

P272

Fungal brain abscess in the era of COVID 19: an experience from a tertiary care Neurosciences Institute in South India

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Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is ruling the world for more than 2 years since 2020. In 2021, the second wave of COVID-19 attributed to the 'delta variant' swept across India, causing significant morbidity and mortality. In addition, the epidemic of COVID-19-associated mucormycosis affected the Indian subcontinent specifically, with a whopping 41 512 cases and 3554 deaths attributed to this dreadful disease.

Methods: The single-center retrospective cross-sectional study was aimed to determine the impact of COVID-19 on fungal brain abscess cases at a non-COVID tertiary care Neurosciences Institute in South India. The study included all cases diagnosed with fungal brain abscess microbiologically (microscopy and/or fungal culture), supported by radiological findings or by histopathological examination. Cases of brain abscess which were negative for fungal elements by microscopy, culture, and imaging were excluded from the study. Fungal culture was done on routine mycological media as per standard procedures. Fungal identification was done by microscopic morphology, MALDI-TOF MS, and ITS sequencing.

Results: A total of 406 cases of brain abscess were recorded between January 2020 and April 2022. Out of these, 26 (6.4%) were cases of fungal brain abscess. In 2020, three out of 153 (2%) cases had a fungal etiology, while it was 10.4% (22/211) in 2021 and 0.24% (1/42) till April 2022. Overall, a male preponderance was observed (20/26, 77% were males). The cases had an even distribution from 6 to 62 years, with no predilection in any particular age group. The most common underlying comorbidity was type 2 diabetes mellitus (13/26, 50%). Four cases had a past history of COVID-19. Radiological suspicion of fungal infection was present in all the cases. Mycological examination (wet mount and 20% KOH mount) of brain abscess pus from all the cases revealed fungal elements. Out of 26 cases, 23 cases showed hyaline, broad aseptate hyphae, 2 showed melanized septate hyphae and 1 showed budding yeast cells with pseudohyphae and arthroconidia on direct microscopy. Culture positivity was observed in 15 cases (57.7%). Out of 23 suspected cases of rhinocerebral mucormycosis based on clinical, radiological, and direct microscopic findings, fungal culture was positive in 13 cases, all of which were identified as *Rhizopus arrhizus*. Out of two cases that showed melanized hyphae in direct microscopy, one grew a dematiaceous mold that was identified as *Cladophialophora bantiana*. The other melanized fungus failed to grow in culture. The single case of brain abscess caused by a yeast-like fungus was attributed to *Trichosporon dohaense*, identified by ITS sequencing. It was initially misidentified as *T. ovoides*/*T. mucoides* by VITEK MS due to lack of mass spectral database for *T. dohaense*.

Conclusions: A significant increase in the incidence of fungal brain abscess has been observed in the COVID-19 era, particularly with each new wave of infection. Clinical features along with imaging and mycological findings are crucial in making an early diagnosis and decision regarding antifungal therapy. Accurate identification to the species level is necessary to guide optimal antifungal therapy as several species exhibit emerging resistance to antifungal drugs.

P273

Diagnostic dilemmas in Pneumocystis pneumonia in case of long COVID -19

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Background: To diagnose Pneumocystis pneumonia in an underlying COVID-19 infection is difficult because of the clinical and radiological indistinguishability of the presentation.

Case Presentation: We report the case of a 67-year-old male background of type 2 diabetes mellitus (DM) and hypertension (HTN), who presented to the emergency department for severe dyspnea for 6 days. He is treated with corticosteroid and other supportive therapy. Initially, the patient responded with that treatment but suddenly his hypoxia is increasing and getting intubated. All possible causes of deterioration hypoxia were evaluated and came negative. Later stage, BAL was done and immunofluorescence test for PCP came positive. Systemic, cotrimoxazole started and gradually hypoxia improved and extubated.

Conclusion: Pneumocystis and COVID-19 co-infection needs serious consideration, particularly for patients with long-term COVID-19, even if patients do not have conventional risk factors for Pneumocystis pneumonia.

P274

COVID-associated invasive pulmonary aspergillosis (CAPA) – a case report

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COVID-associated pulmonary aspergillosis (CAPA) is a severe fungal infection with a high mortality rate. The incidence of CAPA is on the rise possibly due to the prescription of corticosteroids and tocilizumab two repurposed drugs used for treating SARS-CoV-2. Diagnosis is challenging due to the non-specific nature of symptoms. Voriconazole is the mainstay of therapy. We present a case of a 42-year-old male presenting with left hydro pneumothorax post recovery from COVID infection, and later succumbed to this complication. Patients developing pulmonary aspergillosis after short-term steroid therapy is uncommon. The possibility of aspergillosis in immunocompetent patients should be considered in those on systemic steroids and deteriorating pulmonary functions.

