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Invasive Trichosporonosis: an emerging blood stream fungal infection in immunocompromised patients

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Trichosporon is a genus of yeast-like fungi. It is perhaps most widely known as the cause of white piedra, a benign superficial mycosis seen in immunocompetent individuals in tropical and subtropical regions. However, the incidence of invasive trichosporonosis has increased in immunocompromised patients, most notably those with hematologic malignancies. Invasive infections due to *Trichosporon* species are considered rare so far, but during the past two decades, they have emerged as important opportunistic pathogens in immunocompromised individuals.

All patients with blood culture positive for *Trichosporon* species from January 2020 to August 2020 at Woodlands Multispecialty Hospital, Kolkata, India were evaluated. *In vitro* susceptibility testing was performed using the reference broth micro-dilution method. Clinical co-relation was done with the positive culture report and patient's clinical condition to rule out colonization/contamination.

A total of 7 patients were found to have blood culture positive for *Trichosporon* species among which five were true infections. Various predisposing factors previously reported to be associated with invasive trichosporonosis were also considered in the present study. All the cases were associated with either post radiotherapy/chemotherapy with renal failure requiring dialysis via hemodialysis catheter or use of central venous catheter or chemoport. Underlying malignancy was found in all patients. Susceptibility testing has been performed for 5-FC, amphotericin B, and Azoles. Azoles had good *in vitro* activity, whereas amphotericin B had higher MIC values. The all-cause mortality rate was 43%.

Invasive *Trichosporon* infection is a rare, life-threatening infection in immunocompromised patients. Our study highlights the association of central venous catheter and hemodialysis catheter with *Trichosporon* fungemia and its high mortality. Therefore, strict infection control measures while handling these devices are recommended to prevent these infections. Species identification and susceptibility testing are to be attempted for all relevant clinical isolates in view of demonstrable resistance to certain antifungal drugs. Echinocandins are not effective in the treatment of *trichosporon* infection. Amphotericin B should also be avoided. Azoles, in particular, voriconazole is the drug of choice.

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Healthy adult with arm swelling and new onset burning pain

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Introduction: Cladosporium cladosporioides is a dematiaceous fungal agent that is known to produce a variety of clinical manifestations such as cutaneous and subcutaneous infection, corneal infection, pulmonary fungal infection, and rarely central nervous system infection. Several cases of subcutaneous mycosis have been reported from Assam, India. We are describing a similar case from Gujarat, India.

Case History: A 36-year-old healthy, and muscular male farmer residing in central Gujarat presented with painless nodular swelling with normal overlying skin over the posterior aspect of the left arm for the last 3-4 years. He noticed a gradual increase in the size of this swelling and numbness for the last 4 months and burning sensations for the last 10 days before presentation to the surgeon. Local part ultrasound showed a subcutaneous soft tissue lesion. Excision biopsy reported invasive fungal infection and patient was referred for further evaluation to an infectious disease facility (Fig. 1a). He had no other symptoms and comorbidities. Patient didn't recall any trauma in the past. Direct microscopic examination with calcofluor white stain from surgical site scrapping revealed mycelial structure (Fig. 1b) and yielded pure growth of a dematiaceous fungus on Sabouraud dextrose agar medium, brown to blackish colony (Fig. 1c) with olive color on the backside (Fig. 1d) after 6 days. Lactophenol cotton blue stain preparation of culture isolate showed mycelial elements with morphology suggestive of *C. cladosporioides* (Fig. 1e), which was confirmed at the National Culture Collection for Pathogenic Fungi, PGI Chandigarh. Review of histopathology revealed a nodule with dense acute on chronic inflammation composed of lymphocytes, plasma cells with many neutrophils with abscess containing brightly eosinophilic structures with many PAS positive septate, thin and thick walled, branching, irregularly shaped, bullous hyphae surrounded by neutrophilic boarder (Splendor Hoeppli phenomenon) (Fig. 1f).

Patient was treated with capsule itraconazole 200 mg three times a day for three days followed by 200 mg twice a day along with terbinafine and total surgical excision of the subcutaneous nodule. Patient achieved a therapeutic itraconazole level (1.4 mg/l) after 1 week. Patient is currently receiving treatment.

