Fungal infection in Asia, bringing it out of the dark, September 22, 2021, 11:00 AM - 12:30 PM

Immune fungal diseases have been increasing in Asian countries. Recent advances in medical care such as solid organ and stem cell transplantations, chemotherapy for cancer treatment, and corticosteroids therapy, resulted in the increased prevalence of invasive mycoses. Invasive aspergillosis, mucormycosis, and endemic mycoses are among the most common mold infections in Asia. Non-clinical and non-radioligic form of fungal infections have been increasingly recognized in Asia. In contrast to the classical neutropenic patients, most of the patients with invasive mycosis who had non-clinical risk factors are mostly non-neutropenic and may present with an atypical clinical manifestation. These non-clinical risk factors include biological agents or environmental hazards leading to chronic or recurrent fungal cultures or colonization such as fungal conjunctivitis or cryptococcosis disease (2019 COVID-19) pneumonia. Recently, COVID-19-associated aspergillosis (CAP) and COVID-19-associated mucormycosis (CM) have been described. These particular mold infections had high mortality. Treatment of CAPA and CM is challenging due to the onset of COVID-19. However, the interaction between transmit and drugs used for the treatment of COVID-19 must be taken into consideration.

Timely and accurate diagnosis are crucial for the management of invasive fungal infections. Conventional fungal cultures from bone marrow samples or blood are useful but they are time-consuming. Nevertheless, the diagnosis of invasive mold infections is challenging as the imaging is non-specific and the serological tests are not very available in Asian countries. In some situations, such as those with non-clinical risk factors, serology revealed unusually low antibodies. Molecular diagnostic tests are also the utmost needs among Asian countries for timely and accurate diagnosis of invasive fungal diseases. Several factors should be considered for the appropriate choice of antifungal agents, including antifungal coverage, adverse effects, underlying diseases, drug-drug interactions, and cost. Recently, non-mold antifungal agents such as linezolid or newer classes of antifungal agents have been studied and may be promising for the treatment of invasive fungal infections.

4.1d Cryptococcosis

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4.1e Fungal infections in Asia, bringing it out of the dark, September 22, 2021, 11:00 AM - 12:30 PM

Background: Routine laboratory testing for cryptococcal meningitis currently consists of Cryptococcus antigen (GM) testing in blood and cerebrospinal fluid (CSF), CSF India ink, and CSF fungal culture. Quantitative cryptococcal culture (QCC) is less available and not feasible in most settings.

Objective: We evaluated quantitative (qPCR) and reverse transcription (RT-qPCR) assay to quantify cryptococcal load in CSF, plasma, and blood. We also investigated the dynamics of fungal DNA and RNA detection during antifungal treatment.

Methods: We developed a qPCR assay that can differentiate serotypes A and D, and B+C of Cryptococcus neoformans and C. gattii based on the amplification of a unique nuclear eukaryotic sequencing probe (1-PCR) and a multiplex 28S rRNA gene and evaluated the assay on 205 patient samples from the AMFNET trial in Benin and Malawi (2018-2021). CSF; plasma, and whole blood samples were stored per patient and were sampled at day 0 (baseline), day 7 and 14 for CSF and at day 1, day 3, and day 7 for plasma and whole blood post antifungal treatment initiation. A Roche LightCycler 480 and Q5 polymerase were used for data analysis.

Results: A total of 205/209 stored patient samples (85 from Benin, 124 from Malawi), were used. For 1-PCR qPCR results were detected in CSF, D0, 138 (67%) were serotype A, 26 (14%) were serotype B, and 5 (3%) were a mixed infection of serotype A and B. There was no amplification with 16 (7.5%) samples. There was no difference in fungal loads of D0, D7, and D14 between serotypes A, B, and C with the 1-PCR qPCR assay, and QCC showed a good correlation with qPCR quantification with QCC (slope 0.789, R2 = 0.73) and with 28S rRNA qPCR (slope 0.771, R2 = 0.772) assays. The fungal load at D0 was significantly higher in patients who died at week 2 (n = 22) and at week 10 (n = 15) compared with patients who are still alive after week 10. The post-week 10 fungal loads in initial fungal load to both treatment regimens (P < 0.05). Detection of Cryptococcus DNA (28S rRNA) in plasma or whole blood within the first 24 hours of treatment was significantly higher in patients who died at week 2 and at week 10 and mortality at D7 (< 0.01). qPCR 1-PCR assay showed rapid disappearance of DNA was due to viable fungal cells as the quantification of QCC whole RNA nucleic acid was systematically higher (X2 to X3) that of DNA.

Conclusion: Quantification of C. neoformans and C. gattii load in CSF and plasma at D0 is useful in identifying patients at risk of death and may be a promising tool for monitoring treatment response in the future.

5 Epidemiology of mycotic keratitis in developing countries

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5.1 Mycotic keratitis, September 21, 2021, 11:00 AM - 12:30 PM

Mycotic keratitis (corneal infection due to a fungal etiology) is a well-recognized ophthalmological emergency warranting rapid initiation of specific antifungal therapy. However, the magnitude of the problem of mycotic keratitis in the community, especially in the Indian subcontinent and the developing world, is largely unknown. An annual national incidence estimate of 1051, 787 cases (23.6/100,000 population) globally has recently been reported, with the highest rates being in Asia (13.3/100,000 population; an absolute number of 539 897) and Africa (13.0/100,000 population; 77 196). If all culture-negative cases are assumed to be fungal, especially where the incidence of mycotic keratitis is known to be high, then the annual incidence would be about 1480 196 cases. A fungal etiology has been found to account for a very high proportion (41%) of microbial keratitis cases in the Indian subcontinent. However, there is no consensus on the etiologic agents for fungal keratitis despite the burden of disease and the importance of early diagnosis.

The identification of fungal keratitis mostly relies on the anterior chamber. Importantly, the proportion of microbial keratitis patients with a positive fungal etiology shows a significant negative correlation with the gross domestic product per capita. Although it is clear that the most common fungal species are those that can be isolated from the anterior chamber, no solid geographical correlation has been noted. It is important to realize that meningitis of the corneal superficial pathogens can vary, depending on the pathogen, as well as the prevalence of the mycotic agent. For some countries, mycotic keratitis is not a significant cause of keratitis. Furthermore, there has been some evidence of an increasing trend in the proportion of all microbial keratitis cases being diagnosed as mycotic keratitis. Even in a single geographical location, cases of mycotic keratitis may be higher than the yearly average or vary at certain times of the year, such as after the harvest or the rainy seasons. A dermatophyte is the predominant fungal agent to cause keratitis, followed by Trichophyton mentagrophytes, and other related dermatophytes. A dermatophyte was noted to be the predominant fungal agent in 8–11% of patients with mycotic keratitis, the affected eye to be removed, representing an irreversible annual average of 84–155 197 cases. It is recognized that many people suffering from mycotic keratitis in rural distant communities may present late in the course of the disease, and oftentimes, letters and patient information exchanged are not at the disposal of the referring physician due to the costs or the lack of timely medical care. A short period of refractive error could be the reason that, in 8–11% of patients with mycotic keratitis, the affected eye to be removed, representing an irreversible annual average of 84–155 197 cases. It is recognized that many people suffering from mycotic keratitis in rural distant communities may present late in the course of the disease, and oftentimes, letters and patient information exchanged are not at the disposal of the referring physician due to the costs or the lack of timely medical care.