. Out of 40 patients, 31 patients had unilateral involvement. All patients were subjected to CT, followed by MRI. The main spectrum of imaging findings on CT were rectus muscle edema, fat stranding, soft tissue thickening, scleral thickening and optic nerve thickening (table 1). Post contrast examination on CT showed peripherally enhancing intra and peri orbital collections, scleral enhancement. Comparison of CT findings with histopathological and intra operative features showed CT is more sensitive in delineating collections and fat stranding, and more accurate in evaluating fat stranding and scleral involvement (table 5). In three patients CT was more effective in delineating early involvement of bony invasion. The main findings on MRI included rectus muscle edema, intraorbital collections, scleral thickening, optic nerve thickening. MRI is more accurate in delineating scleral involvement, optic nerve involvement and soft tissue thickening (table 4). Intracranial extension of the disease was diagnosed in 18 patients on MRI and 16 patients on CT.

In 30 patients, operative procedures were performed and the samples have been sent to histopathological examination. The findings on CT and MR of involvement of rectus muscle, sclera, optic nerve was compared with the histopathological findings of individual tissue.

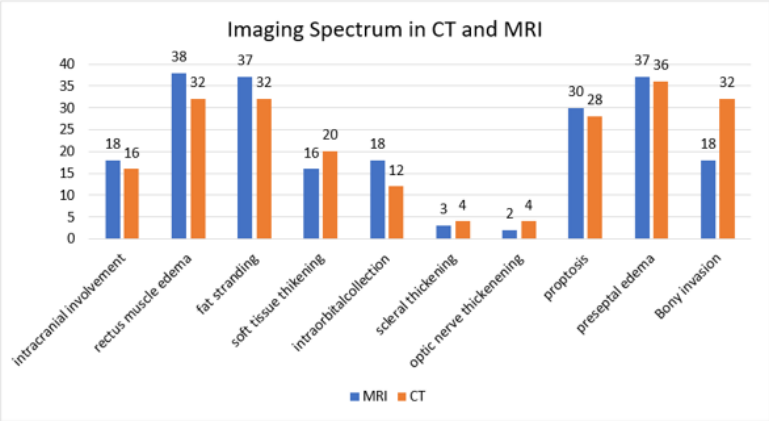

Table 1: Image spectrum in CT and MRI

Table 2: Comparison of CT and MRI in evaluation of finding in orbital mucormycosis.

	Sensitivity	Specificity	PPV	NPV	Accuracy
MRI	91.89	33.33	94.44	25	87.5
CT	72.97	33.33	93	9	70

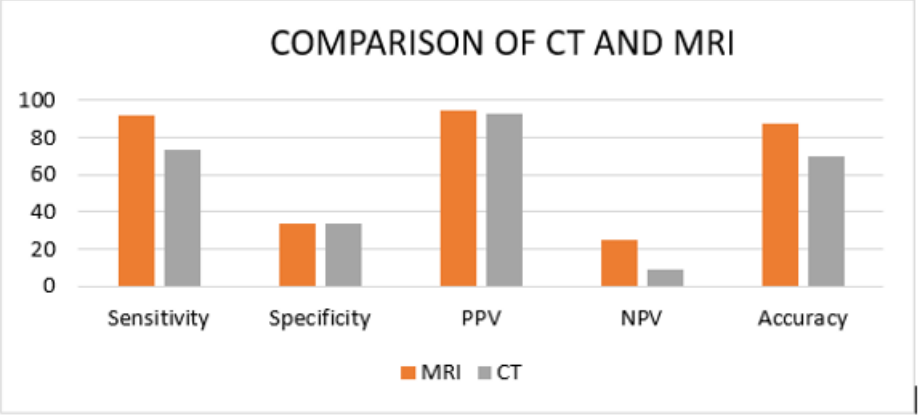

Table 2

Table 4: Efficacy of CT evaluation of finding in orbital Mucor mycosis

	Sensitivity	Specificity	PPV	NPV	Accuracy
Rectus muscle involvement	86%	75%	96%	37.5%	85%
Fat stranding	88%	100%	100v	50%	90%
Soft tissue thickening/ collection	93%	79%	75%	95%	85%
Scleral involvement	50%	92%	25%	97%	90%
Optic nerve involvement	50%	92%	25%	97%	90%

Table 5: Efficacy of MRI in evaluation of findings.