Discussion: Subcutaneous mycosis is endemic in Assam. Several cases of subcutaneous chromoblastomycosis caused by *C. cladosporidiosis* mainly involving the lower limbs were reported from Assam. It mostly affects males engaged actively in outdoor activities during their productive age ranged from 20 to 50 years. It affects a relatively healthy, immunocompetent host and have a long history (in years) of asymptomatic nodule/swelling before diagnosis. Treatment comprises of prolonged antifungal treatment with itraconazole along with surgical excision.

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Bacterial co-infections in Mucormycosis infected COVID-19 patients: experience from a tertiary care center in India

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During the second wave of COVID-19 in India, there was a deluge in Mucormycosis cases; which posed a serious threat as both conditions require extended hospital stay thus serving as an ideal setting for secondary infections.

Objectives: 1. To ascertain the prevalence and anti-microbial profile of hospital-acquired secondary infections in COVID-19 patients with Mucormycosis.

2. To evaluate the outcome in these patients and compare it with the outcome of COVID-19 patients with Mucormycosis but without any other secondary infection.

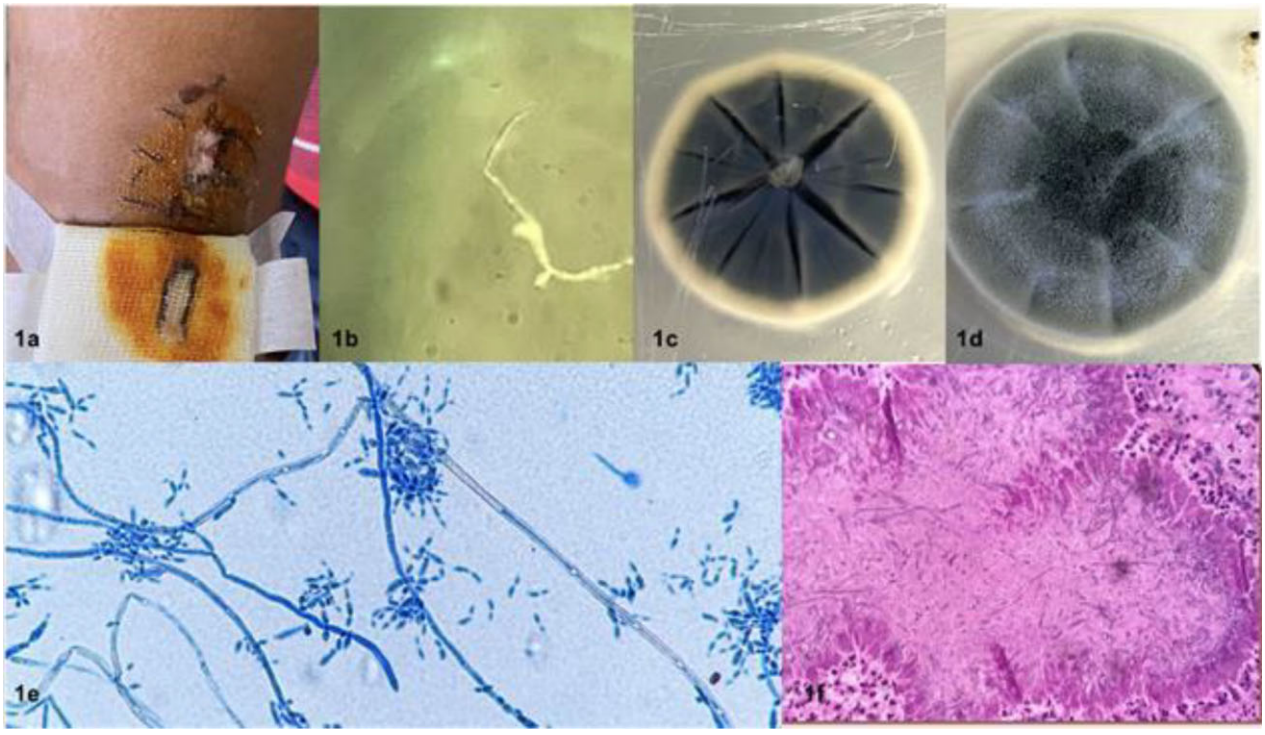
Methods: A 2-month retrospective observational study was conducted, where we compared outcomes in two groups of COVID-19 patients with Mucormycosis, one group being patients with secondary infections and the other group including patients without secondary infections.