P275

Dematiaceous fungi as a rare cause of fungal sinusitis in a tertiary care center

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Objectives: To discuss the occurrence and diagnosis of dematiaceous fungi as a causative organisms of fungal sinusitis in patients at a tertiary care center in North India. Since there is limited data on its prevalence, this study was aimed to know the non-*Aspergillus* causes of fungal sinusitis focusing on the dematiaceous fungi.

Methods: A total of 451 nasal biopsy samples, from the department of pulmonary medicine ward and ICU were received over a period of 3 years, from January 2019 to December 2021. The samples were subjected to conventional mycological diagnostic techniques including direct epifluorescence and light microscopy, culture on solid media and visual identification of growth in culture using lactophenol cotton blue mounts.

Results: Out of 451 samples, no fungi were isolated from 299 samples (66.29%), *Aspergillus* spp from 63 samples (13.96%), dematiaceous fungi from 10 samples (2.21%), and other fungi from 79 samples (17.5%). Among the dematiaceous fungi isolated, 7 isolates were identified as *Alternaria* spp. (70%) and 3 isolates were identified as *Curvularia* species (30%) and described.

Conclusion: Most reported cases of allergic and invasive sinusitis were attributed to *Aspergillus* spp. However, in the current study, dematiaceous 'black' fungi like *Alternaria* and *Curvularia*, were also identified as causes of fungal sinusitis in both immunocompromised and immunocompetent individuals, showing an increasing pathogenic spectrum. Hence a high index of clinical suspicion and appropriate laboratory diagnosis assists in initiating appropriate treatment such as surgical debridement, reducing immunosuppression, and antifungal treatment with newer azoles.

P276

Molecular epidemiology of clinical filamentous fungi in Qatar beyond Aspergillus and Fusarium

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Objectives: Due to an increasing number of patients at risk, (ie, with a highly compromised immune system and/or receiving aggressive chemotherapy treatment), invasive fungal infections (IFI) are increasingly being reported. They are associated with significantly high mortality rates. *Aspergillus* spp., particularly *A. fumigatus*, is the major cause of mold-related IFI around the world followed by *Fusarium* spp., however, other molds are emerging as human pathogens. The aim of this study was to explore the epidemiology and prevalence of the non-*Aspergillus* and non-*Fusarium* molds in human clinical samples over 11 years period in Qatar based tertiary hospital using molecular techniques.

Methods: A total of 91 clinical specimens positive for molds belonging to 90 patients were recorded in about 11 years (September 2003 to November 2014). The isolates were identified based on morphological characteristics and by sequencing the internal transcribed spacer (ITS) gene. To confirm the identifications, a phylogenetic tree based on ITS sequences was constructed.

Results: Most patients were males (72%), 6% were immunocompromised, 12% had IFI, and 7% died within 30 days of diagnosis. The fungal isolates were recovered from a variety of clinical samples, including nails, skin, hair, scalp, nasal cavity, wounds, respiratory samples, body fluids, eye, ear, tissue, abscess, and blood specimens. Dematiaceous fungi were overall the most isolated (33/91, 36%), followed by dermatophytes (25/91, 27%), Mucorales (16/91, 18%), and other hyaline molds (17/91, 19%) (Fig. 1). *Curvularia* was the most isolated genus (22/91, 24%) and Mucorales were the major cause of IFI (5/11, 45.5%) (Table 1). Superficial mycoses were caused by dermatophytes (66%) and non-dermatophytes (34%). Furthermore, rare fungi that are not commonly known to cause human disease were recovered such as *Rhizidhysteron rafatum*, *Subramaniula asteroides*, *Dothichiza pimprina*, and *Quambalaria cyanescens*.

Conclusion: The current study highlights the epidemiology and spectrum of mold genera, other than *Aspergillus* and *Fusarium*, recovered from human clinical samples in Qatar, which can aid in surveillance of uncommon and emerging mycoses other than aspergillosis and fusariosis.

