Incidence of mixed fungal infections in post-COVID-19 outbreak of Macromycosis

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S2.1d Evaluation of new tools for the diagnosis of histoplasmosis

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In sub-Saharan Africa (SSA) and West African countries, histoplasmosis is rarely diagnosed probably due to lack of epidemiological information, insufficient training and awareness of frontline healthcare workers, and clinical features very similar to the symptoms of other tropical diseases that can be confused with histoplasmosis. Moreover, in SSA, the advanced HIV patients with concurrent histoplasmosis and particularly advanced HIV patients, with a high case-fatality rate in the absence of treatment (＞10% to 40%). The clinical diagnostic methods are microscopic observation of yeasts with supportive morphology and a positive culture from a biological sample. Although histoplasmosis can be diagnosed on the basis of clinical suspicion, prolonged hospitalization (often 2-6 weeks) is required, when positive, in a level 3 security laboratory. Implementing new invasive diagnostic tools will allow to improve histoplasmosis diagnosis for the most exposed population and to improve the prevalence of the fungal infection in countries where data are lacking. Rapid diagnostic tests (RDTs) such as the TB LAM for diagnosis of tuberculosis or the Cryptococcal antigen (CAg) lateral flow assay (LFA) for cytomegaly have demonstrated their usefulness for the management of advanced HIV patients in similar contexts.

Recently, two RDTs have been made commercially available for the diagnosis of histoplasmosis, based on urinary monoclonal antigen detection (1: Histoplasma Capillariforme Urinary Antigen Rapid Test from Optimum Imaging Diagnostics (ODI) and (2) Histoplasma Urina-Entamoeba Luminal Flow Assay from MicroVita Diagnostics (MV)).

Objectives and Methods: Our objectives was to evaluate these new tools, by experimenting with their reachability in low- and middle-income countries (LMIC) and by studying their diagnostic performances using different sample collections recovered from patients with disseminated histoplasmosis (culture proven), other HIV-related infections, and proven negative urine culture and other Histoplasma antigen detections.

Materials and Methods: We studied 120 samples collected from the EDARPS study frozen samples from hospitalized patients diagnosed with proven positive and negative histoplasmosis from French Guiana (n = 43) tested with ODI and MV tests.

Conclusions: Our results showed that the two RDTs were able to detect the fungal infection in 82% of urine samples of HIV-infected patients. Results from our study show that the two RDTs can be considered as potential tools for the diagnosis of histoplasmosis in the context of HIV-infected patients in SSA. Further studies are needed to evaluate the diagnostic performances of these RDTs in different clinical settings.

S2.2c African histoplasmosis

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African histoplasmosis caused by Histoplasma capsulatum var. duboisii in Africa with few cases reported from outside this region. It is distributed in the region in sub-Saharan Africa and quickly recognized for its usual subclinical course. The pathogen is not easily isolated in vitro, can be acquired via inhalation of microconidia or by direct inoculation. African histoplasmosis commonly presents with papules, nodules, ulcers, swellings, frank microate, and sometimes, postinfection skin lesions. Subcutaneous abscesses may also develop with draining sinuses containing caseous or frank pus. Although it is generally believed to be acquired through inhalation, the lungs are usually spared. Dermatologic features are usually characterized by the involvement of bones and other extrapulmonary lesions in the general population of Sub-Saharan Africa. Diagnosis, notably in the African tropics, is challenging since the fungal infections are usually subclinical and the symptoms are vague.

Conclusions: To conclude, African histoplasmosis is distributed in Africa in a small-but significant number of cases of post-COVID-19 Rhinoblastina murrillii invades medical infections so while reporting the outbreak-associated clinical suspicion with post-COVID-19 macromycoses one should be aware of the possibility of mixed fungal infections and look for African histoplasmosis as a clinical suspicion. Histoplasma capsulatum var. duboisii is an unusual cause of systemic infections in the African setting and misses the true incidence of mixed fungal infections for which immunotherapy and polychemotherapy are clearly necessary.

S2.2c Talassomycosis in HIV-negative patients: challenges and counter-measures

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Talassomycosis is characterized by the systemic infection caused by Talassomyces marneffei (T. marneffei). It is endemic in tropical regions of Asia and South America and has been recognized far beyond the traditional endemic areas. Talassomycosis was thought to be exclusively associated with HIV infection. However, an increasing number of T. marneffei infections have been reported in non-HIV-infected patients. Although the incidence of talassomycosis in non-HIV-infected patients varies (3-30%), the clinical presentation of this disease can lead to misdiagnosis, inappropriate treatment, and poor outcomes, in addition to tremendous burden and suffering for patients and their families. Screening for immunocompromised patients with talassomycosis is crucial for optimal diagnosis and treatment. One of the main challenges in the diagnosis of talassomycosis is that patients in patients with advanced HIV disease, pathogen-based detection is still limited by atypical clinical presentation. Direct microscopic examination, serologic cultures, and histopathology are the standard diagnostic methods used to isolate T. marneffei from clinical specimens, however, due to time-consuming, it usually has a delay. Metagenomic nucleic acid testing are required to be validated and possibly superior to conventional fungal culture in terms of speed and specificity in the diagnosis of talassomycosis. In terms of clinical diagnostic, nDNA shows a high sensitivity of 97.72% compared with conventional culture (81.66%). Consequently, identification of nDNA would lead to reduced laboratory time and can be useful for diagnosis for talassomycosis. Currently, there is no optimal therapeutic regimen for the treatment of talassomycosis in this specific group of patients. Amphotericin B is the first-line initial antifungal treatment, other antifungal agents such as voriconazole have shown less efficacy against talassomycosis. We investigated the efficacy of voriconazole in the treatment of talassomycosis using population pharmacokinetics. C-reactive protein (CRP) was found to significantly affect voriconazole plasma concentrations. Optimization of voriconazole pharmacokinetics by use of model-based dosing in clinical practice. The nDNA rate in non-HIV talassomycosis is higher than the Spanish population, which may be due to the non-specific and complex clinical manifestations. Failure to achieve antifungal treatment in a timely manner often results in poor response and even death. The course of treatment is protracted, systemic, and depends on the immune status of the patient. Diagnosis and treatment of talassomycosis remain a challenge. Optimization of diagnostic tools and treatment regimens to ensure early detection and prompt antifungal treatment should be considered.