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FATAL CRYPTOCOCCOSIS MIMICKING ACUTE FATTY LIVER OF PREGNANCY (AFLP): A DIAGNOSTIC DILEMMA

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Introduction

Cryptococcosis is an invasive fungal infection caused predominantly by *Cryptococcus neoformans*, associated with advanced immunosuppression, particularly HIV infection and transplant recipients. However, recently cases have been reported in apparently immunocompetent hosts, including pregnant women, where physiological immune modulation may predispose to severe infection. Acute fatty liver of pregnancy (AFLP) is a rare but life-threatening obstetric emergency occurring in the third trimester, characterised by hepatic dysfunction, coagulopathy, encephalopathy, renal failure, and multi organ dysfunction. The clinical and biochemical features of AFLP, HELLP (Haemolysis, Elevated liver enzymes, Low platelets) syndrome, and other systemic illnesses, often overlap with sepsis leading to diagnostic challenges and delayed recognition of alternative etiologies.

We present a fatal case of disseminated cryptococcosis in a primigravida, which closely mimicked AFLP both clinically and radiologically, resulting in delayed diagnosis and fatal maternal outcome.

Case Report

A 31-year-old primigravida at 31 weeks of gestation came to our tertiary care centre with complaints of vomiting for one week, abdominal and epigastric pain, sore throat, and lower backache for four days. She was a known case of hypothyroidism since conception, on levothyroxine therapy. She was diagnosed with gestational diabetes mellitus at six months of gestation, which was well controlled on medical nutrition therapy.

The pregnancy was apparently normal until 20 weeks of gestation. After 24 weeks, she developed progressive loss of appetite, severe vomiting, unintentional weight loss, altered vision at night, and increasing vomiting episodes. This was later associated with polydipsia and bilateral pedal oedema around 30 weeks of gestation. Liver function tests showed elevated enzymes, and she was diagnosed at a peripheral hospital as intrahepatic cholestasis of pregnancy and categorised as a high-risk pregnancy due to associated fetal growth restriction with absent end-diastolic flow on Doppler.

On admission, she was afebrile with gross anasarca. Cardiovascular and respiratory system examinations were unremarkable. Laboratory investigations revealed anaemia (Hb- 7), leukocytosis (TLC- 23000), thrombocytopenia (platelets-40k), prolonged prothrombin time (>14 seconds) suggestive of coagulopathy with liver function tests revealed a hepatocellular pattern of injury, with aspartate aminotransferase (SGOT) of 118 U/L and alanine aminotransferase (SGPT) of 86 U/L, a total bilirubin of 1.2 mg/dL, and profound hypoalbuminaemia (serum albumin 1.2 g/dL). Viral serology, including HIV, hepatitis A, E, and B

Message from the Editor

Dear Friends,

A very warm welcome to the 16th Annual Conference of the Clinical Infectious Diseases Society of India, CIDSCON 2026. On the occasion of this conference we are delighted to bring you this specially curated newsletter which includes cases of invasive infections due to the common five fungi viz Candida, Aspergillus, Mucorales, Cryptococcus and Histoplasma. These cases expertly illustrate the complexities in diagnosis and management of IFI. Also included is a graphical abstract of a recent publication on the prevalence of azole resistance in Aspergillus in India.

You are also invited to visit our website www.fisftrust.org which has many other educational resources including previous issues of the newsletters.

I am sure that you will find the session on invasive fungal infections during the conference engaging and rewarding. Wishing you an academically enriching time at the conference.

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Welcome All Delegates

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surface antigen, was non-reactive. Ultrasonography of the abdomen demonstrated fatty liver changes. She was started on intravenous ceftriaxone, later escalated to meropenem and vancomycin due to clinical deterioration. In view of decreased fetal heart rate, labour was induced; however, the neonate died during delivery.

Post-delivery, the patient developed progressive neurological symptoms, including discomfort in walking and sitting, inability to sleep, and altered sensorium, suggestive of encephalopathy. Cerebrospinal fluid examination was considered but deferred, as lumbar puncture was precluded by thrombocytopenia, coagulopathy and haemodynamic instability. Cryptococcosis was not suspected antemortem, so targeted CSF fungal studies were not performed. She subsequently developed acute shortness of breath, hypotension requiring inotropic support, and sudden cardiovascular collapse necessitating intubation and mechanical ventilation. Computed tomography ruled out pulmonary embolism. After exclusion of other differentials, a provisional diagnosis of AFLP with septic shock was made. Despite aggressive supportive care, the patient succumbed to her illness.

