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Retrospective Study Of Clinic Radiological Profile Of Mucormycosis At A Tertiary Care Centre In Chennai, Tamil Nadu, India.

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ABSTRACT

Mucormycosis, previously called zygomycosis, refers to several different diseases caused by infection with fungi belonging to the order Mucorales. *Rhizopus* species are the most causative organisms of this group. In descending order, the other General mucormycosis-causing species Predisposing factors for mucormycosis include conditions where people are less able to fight infection, have a low neutrophil count, or metabolic acidosis. To assess the clinic radiological profile of Mucor mycosis patients. We performed a retrospective, single-centric, noninterventional, observational study of patients with Rhino-orbital mucormycosis from May- to July 2021, and a concurrent or past history of infection with covid 19 infection was obtained. All patients with probable and possible Rhino orbital mucormycosis were included in the study. Patients with Rhino orbital mucormycosis without concurrent or previous history of COVID-19 infection were also included in the study. Mean age group which was affected by mucormycosis in the study population was found to be 53 years. The youngest among the study population was 18 years old and had type 1 diabetes mellitus as comorbidity and the oldest among the studied population was 82 years old. The most common presenting complaint was found to be retroorbital pain 88% (23). The second most common was found to be headache 76.9% (20). 73% (19) of the study population had eye swelling as the predominant presenting complaint. 46.1% (12) had nasal discharge, 34.6% (9) had proptosis, 23.07% (6) had facial swelling, 11.5% (3) had a fever, 11.5%(3) had nasal bleeding and 7.7% (2) had a loss of vision as the predominant complaint. The majority of the patients presented with left-sided complaints. 65.3% (17) developed mucormycosis after developing covid 19 infection. The mean number of days after the onset of COVID-19 symptoms after which the symptoms of mucormycosis developed was found to be 15 days. 23.07% (6) of them were incidentally found to be COVID-19 positive after presenting with signs and symptoms of mucormycosis. 11.5% (3) of the study population were covid-19 RTPCR negative but radiological imaging done was suggestive of covid-19 infection. Clinicians should have a low threshold for performing an MRI in patients with abnormalities on CT because the MRI will enhance the detection of intracranial, intraorbital, and cavernous sinus involvement. In a study of 23 immunocompromised patients with fungal sinusitis, CT findings included severe soft tissue edema of the nasal cavity mucosa (Turbinates, lateral nasal wall and floor, and septum) in 21 patients, sinus mucoperiosteal thickening in 21patients, bone erosion in 8 patients, orbital invasion in 6 patients, facial soft tissue swelling in 5 patients, and retroental fat pad thickening in 2 patients.

Keywords: Rhino orbital mucormycosis, *Rhizopus* species, CT findings, covid 19 infection

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INTRODUCTION

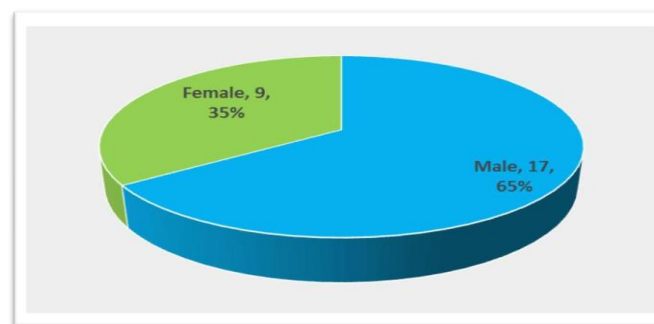
Mucormycosis, a fungal infection caused by ubiquitous environmental molds, such as *Rhizopus arrhizus*, *rhizome*, or *pusillus*, *Apophysomyces variabilis*, and *Lichtheimia corymbifera*, is surging as a COVID-19 association at unprecedented rates throughout India and raising alarming bells around the world. From May 5 to July 12, 2021, 41,512 cases and 3554 deaths were attributed to this rare, but life-threatening fungal infection [1]. The majority of those cases occurred during active SARS-CoV-2 outbreaks in India, prompting the Central Government Of India to declare Mucormycosis infection as an epidemic on May 10, 2021. Fungal infections, including mucormycosis, aspergillosis, and invasive candidiasis, have been reported in patients with severe COVID-19 or those recovering from the disease and have been associated with severe illness and death [2]. India has reported a recent surge in mucormycosis cases. Prevention of COVID-19-associated mucormycosis needs to focus on aiming for better glycaemic control in COVID-19 patients and monitoring the use of systemic corticosteroids in treating severe cases. Outpatient use of systemic corticosteroids/other immunomodulating drugs for mild or moderate patients with COVID-19 should be avoided. Healthcare facilities need to strengthen their infection prevention and control (IPC) programs to prevent healthcare-associated outbreaks. This study was done to determine patient demographics, the population at risk, the role of comorbidities, and imaging findings in Rhinorbital Mucormycosis patients [3].