A total of 180 samples from suspected cases of Mucormycosis, that underwent evaluation by conventional methods, KOH mount and cultures on SDA, were included. Fungal pathogens were identified from the positive cultures, based on macroscopic and microscopic features, as per standard Mycological methods.

Secondary infections inpatients were studied based on conventional bacteriological culture, microbiological profile, alongwith identification and antibiotic susceptibility by VITEK 2. PCT and CRP values were also compared. The outcome was then evaluated. Data analysis was done using SPSS V-20.

Results: A total of 55 patients out of 140 patients, tested positive for Mucormycosis, either by KOH, culture or both. *Rhizopus arrhizus* was the most common isolate identified.

A total of 12/55 (21.8%) people with Mucormycosis developed secondary infections during their stay in the hospital, bloodstream infection being the most common (7/15; 46.67%). Overall, gram-negative (GN) organisms were more common (11/16; 68.75%), in comparison to Gram Positives (GP) (5/16; 31.25%), but the most common organism isolated was *Enterococcus faecium* (5/16; 31.25%), followed by *Klebsiella pneumoniae* (4/16) and *E. coli* (4/16). A total of 4/5 isolates (80%) of Enterococcus faecium were multi-drug resistant (MDR) and two of them were vancomycin-resistant. In all, 10/11 GN isolates (90.9%) were MDR, high resistance to carbapenems was observed, nine out of 11(81.81%) isolates were resistant to imipenem and eight (72.72%) were resistant to meropenem. A total of 3/12 (25%) patients succumbed to their infection in the group with secondary infections, after an average length of stay of 23.33 days. The most common cause of death in these patients was septic shock. A total of 8/43 (18.6%) succumbed to their infection in the group without any secondary infection at an average stay of 9.12 days in the hospital. CRP was found to be consistently elevated, this biomarker might not have a



predictive value for bacterial infections in COVID-19 but PCT had a positive predictive value for the secondary bacterial infections overall (*P*-value <.001). Length of stay in hospital co-related with the development of secondary infection and mortality (*P*-value <.001).

Conclusion: Culture-based testing should be carried out before the administration of anti-microbials. PCT can be used as a guiding tool. Controlled use of antibiotics along with periodic surveillance and hand hygiene practices will immensely contribute to infection control.

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A rare case of vertebral osteomyelitis caused by co-infection of *Candida* and Mycobacterium Tuberculosis: a double trouble

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Introduction: The vertebral osteomyelitis can be pyogenic (bacterial), non-pyogenic-granulomatous (tuberculosis, brucella, fungi), or parasitic. Fungal spondylodiscitis only accounts for 0.7%-2.7% of all spinal infections. Tubercular vertebral osteomyelitis has a high prevalence in developing countries like India. Co-infection of the spine by both fungal and tuberculous organisms is rare, there is only one case that has been reported till now in our literature review.

Case: A 62-year-old man presented with complaints of lower back pain for 3 months and fever with chills for 1 month. He had done multiple OPD visits at other centers for his lower back pain in the past 2 months, where a whole spine MRI was done which was suggestive of prolapsed intervertebral disc at multiple spinal segments- maximum at L4-L5 causing indentation of nerve roots for which he was given 3 days of IV and followed by 15 days of oral methylprednisolone. On steroids, patient developed fever and increased lower back pain for which he was admitted. Repeat MRI spine revealed features s/o axial spondylo-arthropathy. At this point, he was referred to our center for further management and was admitted. He was a known case of diabetes and underwent bilateral DJ stenting for nephrolithiasis 3 months before. On post-operative day 4, he had developed low back ache. He was vitally stable but febrile, unable to sit or walk without support. He also had tingling and numbness in bilateral lower limbs. Laboratory results showed raised inflammatory markers. Vertebral biopsy was done, CBNAAT was negative, while culture revealed growth of *Candida albicans*. He was started on injection of fluconazole 800 mg loading dose followed by 400 mg daily. After 5 days he got afebrile but, lower limb weakness and lower back pain persisted. Hence a repeat vertebral biopsy was planned. Surprisingly, CBNAAT of the biopsy sample detected very low MTB and indeterminate rifampicin resistance, following which the patient was initiated on weight-based HRZE regimen along with fluconazole. Currently, patient is afebrile and his lower limb weakness has improved with lower limb muscles power 0/5 to 3/5 on follow-up after a month.

