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Original Research Article

An Observational Study to Investigate the Head and Neck Mucormycosis in Patients with Prior COVID-19 Infection

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Abstract

Aim: The aim of the present study was to investigate the head and neck mucormycosis in patients with prior COVID-19 infection.

Methods: This cross-sectional study was conducted in the Department of Plastic Surgery, Nalanda Medical College and Hospital, Patna, Bihar, India, We obtained the information by examining the data of patients who visited Hospital with head and neck mucormycosis infection that occurred during or after the course of Covid-19 infection for the period of one year. Among all 50 patients were included.

Results: 30 (60) were men and 20 (40) were women, with a mean age of 56±12.6 years. 21 patients died due to mucormycosis, with a mean age of 60.0 ± 12.0 years (P-value=0.065), and those who survived had a mean age of 52.4 ± 12.0 years. The correlation of the clinical symptoms with the recurrence of mucormycosis and the outcome of the cases showed statistically significant differences in the outcome of patients with positive visual symptoms and orbital bone involvement.

Conclusion: The COVID-19 pandemic has caused an increase in the occurrence of mucormycosis, a fungal infection. This global health challenge has also led to a rise in secondary illnesses, including mucormycosis. Specifically, Rhino-orbito-cerebral mucormycosis (ROCM) in the head and neck area has been found to have a high mortality rate and can cause severe damage to the eyes, bones, and surrounding tissues. This investigation has established a clear connection between mucormycosis and visual impairment, involvement of the ethmoidal bone, and orbital involvement, all of which contribute to a higher mortality rate. Diagnosing mucormycosis in COVID-19 patients is challenging due to the absence of specific clinical features and reliable diagnostic tests.

Keywords: COVID-19, Mucormycosis; Immunocompromised; Diabetes Mellitus

Introduction

Mucormycosis, previously known as zygomycosis and phycomycosis, and recently called the "black fungus". It is a rare, saprophytic, opportunistic, and potentially lethal fungal infection, caused by fungi of the phylum Zygomycota, subphylum Mucormycotina, order Mucorales. [1] Mucormycosis was first reported in humans in the year 1855 and first examined in autopsy in 1956. [2] However, reports of original description by Paultauf in 1885 [3] and A. M. Marchevsky [4] exists. Mucormycosis affects a wide range of ages, from newborns to the elderly. Its global incidence and ecology show remarkable variations. Some studies report equal sex distribution, while others show male predominance. [5]

Mucormycosis presents in different locations and clinical patterns. Unlike the earlier belief that it is a disease of the immunocompromised. [6,7] The type and pattern of Mucormycosis should be identified according to the six well-recognized clinical categories of Mucormycosis, which are: rhino-orbital cerebral Mucormycosis (ROCM), cutaneous, pulmonary, gastrointestinal, disseminated, and miscellaneous. [3] While rhino-orbital cerebral Mucormycosis (ROCM), is prevalent among immunocompromised individuals; cutaneous Mucormycosis is common among the immunocompetent patients. [8] Cutaneous Mucormycosis is regarded as the third most common type of Mucormycosis [1,9] and can be

classified into localized, deep, or disseminated types. Others classify it into superficial or gangrenous forms. However, it is commonly classified into primary and secondary types. Primary Cutaneous Mucormycosis (PCM) occurs due to direct inoculation of infection, while Secondary Cutaneous Mucormycosis (SCM) occurs due to dissemination of infection; usually secondary to rhino-orbital cerebral Mucormycosis (ROCM). [9,10]

Rhinocerebral mucormycosis is a serious invasive fungal infection that is one of the most aggressive and lethal of invasive mycoses. Uncontrolled diabetes, organ transplant, malignancies such as lymphoma and leukemia, immunosuppressive therapy, renal failure, and acquired immune deficiency syndrome (AIDS) are all underlying diseases for mucormycosis. [11] Disseminated rhino-orbital-cerebral mucormycosis is a lethal invasive fungal infection that accounts for 8.3–13 percent of all fungal infections found in hematological patients' autopsies. Hematological malignancy, immunosuppressed children, and Diabetic ketoacidosis (DKA) are all predisposing factors. Uncontrolled diabetes mellitus, periorbital infection, and meningoencephalitis are all part of the mucormycosis triad. [12] Infarction and necrosis of the host tissues are symptoms of mucormycosis, which is caused by hyphae invading the vasculature. Mucormycosis can present as a variety of syndromes depending on the anatomic site involved, including rhino-orbital-cerebral, pulmonary, cutaneous, and less commonly GI, renal, and disseminated diseases. [13] Surgical debridement of the affected tissues and antifungal therapy is used to treat the condition. The drug of choice for initial therapy is intravenous amphotericin B (a lipid formulation). [14] The prognosis for recovery from mucormycosis is poor despite early diagnosis and aggressive combined surgical and medical therapy. [15]

The aim of the present study was to investigate the head and neck mucormycosis in patients with prior COVID-19 infection.