METHODS

We performed a retrospective, single-centric, noninterventional, observational study of patients with Rhinorbital mucormycosis from May- July 2021, and a concurrent or past history of infection with covid 19 infection was obtained. All patients with probable and possible Rhino orbital mucormycosis were included in the study. Patients with Rhino orbital mucormycosis without concurrent or previous history of COVID-19 infection were also included in the study. Type 2 diabetes mellitus 76.9% (20) was found to be the most common co-morbidity found in patients with mucormycosis. 46.15% (12) of the study population had systemic hypertension. 19.23% (5) had coronary artery disease. 11.53% (3) had chronic kidney disease, 11.53% (3) had bronchial asthma, 3.8% (1) had pulmonary tuberculosis, 3.8% (1) had a cerebrovascular accident and 3.8 % (1) had type 1 diabetes mellitus as comorbidities.

RESULTS

Graph 1: Gender

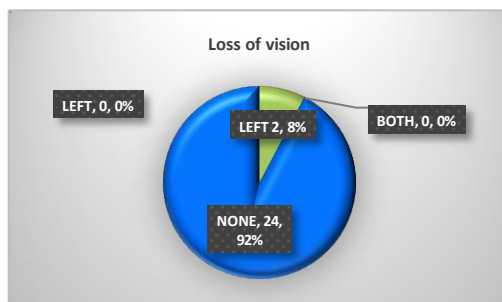
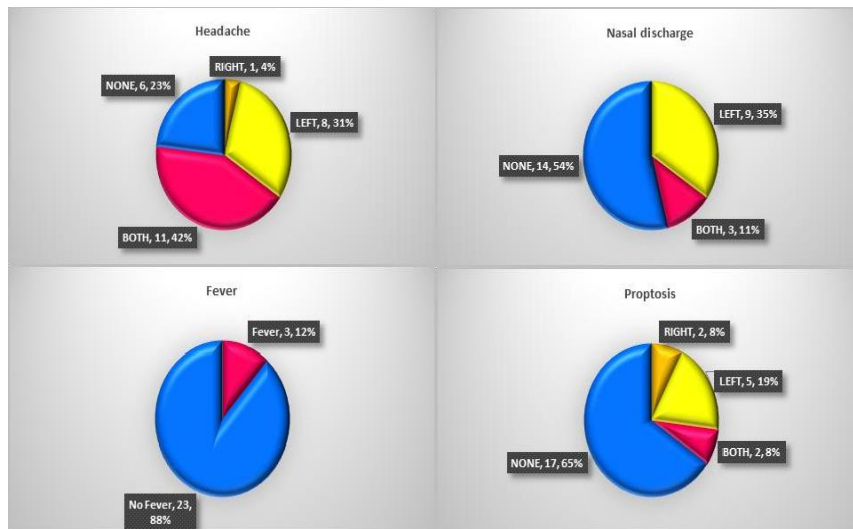


Graph 1: Among the 33 patients studied, 17 (65%) were male and 9 (35%) were female. 53% (14) of the patients who were studied belonged to the age group 40-60 years. 23.07% (6) of them belonged to the age group 60-80. 15.3%(4) of them belonged to the age group 20-40. 1 patient each belonged to the age group less than 20 and more than 80. All 4 patients who belonged to the age group between 20-40 years of age had diabetes mellitus as a co-morbidity. The mean age group which was affected by mucormycosis in the study population was found to be 53 years. The youngest among the study population was 18 years old and had type 1 diabetes mellitus as comorbidity and the oldest among the studied population was 82 years old.