Conclusion: Non-pyogenic vertebral osteomyelitis due to tuberculosis is common in a high TB burden country like India. Even though *Candida* is a rare causative agent, but should always be considered as a differential in patients having risk factors. In our patient abdominal surgery, DM and steroids could have predisposed for developing *Candida* vertebral osteomyelitis. The possibility of co-infection of TB and *Candida* should not be ignored in patients who have risk factors, especially if they present with clinical and radiological signs befitting its manifestations. High suspicion and tissue diagnosis remain crucial factors for early diagnosis and aids in better clinical outcomes.

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A rare case of post covid bilateral renal mucormycosis

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Objective: The most commonly reported sites of COVID-associated invasive mucormycosis till now have been rhinocerebral-orbital followed by pulmonary. This is a rare instance where an apparently healthy male, who had recovered completely from COVID-19, presented with fulminant isolated bilateral renal mucormycosis.

Method: A 60-year-old male was presented with low-grade fever and increased CRP. He had a known history of diabetes, hypertension, and ischemic heart disease since 2007. On examination, he was tachypneic and afebrile; blood pressure and oxygen saturation were within normal limits.

He was also double vaccinated. Also had a history of moderate COVID (Omicron) in January, 2022. His CT score was 18/25. He got admitted for 10 days because of COVID and was treated with oxygen, antibiotics, remdesivir, and steroids.

Later on, patient developed fatigue, anorexia, abdominal discomfort, and pain in lower back. Also vomiting and nausea for 3 months. So patient was treated with tablets Zifi CV for 5 days bd followed by; IV meropenem 1 g tds for 5 days followed/by; tablets faropenem 200 md bd for 3 weeks followed by; tablets nitrilofurantoin 100 mg bd.

Ultrasonography remains the first line of investigation and can show the enlarged echogenic kidneys with hypoechoic areas of abscesses, perinephric fluid collections, hydronephrosis, and cystitis. Cortical thickness appeared normal with raised cortical echo. An unenhanced computed tomography (CT) of his abdomen and pelvis was performed and suggested of mild changes of acute bilateral pyelonephritis. CT features include diffuse patchy nephrogram, inhomogeneous enhancement with areas of low attenuation, perinephric fluid collections, and no contrast excretion.

Fungal culture sensitivity report was done and *Candida albicans* organism was isolated and it was found to be all drug-sensitive. Later on, a biopsy of the urethra was performed and a biopsy specimen revealed a fungal ball composed of thin septate and branching thick abroad aseptate hyphae. And also, which resembled morphologically mucor. spp and *Aspergillus*. A bacterial culture and sensitivity report were suggestive of *E.coli*.

The patient underwent surgical interventions, ie, cystoscopy with B/L RGP with B/L DJ stenting done under SA with a calculated risk of diabetes, hypertension, age, nature of illness, and high creatinine.

Patient started treatment with sulbacin 1.5gm injection with 100 ml sodium chloride 0.9% 6 hourly. As patient's creatinine is not stable so Liposomal Amphotericin B was not given. Later on, as creatinine stabilized patient he began receiving liposomal amphotericin B at a beginning dosage of 300 mg with 25% dextrose 250 ml over 5 h. Also, posaconazole started with a loading dose of 600 mg, and then, 300 mg OD was given to patient.

Result: Patient gradually recovered and a dose of liposomal amphotericin was completed for 4 weeks.

