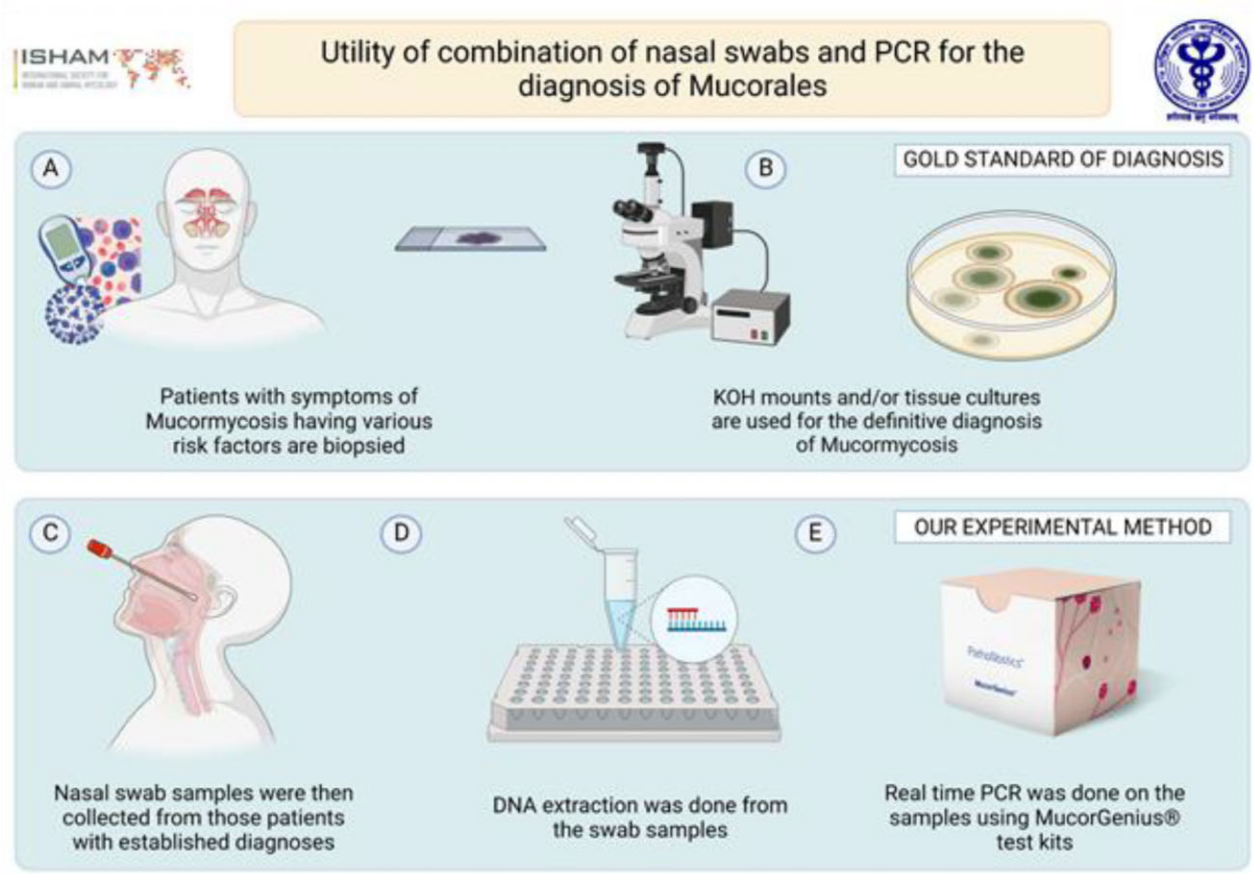

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Influence of underlying conditions on disease presentation and diagnostic strategy during pulmonary mucormycosis: Anational study of 114 cases

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Poster session 3, September 23, 2022, 12:30 PM - 1:30 PM

Objectives: Pulmonary mucormycosis (PM) is a life-threatening invasive fungal infection mostly affecting immunocompromised patients. We aimed to study the influence of underlying conditions on disease presentation and diagnostic strategy during PM.