	Sensitivity	Specificity	PPV	NPV	Accuracy
Rectus muscle involvement	97.2%	25%	92%	50%	90%
Fat stranding	97%	50%	99%	66%	92.8%
Soft tissue thickening/ collection	93%	95.8%	93.7%	95.8%	95%
Scleral involvement	100%	97.3%	66%	100%	97.5%
Optic nerve involvement	100%	100%	100%	100%	100%

Images

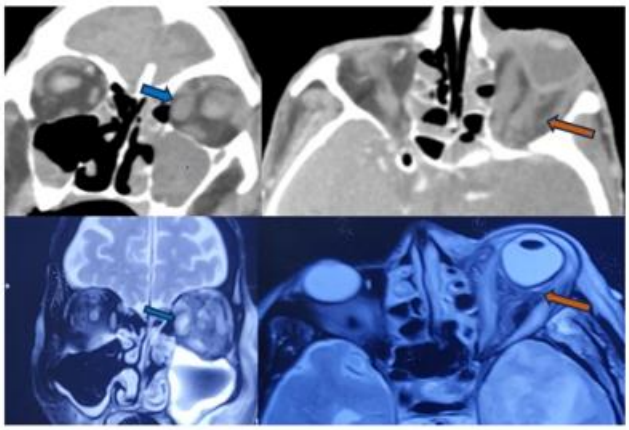

Image 1: Plain CT and T2W MR images showing bulky extraocular muscles (blue arrow) and adjacent fat stranding (orange arrow). Let sided axial proptosis is also seen.

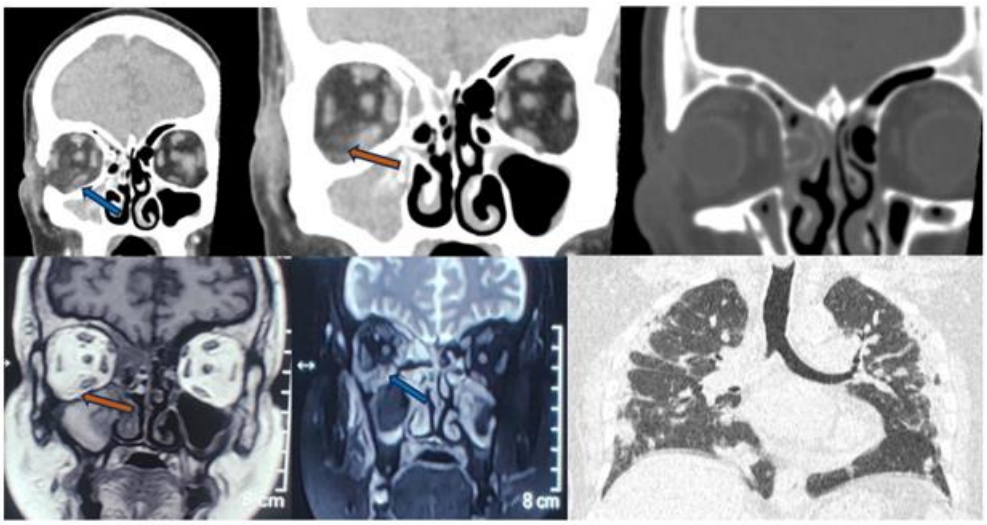

Image 2: Plain CT showing inferior rectus edema (blue arrow) with adjacent fat stranding (orange arrow). HRCT chest showing ground glass opacities and fibrotic opacities S/O COVID-19 sequalae. T1WI and T2FS images showing right inferior rectus edema (blue arrow) with adjacent fat stranding (orange arrow).