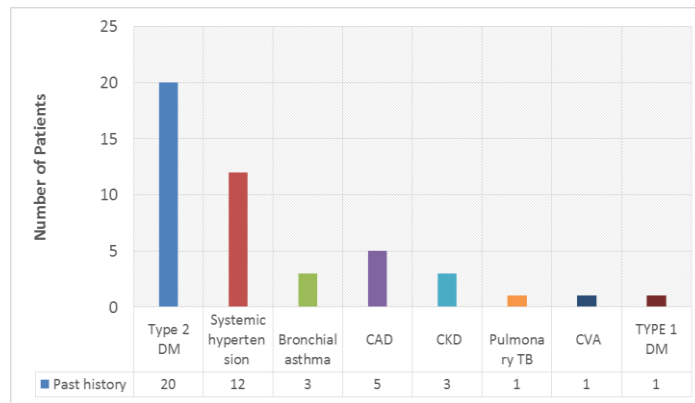
Graph 2: Presenting Complaints



Graph 2: The most common presenting complaint was found to be retroorbital pain at 88% (23). The second most common was found to be headache 76.9% (20). 73% (19) of the study population had eye swelling as the predominant presenting complaint. 46.1% (12) had nasal discharge, 34.6% (9) had proptosis, 23.07% (6) had facial swelling, 11.5% (3) had a fever, 11.5% (3) had nasal bleeding and 7.7% (2) had a loss of vision as the predominant complaint. The majority of the patients presented with left-sided complaints.

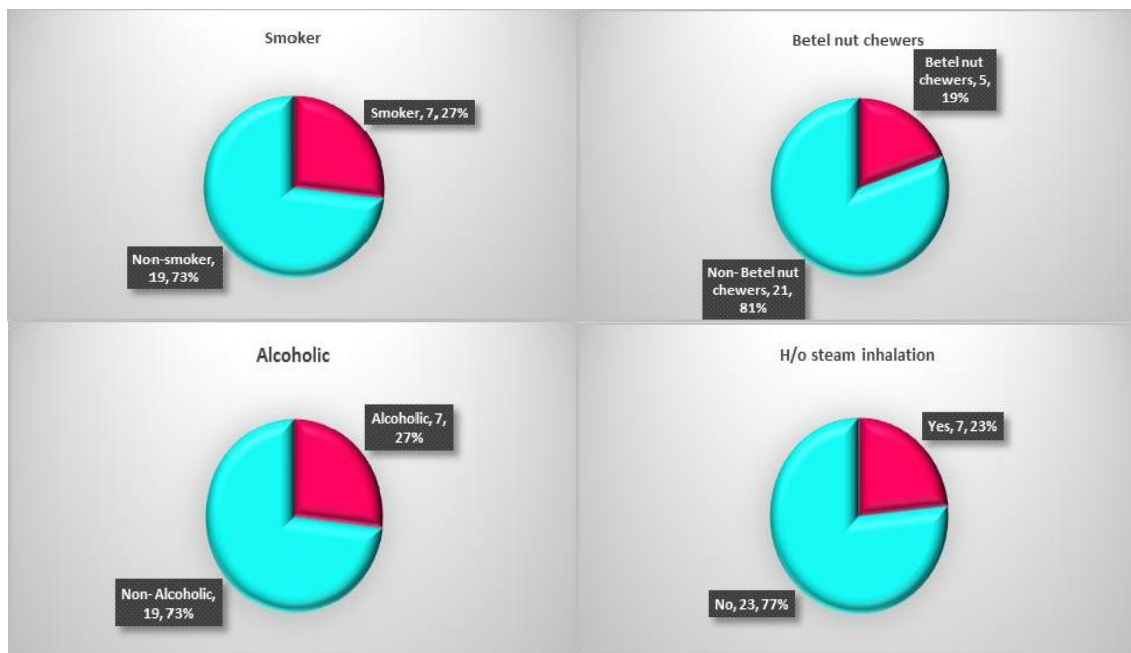


Graph 3: Comorbidities:



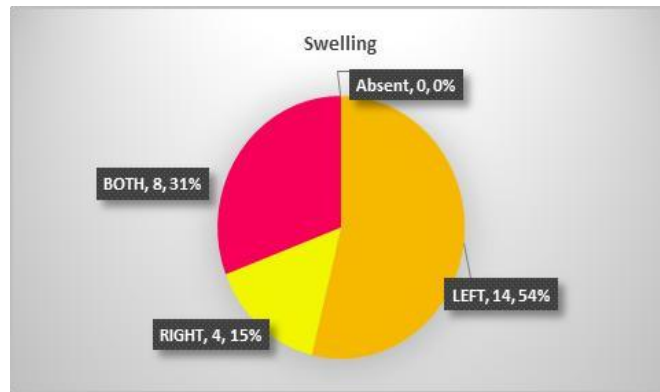
Graph 3: Type 2 diabetes mellitus 76.9% (20) was found to be the most common co-morbidity found in patients with mucormycosis. 46.15% (12) of the study population had systemic hypertension. 19.23% (5) had coronary artery disease. 11.53% (3) had chronic kidney disease, 11.53% (3) had bronchial asthma, 3.8% (1) had pulmonary tuberculosis, 3.8% (1) had a cerebrovascular accident and 3.8% (1) had type 1 diabetes mellitus as comorbidities. 65.3% (17) developed mucormycosis after developing covid 19 infection. The mean number of days after the onset of COVID-19 symptoms after which the symptoms of mucormycosis developed was found to be 15 days. 23.07% (6) of them were incidentally found to be COVID-19 positive after presenting with signs and symptoms of mucormycosis. 11.5% (3) of the study population were covid-19 RTPCR negative but radiological imaging done was suggestive of covid-19 infection.

Graph 4: Personal History And Its Relevance



Graph 4: 27% (7) of the population had a smoking addiction. 27% (7) were alcoholics. 19% (5) were betel nut chewers. 23% (7) of the study population gave a history of steam inhalation after the development of covid 19 symptoms.

Graph 5: Clinical Examination Findings

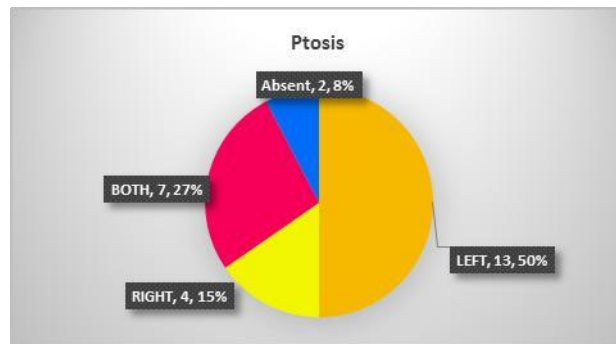


Swelling

Swelling of the face was found to be the most common sign in patients with mucormycosis. All 26 of the study population had facial swelling. 34% (14) of them had left-sided facial swelling, 15% (4) had right-sided facial swelling, whereas 31% (8) of them had swelling on both sides.

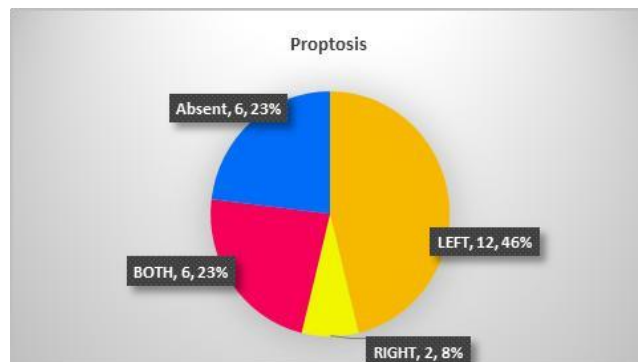
Ptosis

50% (13) of the study population had ptosis in the left eye. 15% (4) had right-sided ptosis. 27% (7) had ptosis of both eyes.