Methods: All PM cases from six French teaching hospitals between 2008 and 2019 were retrospectively reviewed. Cases were defined according to EORTC/MSG 2019 criteria with the addition of diabetes and traumatism as host factors and positive serum or tissue PCR as mycological evidence. Thoracic CT scans were reviewed centrally.

Results: Among 114 cases of PM, 52 (46%) were proven and 62 (54%) were probable, including 12 cases with a positive serum qPCR as the sole mycological criterion. Hematological malignancy was the most common risk factor (49%), followed by allogeneic hematopoietic stem-cell transplantation (21%), and solid organ transplantation (SOT, 17%). Fever was the first symptom for 66% patients and was more frequent in patients with neutropenia than in those without (97% vs 52%, P <.01). A total of 46 (40%) patients had a disseminated infection, which was more frequently reported in neutropenic patients (50% vs 25%, P <.01). Main dissemination sites were the liver (48%), spleen (48%), brain (44%), and kidneys (37%). Sinusitis was present in 13% of cases.

Chest radiological presentation included consolidation (58%), pleural effusion (52%), reversed halo sign (26%), halo sign (24%), vascular abnormalities (26%), and excavation (23%). The excavation was more frequently reported in SOT patients (64%, P <.01) compared with other groups. Vascular involvement was associated with reversed halo sign and Rhizomucor infection. Neutropenic patients presented more frequently than non-neutropenic patients with ground-glass opacities (75 vs 49%, P = .01), halo sign (32% vs 10%, P = .02), and reversed halo sign (35 vs 10%, P <.01).

A total of 83 (73%) patients had a positive fungal culture from any type of respiratory sample. Serum qPCR was positive for 42/53 patients (79%) and respiratory fluid qPCR for 16/21 (76%) patients. In neutropenic patients, BAL culture was less often positive (30% vs 66%, P <.01), and serum qPCR was more frequently positive (91% vs 62%, P = .02). A transthoracic lung biopsy was contributive in 8/11 (73%) patients with negative bronchoalveolar lavage (BAL). Serum qPCR was more frequently positive in patients with the main lesion of >3 cm in diameter (91% vs 62%, P = .02). *Rhizomucor* spp. Was identified in 31 patients (32%), *Rhizopus* spp. In 29 patients (30%), *Lichtheimia* spp. In 24 patients (25%), *Mucor* spp. In 10 patients (10%) and *Cunninghamella* spp. In 4 patients (4%). Neutropenic patients were more frequently infected with *Rhizomucor* (43% vs 13%, P <.01) and less frequently with *Rhizopus* (17% vs 50%, P <.01). Histopathological specimens were available for 48 patients (42%) and revealed Mucorales hyphae in 85% of cases. Patients with a disseminated infection and neutropenia presented more often with angioinvasion than patients with localized disease (50% vs 9%, P <.01 and 38% vs 13%, P = .10). Overall, 90-day mortality was 59%.

Conclusion: Underlying conditions significantly influenced clinical and radiological presentation and diagnostic tools' contribution. Neutropenic patients present more frequently with dissemination, fever, reversed halo sign, pathological angioinvasion, the negativity of BAL culture, the positivity of serum qPCR, and Rhizomucor infection.