Blood cultures were sent during hospitalisation and were initially reported as sterile after overnight incubation. On the third day, the blood culture flagged positive. Gram staining of the flagged sample revealed Gram-positive, round, budding yeast cells. Based on this finding, *Cryptococcus* was suspected. India ink preparation from the blood culture broth demonstrated round budding yeast cells with a prominent peripheral halo, consistent with encapsulated yeast (Figure 1). The Cryptococcal antigen test performed on the sample was positive. The result was immediately communicated to the treating team; however, the patient had expired 1 day prior to culture positivity. Culture on Sabouraud dextrose agar (SDA) yielded mucoid, creamy white colonies. Blood agar showed smooth, creamy, non-hemolytic colonies after incubation (Figure 2). The isolate was identified as *Cryptococcus neoformans* by MALDI-TOF. Antifungal susceptibility testing was performed by broth microdilution according to the Clinical and Laboratory Standards Institute (CLSI) M27 reference method. The minimum inhibitory concentrations (MICs) obtained were: amphotericin B, 0.25 µg/mL; fluconazole, 0.1 µg/mL; voriconazole, 0.12 µg/mL; itraconazole, 0.06 µg/mL; posaconazole, 0.06 µg/mL; and flucytosine, 0.03 µg/mL.

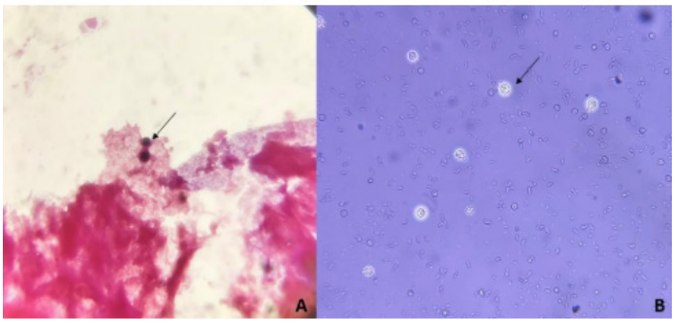

Figure 1: A) Gram stain showing round, gram-positive budding yeast cells with a capsule suggestive of Cryptococcus, B) India ink preparation demonstrating encapsulated budding yeast cells with a characteristic clear halo, consistent with Cryptococcus species.

Discussion

Cryptococcosis in pregnancy remains poorly studied, and available data are limited largely to case reports and small series. Recent systematic reviews have predominantly focused on pregnant women living with HIV, in whom cryptococcosis is associated with high maternal and foetal mortality. In contrast, reports of cryptococcal infection in HIV-negative, apparently immunocompetent pregnant women are scarce, and the true burden in this population remains unknown. This lack of data contributes to low clinical suspicion and delayed diagnosis.

In the present case, the patient was initially diagnosed with intrahepatic cholestasis of pregnancy and later suspected to have AFLP following rapid clinical deterioration after delivery. Notably, AFLP was never confirmed histopathologically; the diagnosis rested on nonspecific ultrasonographic fatty-liver changes and a compatible clinical picture, with liver biopsy precluded by thrombocytopenia and clinical instability. As definitive AFLP requires demonstration of microvesicular steatosis, its diagnosis remains presumptive. In this setting, the hepatic dysfunction may equally reflect hepatic cryptococcosis, a recognised, albeit uncommon, manifestation of disseminated infection rather than true AFLP. This uncertainty is central to the present case and illustrates how disseminated cryptococcosis may closely mimic an obstetric hepatic emergency. Whether AFLP truly co-existed with disseminated cryptococcosis or whether the entire clinical picture, including hepatic dysfunction, coagulopathy, encephalopathy, and multi organ failure, was attributable to cryptococcal sepsis cannot be conclusively determined. To our knowledge, no previously published reports describe cryptococcosis presenting with a clinical phenotype indistinguishable

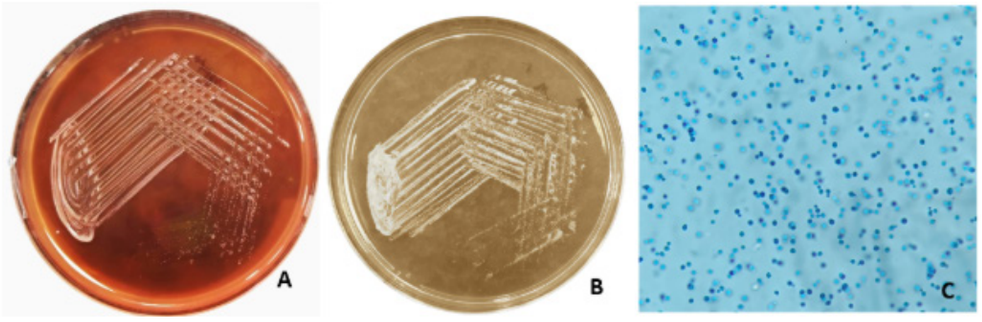

Figure 2: A) Growth on blood agar showing smooth, creamy, non-haemolytic colonies. B) SDA showing mucoid, creamy white colonies. C) Lactophenol cotton blue (LCB) mount showing round budding yeast cells without pseudohyphae, consistent with *Cryptococcus* species

from AFLP, highlighting the diagnostic uncertainty and the novelty of this case.