Conclusion: In conclusion, this paper describes that COVID-associated mucormycosis is a known entity, however, Renal Mucormycosis is a rare disease. Especially, bilateral involvement with limited drug penetration into a urogenital system of the agents which are active in mucormycosis. Its management involves, team approach of diabetologists, infectious disease physicians, urologists, radiologists, and microbiologists. Treatment of mucormycosis is challenging as anti-fungal penetration in renal tissue is difficult. High index of suspicion should be there to make the diagnosis. Early detection and aggressive management may have a favorable outcome.

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Predominance of *Trichophyton* tonsurans causing tinea capitis: a 12-years retrospective study in north of Iran

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Background: Tinea capitis is a common and endemic fungal infection of the scalp that *Trichophyton* spp. and *Microsporum* spp. usually cause. This study aimed to investigate tinea capitis and its etiologic agents for 12 years in northern Iran.

Material Methods: The study is a retrospective analysis involving 11 095 patients referred to the Reference Laboratory of Medical Mycology at Sari, Iran, from July 2009 to April 2022. The skin scraping and hair samples were assessed based on direct microscopy and culture, and causative agents were identified based on macroscopic, and microscopic morphology.

Results: Tinea capitis was confirmed in 209 patients: 157 (75.1%) male and 52 (24.9%) female out of 921 suspected patients with a scalp lesion. The prevalence of tinea capitis in patients who refer to the Reference Laboratory of Medical Mycology varied from 6.1 to 37.5%. In both sexes, a higher rate of tinea capitis was observed in patients younger than 20 years of age. *Trichophyton tonsurans* (146/209; 69.9%) was the most etiological agent, followed by *T. mentagrophytes* (13/209; 6.2), *T. violaseum* (9/209; 4.3), *Microsporum canis* (3/209; 1.4%), *T. verrucosum* (2/209; 1%), and *T. rubrum* (1/209; 0.5%). On direct microscopy examination, endothrix hair invasion in 77.0% cases, ectothrix in 2.3%, septate hyphae in 10.5%, and ecto-endothrix in one case were observed.

Conclusion: In recent decades, the prevalence of tinea capitis caused by anthropophilic fungi has remained high, particularly in younger children. Therefore, it is essential to focus on public and personal health education in this age group to prevent and control the disease.

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Histoplasmosis in Sri Lanka

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Background: Histoplasmosis is a systemic mycosis caused by Histoplasma capsulatum, a dimorphic fungus. More severe disease has been observed in immunocompromised individuals. Most cases occur in certain endemic regions of the world however it seems to have a much wider global distribution. Histoplasmosis is infrequently recognized in Sri Lanka and the dispersion of information on cases is fragmented.

Method: The comprehensive search of medical literature in the English language through databases from any time to February 2022. Either, culture-proven or histopathologically proven cases were selected as diagnostically confirmed histoplasmosis. Duplicate reports were excluded. All available data on demography, clinical presentation, diagnostic method, management, and clinical outcome were appraised for the reported cases.

Result: One survey of histoplasmin skin sensitivity testing and ten cases of histoplasmosis across Sri Lanka were observed during the above period. A total of 5.7% of histoplasmin positivity had been observed in the survey of histoplasmin sensitivity among 1366 Sri Lankan volunteers of the Western and the Central Provinces in 1969. Most of the patients were reported from the Central province which had the positive histoplasmin test previously. In addition, cases were observed in Southern Province, the Sabragamuwa Province, and the Eastern Province. The majority of affected individuals were adult males (90%) and pediatric patients were not observed. The clinical presentation stretched from oral lesions (the most common presentation), skin lesions, and fever of unknown origin, to adrenal crisis. Disseminated histoplasmosis was diagnosed in 50% of the patients however asymptomatic, acute pulmonary, and chronic pulmonary histoplasmosis was not observed. Both diabetes and betel chewing are likely to be linked with oral histoplasmosis and none of the patients were positive for HIV. Both histopathology and fungal culture methods were used for the diagnosis while the use of antigen and antibody testing were not popular. Both itraconazole and amphotericin B were used for the treatment of the patients with variable outcomes.

