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A Mexican case series of COVID-19-associated pulmonary aspergillosis

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The pandemic coronavirus disease 2019 (COVID-19) has been in the scope for invasive pulmonary aspergillosis (IPA) after the first reports worldwide, now known as CAPA.

Objective: to describe a case series of CAPA documented in four intensive care units while treating patients with severe COVID-19 pneumonia in order to describe clinical characteristics, cultures result and MICs from *Aspergillus* isolations, and treatments.

Methods: A prospective and descriptive study was performed from March 2020 to February 2022 in four tertiary level hospitals that treated COVID-19 patients in Mexico. We followed every single culture coming from the COVID-19 ICU. *Aspergillus* positive cultures had morphologic identification, and the MICs were obtained by broth microdilution. We did not interfere in the treatment.

Results: During 24 months of follow-up of patients with severe COVID-19 we found 17 adult cases with a mold identification, from those, 14 patients fit in the possible CAPA definition according to ECMM/ISHAM, and the remaining 3 were treated after expert opinion. The baseline characteristics of overall 47% had diabetes, and 41% were obese. Of the 14 cases included as a possible CAPA all of them had acute severe respiratory syndrome (average PaO₂/FIO₂ 134 mmHg), 64% were in prone position, 78% had steroids at ICU admission, 92% had antibiotics at ICU. The computed tomography pattern predominantly associated were pulmonary infiltrates, nodules and cavitation. Only 2 patients (14%) had a positive galactomannan (>4.5) from non-bronchoscopic lavage. We had 9 *Aspergillus fumigatus* isolations and 4 *A. niger*, 1 *A. flavus*, 6 patients received voriconazole, 3 patients received isavuconazole, 1 anidulafungin and liposomal amphotericin B were used in 1 patient each respectively. The predominant MIC from isolations were ≥64 µg/ml for fluconazole, and <0.5 µg/ml for voriconazole, also all of them had MIC equal or <0.75 µg/ml for isavuconazole and 0.015 µg/ml for anidulafungin. A total of 50% of the patients had a CAPA-related death.

Conclusions: CAPA is still a difficult entity to think of for diagnosis and treatment in severely ill COVID-19 patients. What predominates like other series were obesity, use of steroids, and ARDS. The contribution of small Mexican series like ours (based on the new guidelines) will allow to understand that CAPA could be no longer a rare fungal infectious disease complication in severely ill COVID-19 patients. An extended consensus must be made for those possible CAPA definition cases.

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Oral Candidiasis among inpatients with COVID-19 in the North of Iran

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Objectives: We aimed to characterize oral candidiasis epidemiology, species distribution, and antifungal susceptibility profiles among COVID-19 patients.

Methods: This observational cross-sectional study enrolled patients >18 years old with confirmed oral candidiasis admitted at Razi teaching hospital (a reference infectious disease center in Mazandaran Province). Oral samples from patients with suspected oral candidiasis infection were collected and were confirmed for oral candidiasis by microscopic examination and fungal culture. Fungal isolates were identified using Multiplex polymerase chain reaction (PCR) and PCR-fragment length polymorphism. *In vitro* susceptibility testing for amphotericin B, fluconazole, voriconazole, and micafungin of all identified isolates was performed using broth microdilution according to the Clinical and Laboratory Standards Institute (CLSI) broth microdilution guideline (M27-A3 and M60) standard.

Results: Among 4133 COVID-19 admitted patients during a year in Razi hospital, 120 patients had confirmed oral candidiasis. Totally 172 *Candida* isolates causing oral candidiasis isolated from these patients were identified. Most patients were infected with a single *Candida* species; however, it is notable that mixed *Candida* species caused oral candidiasis in 46 patients. *Candida albicans* (60.46%) was the most common species. Among non-*albicans Candida* species, *C. glabrata* (17.44%) was the most isolates, followed by *C. tropicalis* (11.62%), *C. kefyr* (7.55%), and *C. krusei* (2.9%). Although non-*albicans Candida* species, including *C. glabrata* and *C. krusei* demonstrated high minimum inhibitory concentration (MIC) against azole drugs, in terms of MIC₉₀ values, all tested drugs exhibited superior activity against *C. albicans*. In terms of MIC Geometric mean, amphotericin B and micafungin were more potent than all comparator drugs.

Conclusions: Our study described the high incidence of oral candidiasis caused by non-*albicans Candida* species in COVID-19 patients; most of them, including *C. glabrata* and *C. krusei* exhibits intrinsic decreased susceptibility to the azole class of antifungals. Further studies should design an appropriate prophylaxis program to prevent oral candidiasis in COVID-19 patients.