Proptosis

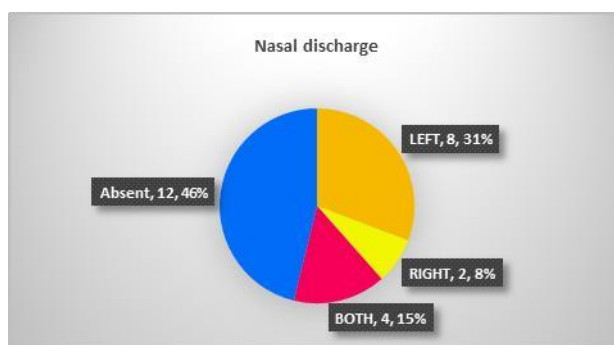
46% (12) of the study population had left-sided proptosis. 8% (2) had proptosis of the right eye. 23% (6) had proptosis of both eyes.



Nasal Discharge

31% (8) of the study population had a left-sided nasal discharge. 8%(2) of them had a right-sided

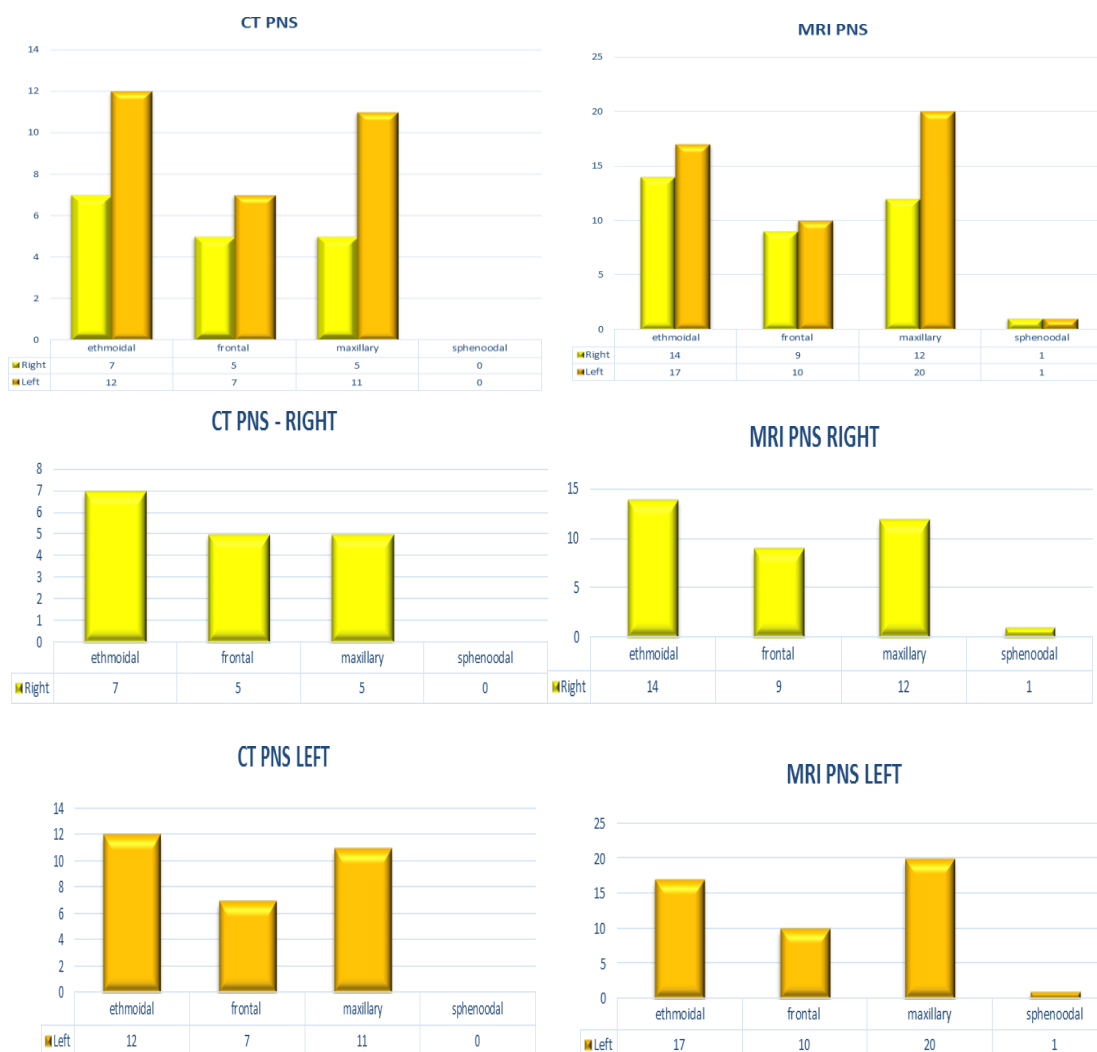
nasal discharge. 15% (4) of them had nasal discharge from both sides. Nasal discharge was absent in 46% (12) of the study population.