Conclusion: Histoplasmosis exists in Sri Lanka. The number of cases could be expected to be much higher than reported along with the increase in at-risk populations. These mandates enhance laboratory diagnostic facilities and increase the awareness of medical professionals in Sri Lanka.

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A case of cerebral aspergillosis in Sri Lanka

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Introduction: Cerebral aspergillosis is a rare disease entity that is usually associated with high mortality. In accordance with most systemic fungal infections, immunocompromised patients are the predominant victims affected. Nonspecific clinical and radiological features may contribute to difficulty and delay in diagnosis, further contributing to the poor prognosis of cerebral aspergillosis. Obtainment of proper specimens for laboratory diagnosis is a key to make a timely diagnosis that may be lifesaving.

Case Report: A 74-year-old female presented with a frontal headache for 2 weeks' duration. She had been diagnosed with a low-grade lymphoma and had completed the chemotherapy and high-dose prednisolone 4 weeks prior to this presentation. Other than the frontal headache, which progressed slowly over 2 weeks, she did not disclose any associated symptoms. Physical examination was normal, with neither sign of raised intracranial pressure nor of a CNS infection. Basic investigations revealed no abnormalities, and the white cell count was 7.5 × 109/l and the CRP was 7 mg/l.

An MRI of the brain indicated right frontal sinusitis with a secondary small abscess in the right frontal lobe inferiorly. Therefore, she was treated with parenteral antibiotics for a bacterial infection and was discharged.

The patient presented with a headache again after 3 months. A repeat MRI of the brain revealed an increase in the size of the lesion in the right frontal lobe and the possibility of a cerebral tumor was suggested. A diagnostic biopsy was performed, and the specimen was subjected to fungal studies. The direct microscopic examination revealed fungal filaments and the culture yielded a pure growth of *Aspergillus fumigatus*.

She was started on intravenous amphotericin B, followed by oral voriconazole. Her headache gradually subsided with antifungal therapy. The duration of therapy was guided by serial radiological imaging, and the patient achieved a complete recovery at the end of 1-year of treatment. She remains asymptomatic to date, after 2 years of treatment completion.

Discussion: Immunocompromised patients with cerebral aspergillosis may present with minimal clinical symptoms and signs. Obtaining a proper specimen for laboratory testing is vital to arrive at a definitive diagnosis. Radiological investigations may play an important role in the diagnosis as well as during the follow-up of a patient with cerebral aspergillosis. Appropriate antifungal treatment for a prolonged duration, with or without neurosurgical intervention and reversal or reduction of immunosuppressive therapy leads to a good prognosis.

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Rhinocerebral mucormycosis due to *Saksenaea vasiformis* in a Sri Lankan patient: A rare fungal infection

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Background: Rhizopus, Rhizomucor, and Mucor species are renowned agents causing rhinocerebral mucormycosis; a disease with a high mortality rate. *Saksenaea vasiformis* is extremely rarely observed in this clinical entity. Minimal sporulation in common laboratory media might be responsible for the under-reporting of this organism. Here we present an uncommon case of rhinocerebral mucormycosis due to *S. vasiformis*. in a Sri Lankan patient with diabetes mellitus.

Case History: A 66-year-old female with diabetes mellitus was admitted with frontal headache, right-sided nasal block, anosmia, and right-side facial swelling. Examination revealed facial edema, maxillary sinus tenderness, and a white patch over the hard palate. Thick pus in postnasal space, growth in posterior tongue base, inflamed palate, and oropharynx, were revealed by rigid nasal endoscopy. She developed ophthalmoplegia along with right V and XII cranial nerve palsies irrespective of antibacterial therapy. Right side pansinusitis was observed in non-contrast computed tomography. She was subjected to right-side full house functional endoscopic sinus surgery with right orbital and optic nerve decompression. Irregular wide, ribbon-like, non-septate hyphae suggestive of Zygomycete fungi were observed in the direct microscopy of a deep surgical tissue sample and started with intravenous amphotericin B. After 5 days of incubation, the culture grew a zygomycetes-like mold with a lack of sporulation on Sabouraud dextrose agar, potato dextrose agar, and slide culture. However, the floating agar technique succeeded