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Entomophthoromycosis: a rare fungal infection case series

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Objectives: To present a case series of entomophthoromycosis (a rare fungal infection of the skin and subcutaneous tissue with a protracted and chronic clinical evolution), which would aid in the early recognition and management of this condition.

Materials and Methods: A total of 7 laboratory-confirmed cases of entomophthoromycosis, diagnosed and treated between May 2018 and March 2022 at our center, were included in the series. Diagnostic criteria were based on the results of conventional mycological diagnostic methods, including direct epifluorescence microscopy and visual identification of isolates obtained by culture on solid media. Clinical histories were collected retrospectively by chart review and correlated with laboratory findings.

Results: Of the seven patients, six were male and one was female, with ages ranging from 2.5 to 42 years. Most of the patients presented with chronic progressive nasal or rhinofacial swelling and nasal obstruction. Aspetate or paucispetate hyphae were observed in direct epifluorescence microscopy of tissue samples from all the patients. *Conidiobolus* spp was isolated from samples from five patients, and *Basidiobolus* spp from the remaining two. Although growth in culture was obtained several days after sample inoculation, specific antifungal treatment for entomophthoromycosis (using a combination of potassium iodide and itraconazole) was initiated early based on concurrence between clinical features, typical fungal elements seen in direct microscopy and histopathological findings. All the patients improved rapidly and made full recoveries.

Conclusion: Entomophthoromycosis is a rare condition whose identification requires a high index of clinical suspicion. The treatment for this condition is specific and different from the treatment for other clinically significant invasive fungal infections, but confirmation of diagnosis by culture may take weeks. Therefore, early diagnosis supported by a combination of suggestive clinical features as well as mycological and histopathological evidence, is vital to ensure successful outcomes.

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Epidemiology of aspergillosis in Kuwait: a nationwide study

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Objectives: *Aspergillus* is the most common filamentous fungi involved in human infections. It is characterized by causing various forms of clinical presentations, ie, invasive, chronic, and allergic forms. It is associated with considerable morbidity and mortality. In spite of this, the epidemiology of *Aspergillus* infections is scarce in Kuwait. This study aims to describe the epidemiology of aspergillosis in Kuwait on a national scale.

Methods: This is a 2-year retrospective observational study designed to analyze the demographic and mycological data on all *Aspergillus* isolates derived from clinical samples processed or submitted to the Mycology reference laboratory (MRL) by all government microbiology laboratories in Kuwait. Using the Mycology reference laboratory surveillance system, the required data was collected. It covers patients' age, gender, type of clinical samples, care settings (outpatient, wards, or ICU), the name of the *Aspergillus* species, and antifungal susceptibility for *Aspergillus fumigatus*. Species-level identification of *Aspergillus* was mostly based on morphological characteristics, except in a few cases where MALDI-TOF or PCR-sequencing of rDNA were performed. Antifungal susceptibility testing was done using Etest method according to manufacturer instructions. EUCAST clinical breakpoints were followed for the interpretation of antifungal susceptibility results for *A. fumigatus* species.

Results: In total, 327 *Aspergillus* isolates from 277 patients were found. A total of 34/277 patients had 2 or more samples yielding either the same *Aspergillus* spp. ($n = 17$) or a different species ($n = 17$). The most prevalent type of clinical specimens was respiratory sample ($n = 196$, 60%), followed by ear swabs ($n = 64$, 19.6%), and nails ($n = 24$, 7.3%). *A. niger* ($n = 147$) was the most isolated species, involving 45% of aspergillosis cases followed by four other species including *A. fumigatus* ($n = 64$), *A. flavus* ($n = 55$), *A. terreus* ($n = 38$), and *A. nidulans* ($n = 13$). A total of 10 cases were caused by rare *Aspergillus* spp. All *A. fumigatus* isolates were susceptible to voriconazole. Itraconazole also exhibited excellent *in vitro* activity against nearly all *A. fumigatus* except 4 isolates that were resistant.

Conclusions: This study reveals the epidemiology of aspergillosis from several perspectives. It gives some insights on the burden of Aspergillosis in Kuwait, especially during the COVID-19 pandemic. Respiratory samples were the predominant positive samples suggesting high rates of pulmonary aspergillosis. *A. niger*, not *A. fumigatus* or *A. flavus*, is the most prevalent agent of aspergillosis in Kuwait. Azole resistance is rare among *A. fumigatus*. Further studies are needed to explore the spectrum of clinical presentations with special emphasis on pulmonary aspergillosis.

