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Press release

For immediate publication

COVID-19-associated fungal infection:

Large international study identifies immunological mechanisms and clinical risk factors

Graz, 29 August 2022: The COVID-19 pandemic has kept the world on its toes for over two and a half years. Yet not only does the acute illness pose difficulties, but those infected are plagued by the consequences to their mental and physical health. Besides long COVID, there is another acute and very alarming side effect of a COVID-19 infection: fungal infections. An international study in which Med Uni Graz participated has identified important immunological mechanisms and clinical risk factors for COVID-19 associated fungal infections.

Three important subspecies

Three important fungal infections have been identified in connection with COVID-19: COVID-19-associated pulmonary aspergillosis (CAPA), COVID-19-associated candidiasis (CAC) and in connection with the Delta variant in India COVID-19-associated mucormycosis (CAM). Although many studies have regarded regional phenomena and issues, none has taken a look at the global development of these COVID-19-associated diseases.

COVID as a risk factor?

One main subject of the study was to find out to what extent the fungal infections are actually related to and influenced by COVID-19. "A basic question and motivation for our study was to clarify whether CAPA and CAM are separate diseases that are influenced by specific immunological mechanisms and interactions or whether they are simply the consequence of clinical risk factors in intensive care units and thus affect COVID-19 and non-COVID-19 patients equally," said Martin Hönipl. In fact, there are specific immunological connections between both CAPA and CAM and COVID-19 infection that largely do not exist with CAC/candidiasis.

CAPA infectious pathway

The destruction of tissue that occurs during COVID-19 infection and the subsequent release of a large number of cytokines provide the perfect basis for growth in the lung tissue of the fungus that causes aspergillosis. "The suppression of a specific immunological mechanism, the type 1 interferon response, that occurs in severe COVID-19 cases predisposes these patients to develop CAPA. Naturally, COVID-19 treatment with dexamethasone and tocilizumab in the intensive care unit is also a risk factor," says Hönipl.

CAM infectious pathway

With CAM, this process appears to be different and more complex. Mucormycosis occurs around the world but most frequently in India, and CAM (also referred to in the media as the black fungus pandemic) gained notoriety in India during the Delta wave. Diseases such as untreated diabetes can make it easier for SARS-CoV-2 as well as the pathogens that trigger CAM to find their way into the body through the mucous membrane in the nose. In India this has primarily led to rhino-orbital or rhino-orbital-cerebral mucormycosis, a fungal disease that can destroy facial structures in the area of the eyes and nose and ultimately structures in the brain. CAM rarely occurs in western and rich countries and if it does, it is normally the pulmonary or disseminated type.

CAC infectious pathway

In contrast to CAPA and CAC, there is no direct correlation between COVID-19 infection and candidiasis. The latter is an infection that is primarily acquired nosocomially, i.e., in medical facilities. Important factors are overcrowded intensive care units, central venous catheters, artificial feeding and longer stays in the intensive care unit.

High mortality

Fungal infections in COVID-19 patients are unfortunately associated with high mortality. Depending on the time of diagnosis, 50 to 80% of them die. In rhino-orbital-cerebral mucormycosis, survivors have facial disfigurements for the rest of their lives from the necessary operation and frequently lose one or both eyes.

Treatment options

At present, treatment options for COVID-19-associated diseases are no different than for their counterparts that are unrelated to COVID-19 infections, yet new classes of antimycotics are under investigation and should provide better results. Also being examined are specific interventions that address the immunological mechanisms that predispose COVID-19 patients to developing infections such as CAPA.

Further information and contact

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Profile of Martin Hoenigl:

Following his habilitation on the subject of systematic fungal infections in 2012, Martin Hoenigl spent several years at the Division of Infectious Diseases at the University of California-San Diego. Since 2021 he has been an associate professor of translational mycology at the Medical University of Graz. Martin Hoenigl is the current president of the European Confederation of Medical Mycology, one of the largest societies in this subject area, and the author of over 250 scientific publications.

To the publication: <https://www.nature.com/articles/s41564-022-01172-2>