Recent evidence indicates that pregnancy is characterised not by generalised immunosuppression, but by immune-metabolic set-point changes that predispose to maladapted host responses to infection. Hormonal and metabolic adaptations during pregnancy result in reduced cell-mediated immunity, altered antigen presentation, and suppression of natural killer and cytotoxic T-cell responses, creating a physiological state that partially mirrors sepsis itself. In this context, pregnancy may lower the threshold for dissemination of intracellular pathogens such as *C. neoformans* and facilitate rapid progression to septic shock, even in the absence of classical immunosuppression. The overlap between pregnancy physiology, sepsis, and AFLP likely contributed to diagnostic anchoring and missed opportunity for early antifungal therapy in this patient.

Discussion

This case highlights a fatal presentation of disseminated cryptococcosis in pregnancy masquerading as acute fatty liver of pregnancy, resulting in diagnostic delay and adverse maternal and foetal outcomes. Cryptococcemia may present with nonspecific features that closely resemble obstetric emergencies and sepsis, particularly in the setting of pregnancy-associated immune modulation. Clinicians should maintain a high index of suspicion for invasive fungal infections in pregnant patients with unexplained hepatic dysfunction, encephalopathy, or sepsis that does not respond to antibacterial therapy. Early blood cultures and rapid fungal diagnostics, including cryptococcal antigen testing, are crucial and may be life-saving. This case underscores the need for heightened awareness and timely evaluation of fungal etiologies in complex obstetric presentations to prevent fatal outcomes.

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UNMASKING CULTURE NEGATIVE CNS ASPERGILLOSIS IN AN APPARENTLY IMMUNOCOMPETENT ADOLESCENT

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Introduction

Central nervous system aspergillosis is an uncommon manifestation of invasive aspergillosis, classically described in patients with profound immunosuppression. However, an increasing number of cases are now being recognized in individuals without apparent predisposing conditions, making diagnosis particularly challenging. The clinical presentation is often variable; neuroimaging findings overlap with more common infectious etiologies such as tuberculous meningitis and conventional fungal cultures have poor diagnostic sensitivity. Consequently, diagnosis is frequently delayed, contributing to the high mortality associated with this condition. We report an unusual case of culture-negative CNS aspergillosis presenting as meningo-myeloradiculitis in an apparently immunocompetent adolescent, where fungal biomarkers and molecular diagnostics proved pivotal in establishing the diagnosis.

Case Report

A 16-year-old obese, prediabetic (HbA1c -6.2%), school student presented with fever, which began 10 days prior to admission, The fever subsided for a while and then he had a family trip to a village nearby Pune. His fever reappeared during the trip with abdominal pain, vomiting and loose stools. Following this, he developed imbalance while walking, hesitancy followed by retention of urine and progressive lower limb weakness. He eventually became unable to walk. He was initially admitted elsewhere, where empirical antibiotics and dexamethasone resulted in transient clinical improvement. However, fever recurred soon after discharge, with persistent neurodeficit and hence referred to our hospital.

On admission, he was febrile but hemodynamically stable. Neurological examination revealed mild neck stiffness, truncal weakness, flaccid paraplegia with absent lower limb reflexes and a well-defined sensory level at T6. Initial working diagnosis was Guillain- Barre syndrome (GBS) but continued high grade fever was atypical. MRI of the brain and spine demonstrated diffuse leptomeningeal enhancement involving the bilateral temporo-occipital sulci, prepontine cisterns, cervical cord, thoracic meninges, conus medullaris and cauda equina nerve roots, suggestive of extensive meningo-myeloradiculitis. (Figures 1,2,3). This made diagnosis of GBS unlikely.