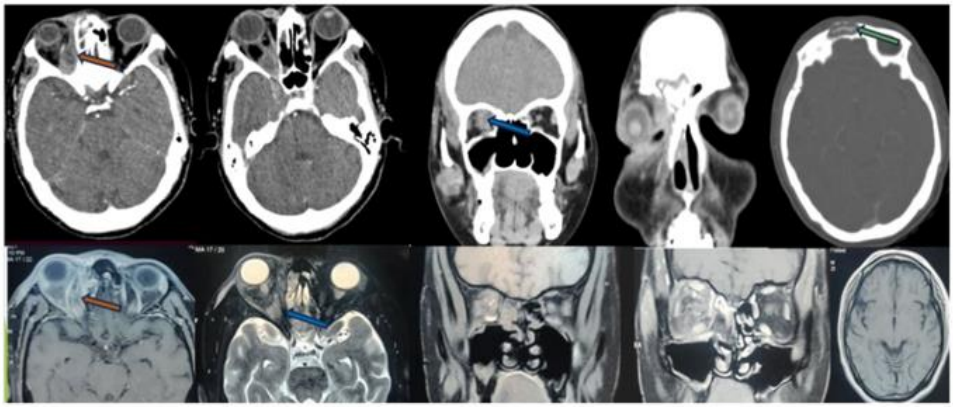

Image 3: Plain and contrast CT showing peripherally enhancing collection (Orange arrow) along medial wall of right orbit extending into apex (Blue arrow). There are also osteomyelitis changes of frontal bone on right side (green arrow). T1 contrast and T2 FS images showing peripherally enhancing collection along medial wall extending into apex with fat stranding Axial T1 showing no bony changes.

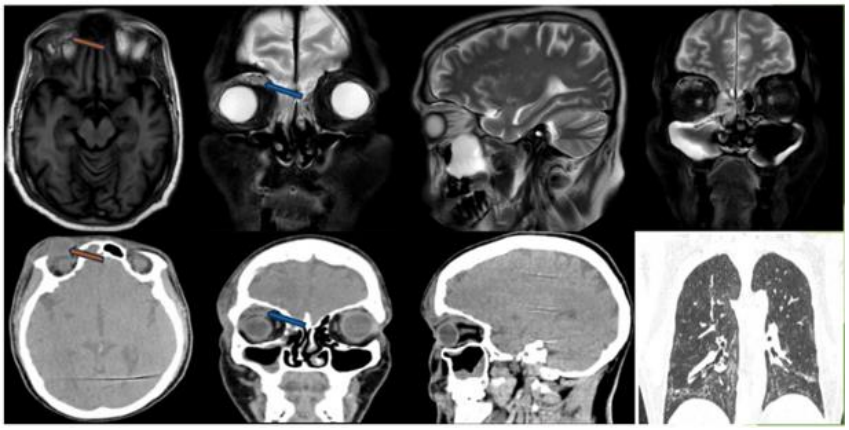

Image 4: Plain CT showing ill-defined hypodense extraconal collection along roof of right orbit (orange awwrow). T1W, T2W and FS images showing ill-defined collection around superior rectus muscle (blue arrow) with fat stranding. There is mucosal thickening in right maxillary sinus. HRCT chest showing patchy GGOs with fibrotic opacity.
S/O orbital cellulitis with COVID-19 sequalae.