Materials and Methods

This cross-sectional study was conducted in the Department of Plastic Surgery, Nalanda Medical College and Hospital, Patna, Bihar, India. We obtained the information by examining the data of patients who visited Hospital with head and neck mucormycosis infection that occurred during or after the course of Covid-19 infection for the period of one year. Among all 50 patients were included. We defined the conditions for inclusion in the study as patients must have been infected with covid-19 before developing mucormycosis, and their covid-19 was confirmed by at least one of the following methods: polymerase chain reaction (PCR) or rapid antigen test or Computed tomography (CT) of the chest which was diagnosed by infectious and radiology specialists. According to clinical evidence and radiological interventions such as magnetic resonance imaging (MRA) or CT, possible mucormycosis patients were found and finally confirmed by culture.

A checklist was designed that includes demographic information such as gender and age were included in the checklist. In addition, the clinical presentation of the cases like pain, paresthesia, facial swelling and visual symptoms was noted. Past medical history of patients such as diabetes mellitus status, hypertension status, Renal Failure and malignancy were gathered. Lab data such as anemia, and leukocytosis were added to the checklist. Also, with the cooperation of several specialists, the imaging data of various head and neck anatomical parts such as the nose, maxillary, palate, orbital, ethmoid, sphenoid, frontal, and scalp were analyzed and added to the above collection.

Statistical Analysis

Statistical analysis was performed using SPSS software version 22 (IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as number and frequency (%) for categorical variables. Quantitative variables are presented by means with standard deviation (mean ± SD) or median with interquartile ratio (median, IQR). For data analysis, the Shapiro- Wilk test was used to assess the normal distribution of quantitative variables. Chi-square, exact fissure test, and independent sample T-test were used to investigate the correlation of each independent factor with the outcome and recurrence. Multivariate logistic regression was used to correlate the chosen variables with the outcome. P-value of less than 0.05 was considered as significantly different.

Results

Table 1: Demographic information and their correlation with recurrence and outcome

Number (%) Mean±SD			Recurrence N(%) Mean±SD Positive Negative		*P*-value	Outcome N (%) Mean±SD Death Alive		*P*-value
Age		56±12.6	52.8 ± 14.4	59.0 ± 12.6	0.087	60.0 ± 12.0	52.4 ± 12.0	0.065
Sex	**Female**	20 (40)	13	7	.078	11	9	.314
	Male	30 (60)	14	16		10	20	
Anemia		23(46)	14	9	.290	9	14	.912
Leukocytosis		23(46)	11	12	.480	9	12	.942

Diabetes mellitus (DM)	39(78)	22	17	.512	16	23	.176
Hypertension (HTN)	26(52)	15	11	.480	13	13	.078
Renal Failure (RF)	7 (14)	3	4	.428	4	3	.242
Malignancy	4 (8)	1	3	.358	2	2	.350

30 (60) were men and 20 (40) were women, with a mean age of 56±12.6 years. 21 patients died due to mucormycosis, with a mean age of 60.0 ± 12.0 years (P-value=0.065), and those who survived had a mean age of 52.4 ± 12.0 years.

Table 2: Clinical presentation information and their correlation with recurrence and outcome

Variables	Number (%)	Recur Positive	Rence Negative	*P*-value	De Positive	Ath Negative	*P*-value
Visual symptom	32	18	14	.525	16	16	.034
Nasal bone involvement	18	10	8	.780	9	9	.212
Ethmoid bone involvement	24	12	12	.670	14	10	.026
Maxillary bone involvement	45	25	20	.260	18	27	.525
Orbital bone involvement	26	14	12	.880	14	12	.046
Frontal bone involvement	2	0	2	.220	0	2	.390
Palatine bone involvement	14	5	9	.055	7	7	.352
Sphenoid bone involvement	6	3	3	.440	1	5	.372
Scalp involvement	1	0	1	.456	0	1	.632

The correlation of the clinical symptoms with the recurrence of mucormycosis and the outcome of the cases showed statistically significant differences in the outcome of patients with positive visual symptoms and orbital bone involvement.