Cerebrospinal fluid (CSF) examination revealed lymphocytic pleocytosis (162 cells/Cmm with 90% lymphocytes), 196 mg/dL protein and 38 mg/dL sugar. Given the clinical presentation and imaging findings, empirical antitubercular therapy (ATT), corticosteroids and broad-spectrum antibiotics were initiated. An extensive parallel diagnostic evaluation while administering ATT was being done. CSF Biofire Assay Meningo-Encephalitis panel, bacterial culture, MTB pyrosequencing, Brucella PCR, Lyme serology, cryptococcal antigen, tropical fever panel by PCR were negative. Urinary Histoplasma antigen test was negative. TB-MGIT culture reports were awaited. Whole-body PET-CT did not identify any occult infective or malignant focus. Fever was persistent despite higher (weigh-based) dosing of ATT and neurological recovery remained unsatisfactory at 2 weeks, prompting reconsideration of the diagnosis. A decision was made to repeat CSF examination.

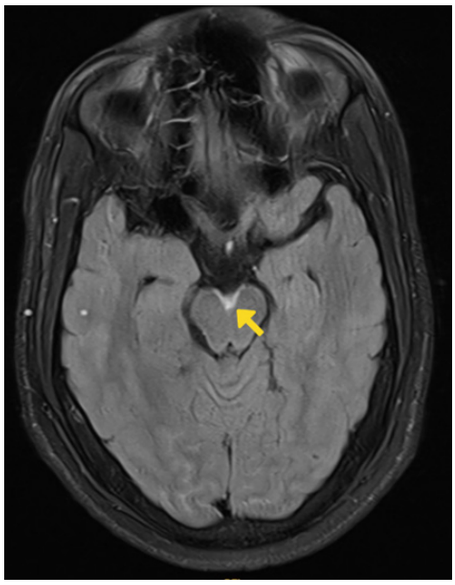

Figure 1: Leptomeningial enhancement along the prepontine cistern (along the ventral surface of pons).

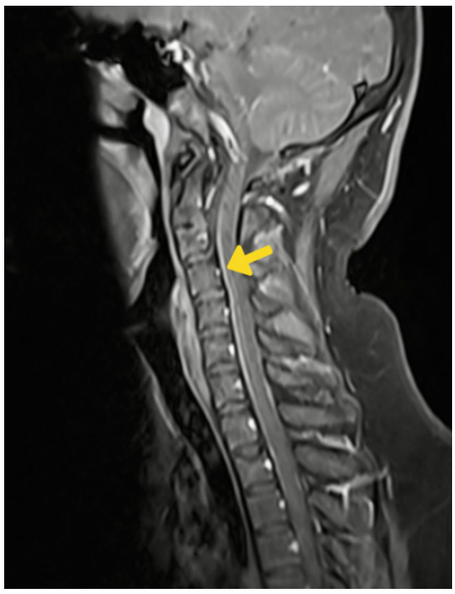

Figure 2: Smooth anterior and patchy posterior dural enhancement in cervical and upper dorsal region, from cervico vertebral junction to D1-D2 vertebral body.

The second CSF examination demonstrated increased total nucleated cell count to 536 cells/cmm with 85% lymphocytes and proteins 129 mg/dl with sugar of 68 mg/dl. CSF revealed strongly positive galactomannan (2.312 index value) and raised 1,3-β-D-glucan (344 pg/mL). CSF Aspergillus PCR by Multiplex Real Time Qualitative PCR was positive for Aspergillus species but negative for *A. fumigatus, A. terreus* and *A. flavus* raising possibility of infection by cryptic aspergillus species. CSF fungal cultures did not report any growth.

Based on these findings, antitubercular therapy and antibacterial agents were discontinued, steroids were rapidly tapered and stopped and a combination of liposomal amphotericin B and voriconazole was initiated. Voriconazole was subsequently continued after 2 weeks of combination therapy and achieving adequate serum voriconazole level. Fever spikes settled and the patient showed gradual neurological improvement, started walking with walker support and was discharged on prolonged oral voriconazole 400mg twice daily with continued neurological rehabilitation. Removal of Foley's catheter is planned at a latter date.

Discussion

The most intriguing aspect of this case was not merely the diagnosis but the host. Our patient was 16 years old with no identifiable predisposing condition. HIV testing was negative, CD4 counts were normal and there was no clinical or radiological evidence of pulmonary, sinonasal or cardiac valvular aspergillosis. Consequently, an extensive search for occult immune dysfunction was also done, including evaluation for chronic granulomatous disease by dihydrorhodamine (DHR) test and quantitative immunoglobulin deficiencies by immunoglobulin panel; both were negative. A primary immunodeficiency panel to look for inherited defects affecting antifungal immunity such as CARD9 and STAT pathway abnormalities is awaited. Whether this represents an unrecognized primary immunodeficiency or an unusual environmental exposure remains uncertain.