Figure 2. Distribution of fungal isolates

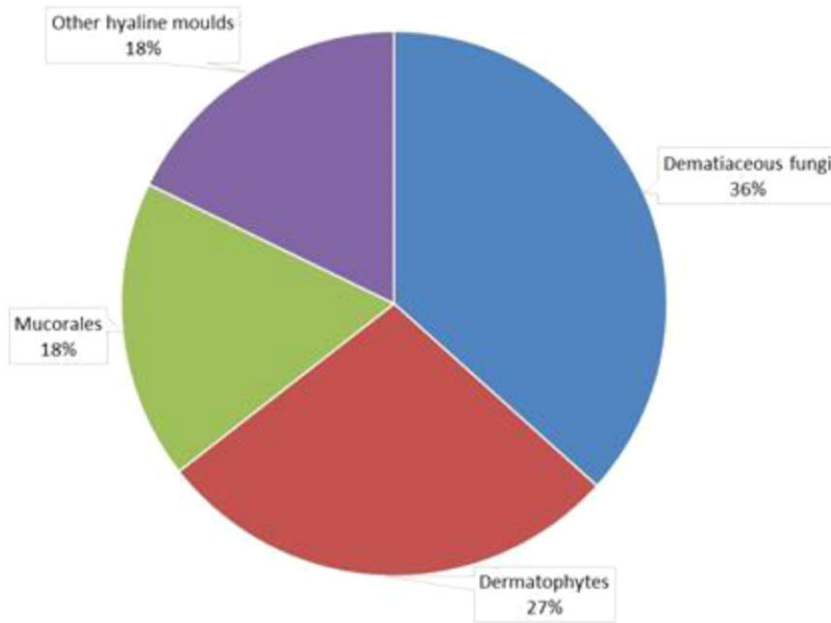


Table 1. Risk factors associated with invasive fungal infections

Group of fungi	Organism (n)	Risk factor	Specimen
Mucorales (5)	<i>Mucor indicus</i> (1)	Liver transplant	BAL
	<i>Rhizopus oryzae</i> (2)	Renal transplant	Nasal
		NA*	Nasal
	<i>Rhizopus microsporus</i> (2)	Abdominal surgery	Abdominal tissue
Fracture		Wound tissue	
Dematiaceous fungi (4)	<i>Curvularia</i> spp. (3)	NA	Nasal
		NA	Nasal
		NA	Nasal
	<i>Rhinocladiella mackenziei</i> (1)	Breast Cancer	Brain abscess
Hyaline fungi (2)	<i>Sarocladium kiliense</i> (1)	Breast Cancer	Blood
	<i>Acremonium breve</i> (1)	Eumycetoma	Foot Pus

*Data not available.

P277

The epidemiology, clinical manifestations and outcomes of cerebral mucormycosis: A systematic review

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Objectives: Mucormycosis is a devastating infection caused by Mucorales order ubiquitously existing in the environment. Cerebral mucormycosis, the mortal manifested type of brain infection, is commonly seen in association with deep immunocompromised status. Despite lethality of brain mucormycosis, the lack of consensus data specifically concerning clinical manifestations, radiographical characteristics, diagnosis methods, and management are severely felt.

Methods: In this systematic review and meta-analysis, we searched PubMed and Scopus (up to December 31, 2018) using the combination of the following keywords: ('Mucor*' or 'Zygomyc*') and ('cereb*' or 'brain' or 'central nervous system' or 'intracranial') and found ~1462 articles.

Only published case reports or case series with the definition of cerebral mucormycosis (finding the signs of this invasive mold in histopathological section or mycological examination and the presence of histopathological or radiological signs of brain involvement) were included. However, animal mucormycosis and papers in languages other than English or duplicates were excluded. Overall, 287/1462 articles were reviewed and included consisting of 345 cases of cerebral mucormycosis.

Results: A total of 206 (59.7%) patients were male. The most common risk factor was diabetes mellitus (51%), followed by hematological malignancies (23.8%). Remarkably, among hematological malignancies, acute lymphoblastic leukemia was significantly associated with cerebral mucormycosis ($P < .001$). In terms of reported risk factors, only 16.3% of patients had hematological malignancies till 2000, while the percentage of cases (29.7%) with this risk factor increased significantly after 2000 ($P = .04$). The most common clinical symptoms were orbital (46.4%) and neurological symptoms (41.2%), while headache was present in 35.9% of patients and fever only in 0.6%. Of the patients reported, 60.6% died and there was a significant correlation between mortality rate and diabetes mellitus ($P = .003$), while the mortality rate was not associated with other risk factors such as hematological malignancies.

Conclusions: In patients with mucormycosis, the presence of orbital clinical symptoms may suggest cerebral involvement as much as the presence of neurologic symptoms. Finally, it can be said that Cerebral Mucormycosis is a very fatal mold infection, especially if it occurs in diabetic patients.