Ophthalmological Examination

30.7% (8) of the study population developed ophthalmoplegia – out of the 8 patients, 6 developed bilateral ophthalmoplegia. 30.7% (8) of the study population developed facial nerve palsy. Out of the 5 who developed unilateral facial nerve palsy, 4 developed left-sided facial nerve palsy whereas 1 developed right-sided facial nerve palsy. 15.38% (4) of the study population developed central retinal artery occlusion – all of them developed it on the left side patients among the study population developed bilateral cavernous sinus thrombosis.

Graph 6: Radiological Examination



Graph 6: All 26 of the study population had CT and MRI of the brain including the PNS and orbit. The most common sinus involved was found to be the maxillary sinus in both CT and MRI. The most common side involved was found to be the left side in both CT and MRI. 2 among the study population had developed left optic neuritis and 2 developed bilateral cavernous sinus thrombosis.

DISCUSSION

Mucormycosis is manifested by a variety of different syndromes in humans, particularly in immunocompromised patients and those with diabetes mellitus. The general in the order Mucorales causes most human infection [4]. These organisms are ubiquitous and can be found on decaying vegetation and in the soil. These fungi grow rapidly and release large numbers of spores that can become airborne. Because the agents of mucormycosis are common in the environment, they are relatively frequent contaminants in the clinical microbiology laboratory; all humans have ample exposure to these fungi during day-to-day activities [5]. The fact that mucormycosis is a rare human infection reflects the effectiveness of the intact human immune system. This is further supported by the finding that almost all human infections due to the agents of mucormycosis occur in the presence of some underlying compromising condition. *Rhizopus* organisms have an enzyme, ketone reductase, which allows them to thrive in high glucose and acidic conditions [6]. Serum from healthy individuals inhibits the growth of *Rhizopus*, whereas serum from individuals in diabetic ketoacidosis stimulates growth. Rhino-orbital-cerebral and pulmonary mucormycosis are acquired by the inhalation of spores [7]. In healthy individuals, cilia transport these spores to the pharynx, and they are cleared through the gastrointestinal tract. In susceptible individuals, infection usually begins in the nasal turbinates or the alveoli. The agents of mucormycosis are angioinvasive; thus, infarction of infected tissues is a hallmark of invasive disease [8]. Almost all patients with invasive mucormycosis have some underlying disease that both predisposes them to the infection and influences the clinical presentation. The most common underlying diseases are Diabetes mellitus - particularly with ketoacidosis, treatment with glucocorticoids, hematologic malignancies, hematopoietic cell transplantation, solid organ transplantation, treatment with deferoxamine, iron overload, AIDS, injection drug use, trauma/burns, malnutrition [9]. Diabetes appears to be more likely than other conditions to predispose to rhino-cerebral infection, but the reason for this is unknown. There have been case reports of mucormycosis in patients diagnosed with coronavirus disease 2019 (COVID-19), but the relationship between these two infections is unclear [10]. Some of the infections of mucormycosis were diagnosed several days to a couple of weeks after being admitted for COVID-19, and it seems reasonable to assume that the mucormycosis (rhinocerebral and pulmonary in these cases) was a secondary infection arising in a critically-ill patient on steroids. Almost 90 percent of cases involved the nose and sinuses, and overall mortality was 31 percent. Clinicians should be aware of the potential for rhinocerebral mucormycosis as a complication of COVID-19, especially in patients with underlying diabetes mellitus [11]. Mucormycosis is characterized by infarction and necrosis of host tissues