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The impact of COVID-19 pandemic on invasive *Candida auris* infections in Kuwait

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Objectives: To evaluate the impact of the coronavirus disease (COVID-19) pandemic on the incidence of *Candida auris* invasive infections at a national level.

Methods: This is a laboratory-based, three years-period retrospective study. The demographic and mycological data were obtained from the mycology reference laboratory (MRL) active surveillance system. The number of *C. auris* blood isolates was retrieved for the following years: 2019, 2020, and 2021. *C. auris* blood isolates from all hospitals were sent to the MRL as part of patient care. Species-level identification was confirmed by chromogenic media, VITEK 2 yeast identification system, and/or MALDI-TOF MS (VITEK MS). Antifungal susceptibility was performed using Etest according to manufacturer instructions. The following antifungal agents were tested: amphotericin B, fluconazole, voriconazole, and caspofungin. If the strain was resistant or intermediate to caspofungin, other echinocandins (micafungin or anidulafungin) were tested for confirmation. Since there were no established clinical breakpoints for *C. auris*, tentative minimum inhibitory concentrations were used based on experts' opinions. Incidence rates of COVID-19 during the years 2020 and 2021 (COVID-19) were obtained from the World Health Organization website. All data were numerically coded and labelled for each variable using Microsoft Excel (Version 16.57, 2021), then analyzed by SAS 9.4 (SAS Institute., USA). P -value < .05 was considered statistically significant.

Results: A total of 307 samples isolated from invasive infections were reported with *C. auris* in this study (50 in 2019, 102 in 2020, and 155 in 2021). The number of patients reported with *C. auris* invasive infection increased significantly ($P < .05$) from 50 in 2019 (pre-COVID-19) to 155 in 2021 (post-COVID-19). This was associated with the waves of the COVID-19 pandemic in Kuwait. Of 307 *C. auris* isolates tested, all were resistant to fluconazole. Resistance to amphotericin B and caspofungin was 29/307 (9%) and 3/285 (1%) respectively.

Conclusion: Patients infected with COVID-19 are at considerable risk of invasive candidiasis especially critically ill patients staying in ICU. The significant increase in *C. auris* invasive infections as seen during this pandemic clearly demonstrates the great ability of this opportunistic pathogen to cause secondary lethal infections among COVID-19 patients. In addition, the spread of *C. auris* among patients in care facilities results in outbreaks, which further compromises the health care services and threatens patient safety. Therefore, a greater understanding of its epidemiology and awareness among healthcare staff about its identification methods, antifungal resistance profile and infection control measures are essential to improve outcomes and prevent further hospital transmission.

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Paracoccidioidomycosis severe: Bizarre presentation in the face

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Introduction: Paracoccidioidomycosis is a systemic mycosis caused by the dimorphic fungus *Paracoccidioides brasiliensis*. The disease is restricted to Latin America. It is the principal systemic mycosis in Brazil, with higher incidences in the southern, southeastern and central regions.

Objectives: It's to report a case of paracoccidioidomycosis with a bizarre presentation on the face.

Case Report: A 54-year-old male farmer from Açailândia, Maranhão, with a history of an extensive ulcerated lesion that started in the right wing of the nose. After 6 months of evolution, the lesion had already spread reaching the nasal and oral mucosa, evolving with acute respiratory failure, requiring tracheostomy (Fig.1). He was referred to the Cancer Hospital for a biopsy, which was referred for pathological examination, showing an intense inflammatory infiltrate consisting of lymphocytes, histiocytes, neutrophils with giant, multinucleated cells that phagocytize refringent bodies, compatible with paracoccidioidomycosis. Material sent for direct examination and culture, showed positive for *Paracoccidioides* sp. After PCR amplification of the genetic material and sequencing, *P. brasiliensis* was identified. Chest tomography showed sparse ground-glass attenuation, but affecting both lungs and radiodense striations in the lower lobes bilaterally. Treatment was established with liposomal amphotericin B, with a good therapeutic response (Fig. 2). The patient was discharged from the hospital using itraconazole and still upper outpatient follow-up, with good healing of the lesions.

Conclusion: Paracoccidioidomycosis can get a severe presentation, distancing the physician from the diagnosis, showing that in all these situations, simple tests, such as the direct examination of lesional material or sputum can elucidate the diagnosis. We need to think about it in endemic area.