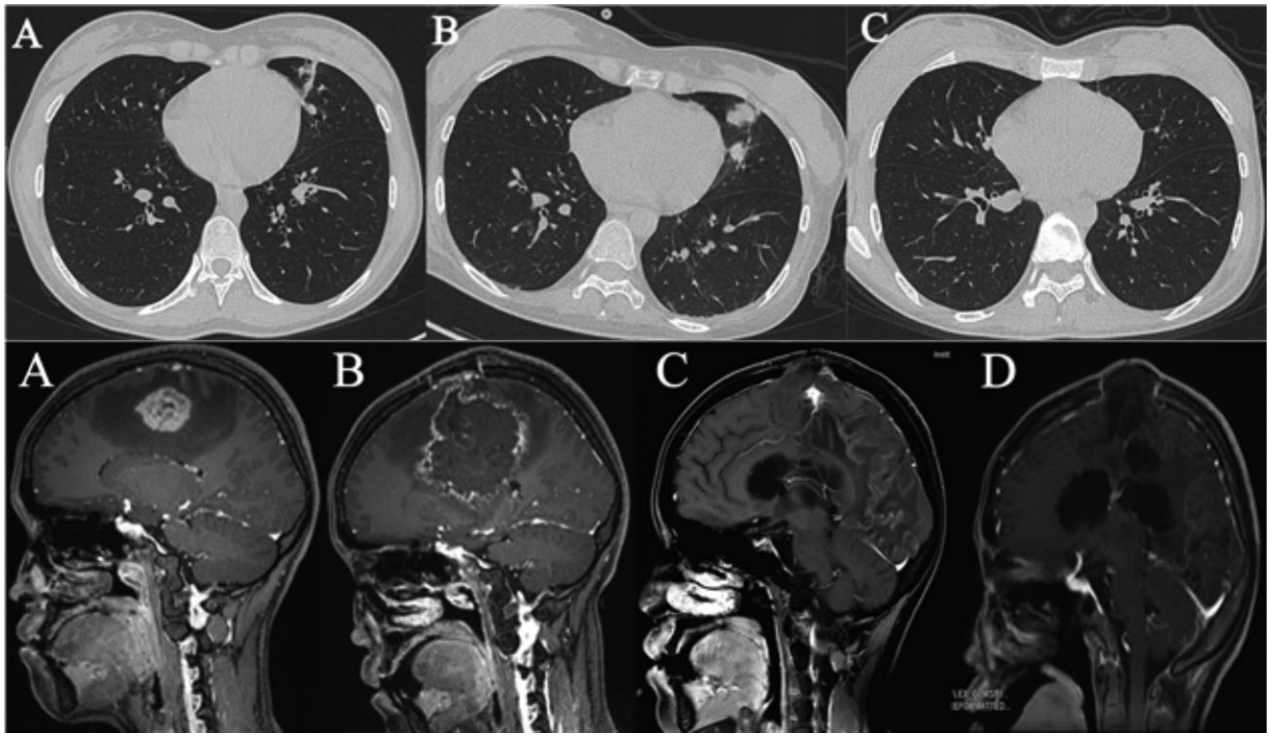

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Anti-granulocyte-macrophage colony-stimulating factor (Anti-GM-CSF) autoantibodies—the underrecognized cause of Cryptococcosis in non-HIV individuals in Thailand: Case series from a single tertiary care hospital

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Background: Cryptococcosis is an opportunistic fungal infection in immunocompromised patients. Granulocyte-macrophage colony-stimulating factor (GM-CSF) regulates the functions of phagocytes and alveolar macrophages, which are crucial in cryptococcal control. Anti-granulocyte-macrophage colony-stimulating factor (Anti-GM-CSF) autoantibodies have been found to be associated with cryptococcosis in non-HIV individuals but this syndrome has never been described in Thai population.

Methods: We report here the case series of patients hospitalized in a tertiary care hospital in Northern Thailand.

Results: Three apparently immunocompetent patients, 34, 38, and 45 years old, were presented with neurological manifestations. Brain computed tomography scans and lumbar punctures were performed and the results showed evidence of cryptococcal meningoencephalitis. Two of the patients also had pulmonary cryptococcosis. We performed Anti-GM-CSF autoantibody ELISA assays in the patient's sera and all of three serum samples revealed a high titer of anti-GM-CSF autoantibodies. The patients were treated with amphotericin B deoxycholate with or without flucytosine for induction antifungal therapy, followed by fluconazole consolidation treatment. All patients were cured and had favorable outcomes.

Conclusions: Anti-GM-CSF autoantibodies syndrome is underrecognized in Thai patients and is a new entity of immunodeficiency associated with cryptococcal meningoencephalitis and disseminated cryptococcosis in Thai patients.