that results from invasion of the vasculature by hyphae. A review of 179 cases of rhino-orbital-cerebral mucormycosis found that 126 (70 percent) of the patients had diabetes mellitus and that most had ketoacidosis at the time of presentation. There are rare reports of rhino-orbital-cerebral mucormycosis in the absence of any apparent risk factors. The infection usually presents as acute sinusitis with fever, nasal congestion, purulent nasal discharge, headache, and sinus pain [12]. All of the sinuses become involved and spread to contiguous structures, such as the palate, orbit, and brain usually progress rapidly over a few days. However, there have been some reports of rhino-orbital-cerebral mucormycosis with an indolent course that progresses over weeks [13]. The hallmarks of spread beyond the sinuses are tissue necrosis of the palate resulting in palatal eschars, destruction of the turbinates, perinasal swelling, and erythema and cyanosis of the facial skin overlying the involved sinuses and/or orbit [14]. A black eschar, which results from necrosis of tissues after vascular invasion by the fungus, may be visible in the nasal mucosa, palate, or skin overlying the orbit. Signs of orbital involvement include periorbital edema, proptosis, and blindness [15]. Facial numbness is frequent and results from infarction of sensory branches of the fifth cranial nerve. The spread of the infection from the ethmoid sinus to the frontal lobe results in obtundation. Spread from the sphenoid sinuses to the adjacent cavernous sinus can result in cranial nerve palsies, thrombosis of the sinus, and involvement of the carotid artery. Hematogenous spread to other organs is rare unless the patient has an underlying hematologic malignancy with neutropenia. A review of 208 cases of rhino-orbital-cerebral mucormycosis published in the literature between 1970 and 1993 found the following frequency of symptoms and signs [16]. Fever - 44 percent, Nasal ulceration or necrosis - 38 percent, Periorbital or facial swelling - 34 percent, Decreased vision - 30 percent, Ophthalmoplegia - 29 percent, Sinusitis - 26 percent, Headache - 25 percent. Rhino-orbital-cerebral mucormycosis is most commonly caused by *R. oryzae*. The

presence of mucormycosis should be suspected in high-risk patients, especially those who have diabetes and metabolic acidosis and who present with sinusitis, altered mentation, and/or infarcted tissue in the nose or palate [17]. Endoscopic evaluation of the sinuses should be performed to look for tissue necrosis and to obtain specimens. The specimens should be inspected for characteristic broad, non-septate hyphae with right-angle branching using calcofluor white and methenamine silver stains. The presence of the characteristic hyphae in a clinical specimen provides a presumptive diagnosis that should prompt further evaluation [18]. However, the absence of hyphae should not dissuade clinicians from the diagnosis of mucormycosis when the clinical picture is highly suggestive. Further evaluation includes imaging to gauge sinus involvement and to evaluate contiguous structures such as the eyes and brain. We generally perform a computed tomography (CT) scan as the initial imaging study as it can often be obtained quickly and is more sensitive than magnetic resonance imaging (MRI) for detecting bony erosions. [19,20].

CONCLUSION

Clinicians should have a low threshold for performing an MRI in patients with abnormalities on CT because the MRI will enhance the detection of intracranial, intraorbital, and cavernous sinus involvement. In a study of 23 immunocompromised patients with fungal sinusitis, CT findings included severe soft tissue edema of the nasal cavity mucosa (turbinates, lateral nasal wall and floor, and septum) in 21 patients, sinus mucoperiosteal thickening in 21 patients, bone erosion in 8 patients, orbital invasion in 6 patients, facial soft tissue swelling in 5 patients, and retroental fat pad thickening in 2 patients.

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