Table 3: Multivariate logistic regression of selected variables and outcome (alive, death)

Variables	B	*P*-value	OR	95% CI
Age	.072	.034	1.082	1.007-1.161
Sex	-1.672	.068	.186	.033-1.092
Visual symptom	1.432	.116	4.206	.697-25.397
Ethmoid bone involvement	1.216	.124	3.372	.715-15.876
Orbital bone involvement	1.758	.050	5.808	1.001-33.702
constant	-6.474	.007	.002	

The logistic regression multivariable analysis was presented in Table 3.

Discussion

Among COVID-19 patients admitted to intensive care units (ICUs) with acute respiratory failure, the most prevalent fungal pathogens are Aspergillus, Candida, and Mucor. [16,17] Mucormycosis is a common invasive fungal infection that primarily affects immunocompromised individuals, along with aspergillus. [18] Mucormycosis is caused by fungi belonging to the order Mucorales, which are ubiquitous in nature. [19] These infections are characterized by their severe and rapidly progressive nature, leading to significant morbidity and mortality. [20] The COVID-19 pandemic has witnessed a sudden surge in the number of mucormycosis cases worldwide. [21,22] One of the countries hit hardest by the COVID-19 pandemic, India experienced a significant increase in mucormycosis cases. In May 2021, India reported thousands of mucormycosis cases, with estimates suggesting over 11,000 cases. [23,24]

30 (60) were men and 20 (40) were women, with a mean age of 56±12.6 years. 21 patients died due to mucormycosis, with a mean age of 60.0 ± 12.0 years (P-value=0.065), and those who survived had a mean age of 52.4 ± 12.0 years. Mucormycosis can invade different body systems including head and neck region. Rhino-orbito- cerebral mucormycosis (ROCM) refers to Mucorales infection of this region, which has a high mortality rate. [25,26] Some ocular signs and symptoms associated with ROCM include eye pain, ophthalmoplegia, impaired vision, orbital cellulitis, necrosis, and ptosis. [27]

The correlation of the clinical symptoms with the recurrence of mucormycosis and the outcome of the cases showed statistically significant differences in the outcome of patients with positive visual

symptoms and orbital bone involvement. Diagnosing mucormycosis in COVID-19 patients presents a significant challenge due to the lack of specific clinical features and reliable diagnostic tests. The clinical manifestations of mucormycosis can overlap with other fungal or bacterial infections, making it difficult to differentiate and diagnose accurately. However, a high index of suspicion is crucial in identifying potential cases. Imaging techniques such as computed tomography (CT) scans can aid in detecting characteristic findings. [28]

Biopsy-proven Mucormycosis is the gold standard for a precise definitive diagnosis. However, to avoid false-negative histopathological results, the harvested tissue biopsy should be deep enough and include subcutaneous fat to facilitate recovering the characteristic hyphae. These are broad, branching, aseptate hyphae that are the cause of thrombosis and tissue necrosis. Fungal Rhinosinusitis (FRS) can be divided into invasive and non-invasive types according to histopathological evidence of fungal tissue invasion. [29] However, surgical debridement of progressive disease or necrotic tissues should not be delayed due to an unavailable or negative histopathological result, especially at the time of covid-19. Surgical eradication of diseased tissues provides a life-saving measure, initially at the cost of esthetics and function. However, advances in free flaps allow surgical reconstruction of defects once considered inoperable, and bring vascularized tissue into a previously compromised area. Anterolateral thigh (ALT) flap was chosen as it offers a highly versatile reconstructive option when different coating surfaces are needed. It provides sufficient volume to ablate the previously excised sinus cavities, adequate bulk to cover the complex orofacial defect with reasonable projection to the malar region. Survivors of Mucormycosis are high-risk patients, and planning their reconstruction by free flaps is an added challenge. Many authors [30] prefer delayed reconstruction after surgical debridement of Mucormycosis. The study revealed that there is no notable connection between the recurrence or mortality of mucormycosis and certain factors such as leukocytosis, blood group, frontal bone involvement, maxillary bone involvement, sphenoidal bone involvement, or scalp involvement.

Conclusion

The COVID-19 pandemic has caused an increase in the occurrence of mucormycosis, a fungal infection. This global health challenge has also led to a rise in secondary illnesses, including mucormycosis. Specifically, Rhino-orbito-cerebral mucormycosis (ROCM) in the head and neck area has been found to have a high mortality rate and can cause severe damage to the eyes, bones, and surrounding tissues. This investigation has established a clear connection between mucormycosis and visual impairment, involvement of the ethmoidal bone, and orbital involvement, all of which contribute to a higher mortality rate. Diagnosing mucormycosis in COVID-19 patients is challenging due to the absence of specific clinical features and reliable diagnostic tests.

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