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Fatal secondary fungemia due to *Trichosporon asahii* onychomycosis in a diabetic patient

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Objectives: We describe a fatal case of trichosporonosis caused by *Trichosporon asahii*. The aim was to molecularly characterize the *T. asahii* strains from blood and foot tissue samples to investigate their genetic relatedness.

Case: An 85-year-old morbidly obese female with a prior cerebrovascular accident, hypertension, and diabetes mellitus was admitted to a peripheral hospital with type II respiratory failure, metabolic acidosis, and chronic anemia. Three weeks post-hospitalization the patient remained febrile, physical examination showed that the patient had paronychia, nail pigmentation, subungual onychomycosis, and a diabetic foot ulcer. Blood culture, as well as nail and ulcer samples, became positive for *Trichosporon* yeasts.

Methods: *Trichosporon* yeasts were subjected to molecular identification by sequencing the intergenic spacer (IGS1) region. Minimal inhibitory concentrations (MICs) were determined by the EUCAST microdilution method. Long-read nanopore sequencing was performed for the three clinical strains, the type-strain of *T. asahii* (CBS2479), and two IGS-genotype 7 strains (CBS2936, CBS7632) using the native barcoding kit v12 (SQK-LSK112; Oxford Nanopore Technologies). Raw data were base-called with Guppy v6, Flye v2.9 was used to *de novo* assemble the genome of CBS2479, this was used as a reference for variant calling using the genomic reads of all strains.

Results: The three clinical strains were found to belong to the rare IGS-genotype 7 and had similar MICs for amphotericin B (4 µg/ml), 5-fluorocytosine and fluconazole (2 µg/ml), voriconazole (≤ 0.015 µg/ml), posaconazole (0.0625 µg/ml), itraconazole (0.125 µg/ml), caspofungin (8 µg/ml), anidulafungin and micafungin (> 16 µg/ml). Strains from the ulcer and nail were genetically very closely related with 10 836 SNPs differences, the blood-derived strain differed more from these two strains with 94 729 SNPs and 94 913 SNPs, respectively. Strains CBS2936 and CBS7632 were only distantly related to CBS2479 with 328 221, and 436 060 SNPs, respectively.

Conclusion: The *T. Asahii* IGS-genotype 7 strain causing fatal fungemia was genetically nearly identical to that obtained from nail and foot ulcers, making it highly likely that this was the port d'entrée for *T. asahii*.

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***Scedosporium Apiospermum* brain abscess in an immunocompetent host: Rare case from Southern India**

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Objectives/Introduction: *Scedosporium apiospermum* is a filamentous fungus that causes a broad spectrum of diseases in an immunocompromised host involving the lungs, skin, bones, eyes, joints, and the central nervous system. It is a rare cause of fungal brain abscess, more so in an immunocompetent individual. Here, we report a case of brain abscess in an immunocompetent host caused by *S. apiospermum*.

Methods: A 78-year-old retired railway officer from Chennai, presented to our hospital on May 4, 2022, with a 3-month history of weakness, gait instability followed by difficulty in walking, and left hemiparesis. In all, 20 days before the presentation, he had an episode of generalized tonic-clonic seizure with worsening of his neurological state resulting in bed-bound status. His medical history included *Pemphigus vulgaris* for which he was on topical treatment, well-controlled diabetes mellitus, hypertension, and coronary artery disease.

He underwent an MRI brain which revealed a T2 heterointense intra-axial right parietal lesion with significant perilesional edema. A provisional diagnosis of a cerebral abscess and malignancy was entertained. He was subjected to craniotomy and the surgical findings were consistent with a brain abscess and the pus was evacuated and sent for microbiological analysis. The pus fungal stain was consistent with septate hyphae and the cultures grew *S. apiospermum*. The histopathological findings were also consistent with a brain abscess caused by septate fungi (*Aspergillus* like fungi).

Results/Treatment: He was started on Liposomal Amphotericin B 5 mg/kg dose IV OD and injectable voriconazole. There was an initial clinical improvement with respect to sensorium and neurological status. He subsequently developed bradycardia with worsening sensorium to which he finally succumbed.

Conclusion: *Scedosporium apiospermum* is an asexual form of *Pseudoallescheria boydii*, a fungus found in soil, contaminated water, and sewage. It is a rare cause of brain abscess in immunocompromised individuals. Near drowning or trauma may be the causative factors for immunocompetent individuals. Our patient was a well-controlled diabetic host with no apparent immunosuppression.

Scedosporium apiospermum is diagnosed on the basis of culture and microbiological examination. Due to the similarities in the clinical and histopathological presentation of *Scedosporium* with other similar fungi, culture becomes the gold standard tool for diagnosis.

Treatment includes surgical drainage of the abscess along with intravenous voriconazole for at least 8-12 weeks. The prognosis depends upon the immune status, surgical intervention, and medical antifungal therapy.