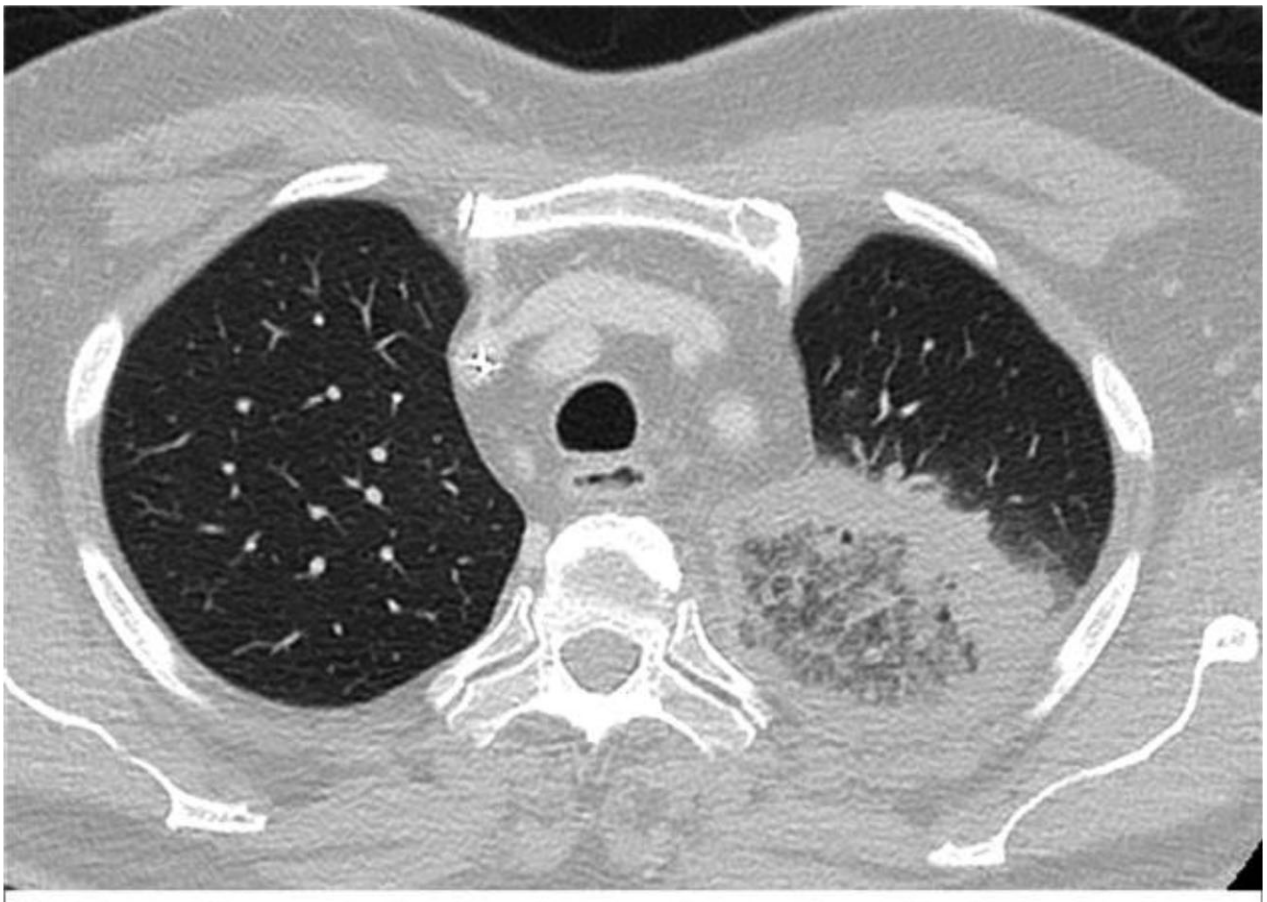

Figure 1. Reverse halo sign in a neutropenic patient

Figure 2. Thrombosis of the subclavian artery due to fungal angioinvasion in a neutropenic patient

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COVID-19-associated pulmonary aspergillosis: Species distribution and susceptibility profiles

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Objectives: This study aimed to investigate the species distribution and susceptibility profiles of *Aspergillus* species isolated from patients admitted to the intensive care unit with severe COVID-19 in Isfahan, Iran, between April 2021 and March 2022.

Methods: This retrospective study included intubated patients with COVID-19 in three referral COVID-19 hospitals. Tracheal aspirate (TA) samples were taken from 267 patients to investigate pulmonary co-infections. COVID-19-associated aspergillosis (CAPA) was defined according to the 2020 European Confederation of Medical Mycology/International Society of Human and Animal Mycosis consensus criteria. *Aspergillus* species obtained from samples were characterized based on conventional and molecular assays. *In vitro* antifungal susceptibility testing was performed on the obtained isolates according to the guidelines from the Clinical and Laboratory Standards Institute.