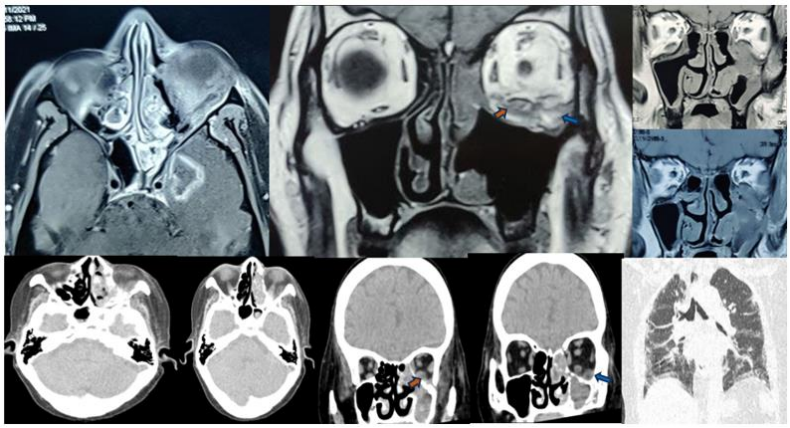

Image 5: There is hypodense collection (blue arrows) along inferior wall of left orbit in extraconal compartment with bulky inferior oblique muscle (orange arrows) with adjacent fat stranding. HRCT chest showing GGOs and fibrotic opacities S/O post COVID-19 sequalae.

Image 6: Plain CT and MR image showing diffuse scleral thickening (blue arrows) and bulky extraocular muscles with intraconal fat stranding on right side

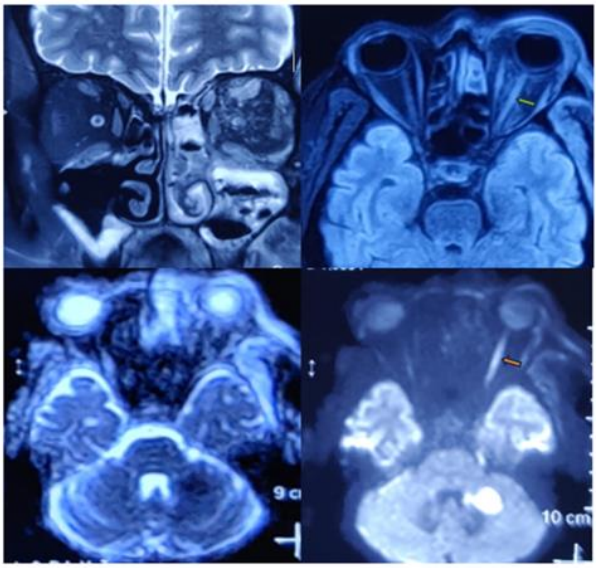

Image 7: T2 FS, FLAIR, DWI, ADC images showing bulky left optic nerve (green arrow) with adjacent fat stranding showing restriction on diffusion (orange arrow) and hypointense signal on ADC image.

Discussion

Mucormycosis primarily involves nasal cavities and paranasal sinuses, spreads into para-antral soft tissues, adjacent bones, and also extends into orbital tissues, base of skull and central nervous system. The spread of mucor mycosis is common and more rapid in COVID-19 patients, during the second wave. Many factors contributed to this, some of which include COVID-19 associated immune suppression, hyperglycaemic state due to pre-existing diabetes mellitus. Orbital extension occurs via nasolacrimal duct and through erosion of medial orbital wall. Such invasion is facilitated by the thinness of the lamina papyracea, congenital dehiscence often presents along the medial wall, and the perforations of the medial wall by arteries and

veins [3,4].Facial, orbital fat stranding, and retro-antral soft tissue extension are the early indicators of the aggressive course of the disease [5,6].

Shinde et al, in their study of ROM described that diabetes is one of the most common etiological factors and associated with high mortality [7]. 60% of the patients had history of Diabetes and few of them discontinued treatment. Most of the patients were diagnosed with new onset diabetes during COVID-19 infection. In our study 18 (22%) of patients showed intracranial extension of infection in which 16 (90%) were having diabetes.

Common Signs/symptoms associated with mucormycotic are fever, headache, cranial nerve palsy, decreased vision, exophthalmos, diplopia, blepharoptosis, periorbital enema, facial swelling and pain, ocular purulent secretion, nasal blockage/crusting, blood-stained discharge. In our study most of the patients presented with pain and swelling of eye, 60% patients had blackish discharge and in 20% there was bilateral involvement.