Results: The mean age of the patients was 61.73 ± 12.69 years. The mean length of hospitalization and admission in ICU were 18.77 ± 12.94 and 13.51 ± 9.83 days, respectively. A total of 61 (22.9%) patients presented with a single cavity lesion. Pulmonary artery pseudoaneurysm was seen in seven patients and post-COVID-19 changes were seen in all patients. Based on the conventional and molecular techniques, 72 isolates of *Aspergillus* species (26.9%), including *A. flavus* (10.1%%), A. *fumigatus* (8.6%%), *A. niger* (3.3%), *A. tubingensis* (2.9%), *A. terreus* (1.1%), *A. luchuensis* (0.37%) *A. quadrillineatus*, and (0.37%), were obtained from 267 patients. MIC results showed that all *Aspergillus* species were susceptible to all tested antifungal drugs.

Conclusion: Access to priority clinical groups, improving the care of patients with simultaneous pulmonary aspergillosis with COVID-19, and identifying *Aspergillus* species are essential steps in the care cascade to manage those affected by them.

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Diagnostic value of *Candida* coloni zation index and serum *Candida mannan* antigen for candidemia in febrile episodes of pediatric lymphoreticular malignancies

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Objective: To evaluate the diagnostic performance of *Candida* colonization index and serum *Candida mannan* antigen predicting candidemia in febrile episodes of pediatric lymphoreticular malignancies

Methods: It was a prospective observational study done for 18 months, from November 2018 to April 2020 at the pediatric oncology unit of a multispecialty tertiary care center. Based on our patient load, duration of the proposed study, and available resources, a sample size of 49 ($n = 49$) was decided and 100 febrile episodes in children with lymphoreticular malignancy were studied. Children below 12 years, receiving chemotherapy for hematological malignancy having oral or axillary temperature >38.3˚C for >1 h were included in this study. Children receiving the antifungal treatment in last 7 days were excluded from the study. Blood collected on day1 and day4 was cultured in BACTEC-9120. For colonization, swabs and samples were collected and cultured on SDA on day1, day4, and day8. All *Candida* isolates were subcultured on SDA and subjected to Gram's stain, germ tube test followed by Microscan identification. DNA sequencing followed by phylogenetic analysis was done for all the isolates of *Candida* recovered from blood. Antifungal susceptibility of yeast stains was done. Serum collected on day1 was used for *C. mannan* antigen detection using ELISA system.

Results: Prevalence of candidemia was 5%. Non-*albicans Candida* spp were isolated from blood cultures on day 4. *Candida* colonization decreased from day1 to day8. Colonization index (CI) day1 showed 80% sensitivity 98.9% specificity, and 98.9% negative predictive value. Significant colonization (CI ≥0.5) was seen in a larger proportion of cases that developed candidemia. There was a significant association of *Candida* colonization (CI ≥0.5) with occurrence of candidemia on day1 and day4. A total of 4 (80%) of candidemia episodes were positive for serum mannan antigen while 1 (20%) was negative. Mannan antigen was detected earlier with 80% sensitivity, 92.6% specificity, and 98.9% negative predictive value. All *Candida* isolates were sensitive to fluconazole, amphotericin-B, and caspofungin.

Receiver operator characteristic curves for diagnostic performance of various parameters in predicting candidemia show the following trends:

- Best parameter in terms of AUROC is the CI (Day 1).
- Best parameters in terms of sensitivity are the CI (Day 1), CI (Day 4), and mannan antigen level.
- Best parameter in terms of specificity is the CI (Day 8).
- Best parameter in terms of positive predictive value is the CI (Day 1).
- Best parameters in terms of negative predictive value are the CI (Day 1), CI (Day 4), and mannan antigen level.
- Best parameters in terms of diagnostic accuracy are the CI (Day 1), CI (Day 8).

Conclusion: The CI can predict candidemia but the threshold value needs to be explored in pediatric patients with lymphoreticular malignancies. Mannan antigen detection gives early results with a high negative predictive value.