All the diagnosed patients received different treatments and surgical procedures depending on the involvement and extension of the fungus. Some of the patients underwent endoscopic debridement of devitalized fungal infected tissue, while others underwent inferior maxillectomy, advanced cases underwent facial resection. Few patients with partial visual loss underwent orbital debridement.

The imaging findings in ROCM in CT are mucosal thickening, sinus wall erosions, soft tissue thickening in intra or extraconal compartment, rectus muscle edema, optic nerve thickening & preorbital edema. Safder S [8] in their study described Rhino cerebral mucormycosis should be a strong consideration when there is a lack of enhancement of the mucosa, given its Angio invasive nature, because the hyphae likely invade smaller vessels supplying the mucosa and common findings in MR are mucosal enhancement within the sinuses and non-enhancement of left nasal turbinates (Black turbinate sign).

Son et al found that in ROCM the tendency for infraorbital extraocular muscle involvement and thickening of sinus mucosa was higher compared to patients with bacterial orbital cellulitis (BOC). Orbital involvement in our study varied from thickening of ocular muscles, preseptal cellulitis, extraconal and intraconal space involvement, proptosis, optic nerve involvement.

We selected five findings that is rectus muscle involvement, fat stranding, soft tissue collection, scleral involvement and optic nerve thickening to compare CT and MR with HPE findings.

CT has more sensitivity for soft tissue thickening and highest specificity for fat stranding. The Positive predictive value for fat stranding was 100% and Negative predictive value was more for scleral involvement and optic nerve involvement. Studies conducted by Thomas et al and Agarwal et al [9-10] demonstrated that soft tissue thickening and orbital apex involvement appears to be more specific for Mucor mycosis infection, in our study 95% of patients demonstrated soft tissue thickening and 40% showed orbital apex involvement.

Optic nerve involvement was demonstrated in a study by Werthmn et al [11]. Mandeep Singh Guhamen et al [12]in a study demonstrated the involvement of optic nerve in Mucor mycosis and perineural spread which is a rare complication. They explained that Ischemic involvement of the optic nerves, although a rare complication, should be considered in cases presenting with visual symptoms. In our study three patients presented with visual loss, more than 50% patients complained of blurring of vision. In our study four cases demonstrated optic nerve involvement. CT demonstrated thickening of optic nerve with adjacent fat stranding. In MRI there was nerve thickening and fat stranding along with that there was diffusion restriction and hypointense signal on ADC.S Mathur et al [13] explained in a study that restricted diffusion on MR imaging may be the earliest abnormality detectable in acute ischemic optic neuropathy due to rhino cerebral Mucor mycosis. Optic nerve infarction is seen as high-signal intensity of the nerve on diffusion-weighted imaging. In our study MR showed more sensitivity for scleral involvement and optic nerve involvement and 100% specificity for optic nerve involvement.

CT is a widely available, fast, effective, and relatively inexpensive imaging modality. Compared to MR, it has significant shorter acquisition time. In one patient we observed osteomyelitis changes in the frontal bone, seen as patchy areas of lysis, which were better demonstrated on CT and there was no signal abnormality in the corresponding region on MR. In 60% of the cases, there was bone destruction specially in medial wall of orbit through which there was spread of infection and it was better demonstrated on CT. Better delineation of Sino nasal anatomy at CT helps in directing surgical approach.
MRI is an inherently multiplanar imaging modality, which has excellent soft tissue contrast resolution.
Overall, when we compared CT and MR with HPE, the accuracy of MR was 87.5% and CT 70%. The NPV of MR was 25% and CT was 9%.

Conclusion

Comparing MR and CT findings with histopathology, statistics revealed that MRI determines the extent of invasion very well, and demonstrates involvement of sclera and optic nerve at an earlier stage. DWI added specificity to the diagnosis by showing restricted diffusion in the path of fungal invasion. Whereas on CT, soft tissue collections earlier demonstrate fungal invasion. But CT is a widely available, fast, effective, and more feasible imaging option specially in sick and uncooperative patients. CT is useful in preoperative planning and in directing the surgical approach.

DISCLOSURE:
No conflicts of interest

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