Our experience also mirrors observations from the largest systematic review of aspergillus meningitis published to date. Although traditionally

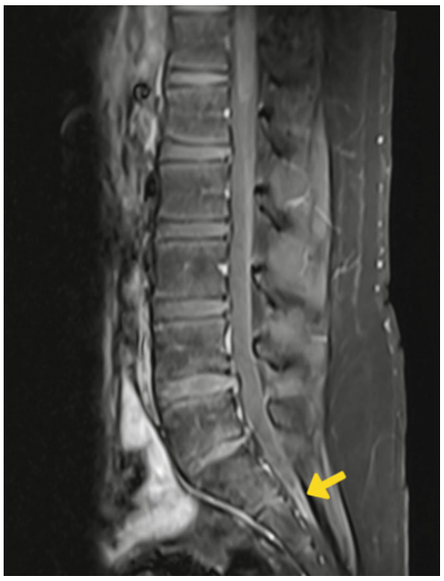

Figure 3: Subtle meningeal enhancement along conus medullaris.

regarded as an opportunistic infection, more than half of the reported cases occurred in patients without predisposing factors, emphasizing that the absence of immunosuppression should not preclude consideration of the diagnosis. Clinical manifestations are highly variable, with acute or chronic meningitis accounting for nearly two-thirds of presentations, followed by meningoencephalitis, ventriculitis and spinal arachnoiditis. Fever, headache, altered sensorium, cranial nerve palsies, stroke-like deficits and radicular pain are among the most frequently reported features, while neuroimaging may demonstrate basal meningeal enhancement, cerebritis, infarctions, abscesses or vascular complications owing to the angio-invasive nature of Aspergillus. Cerebrospinal fluid findings are nonspecific and often closely resemble tuberculous meningitis, typically showing lymphocytic pleocytosis, elevated protein and reduced glucose. *Importantly, conventional CSF fungal culture has poor diagnostic sensitivity (as in our case), whereas CSF galactomannan and aspergillus PCR have emerged as significantly more sensitive diagnostic tools that permit earlier diagnosis and treatment.* Despite advances in antifungal therapy, CNS aspergillosis continues to carry a high mortality, highlighting the importance of maintaining a high index of suspicion and incorporating fungal biomarkers early in the evaluation of culture-negative subacute to chronic meningitis.

This case reinforces several important lessons. First, the absence of immunosuppression should not exclude invasive fungal disease from the differential diagnosis of subacute/chronic meningitis or meningo-myeloradiculitis. Second, clinicians should remain cautious of diagnostic anchoring, particularly in tuberculosis-endemic settings where lymphocytic meningitis with low CSF glucose may naturally favour a diagnosis of TB. A persistent clinical deterioration despite appropriate empirical TB therapy should prompt search for alternative diagnosis such as brucellosis, cryptococcosis and aspergillosis. In our patient, fungal biomarkers and molecular diagnostics transformed an unexplained, culture-negative neurological illness into a treatable diagnosis, allowing targeted therapy to be instituted before irreversible neurological injury and death occurred.

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GRANULOMATOUS ASPERGILLOSIS – A DIAGNOSTIC CHALLENGE

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Introduction

Granulomatous aspergillosis is an uncommon manifestation of Aspergillus infection, typically caused by *Aspergillus flavus* and often occurs in immunocompetent hosts. Its indolent course and mass-forming nature may closely mimic malignancy and a number of other conditions.

Case report

A 38-year-old male with no known comorbidities presented with progressive dysphagia, vomiting, breathlessness, and significant weight loss over 3 months. There was luminal narrowing with a large submucosal mass at the lower end of the oesophagus on video gastroscopy. CECT revealed circumferential thickening of the distal oesophagus and gastroesophageal junction with infiltration of adjacent mediastinal structures, bilateral hilar masses, mediastinal and right hilar lymphadenopathy. In addition to these, PET-CT demonstrated FDG-avid right peribronchial mass, subcapsular liver lesion and encasement of suprahepatic IVC with a thrombus within, extending into right atrium (Figure 1).

CT-guided biopsy of lung and oesophageal mass showed non-necrotizing granulomatous inflammation with giant cells and no evidence of malignancy.. Subsequently, endoscopic ultrasound-guided biopsy of the oesophageal mass revealed numerous non-necrotizing granulomas and giant cells containing fungal elements (Figure 2). The organisms demonstrated septate hyphae with a beaded appearance and intercalary chlamydospore like forms, commonly described with *Aspergillus flavus*.

The patient was advised per oral isavuconazole but he was unable to swallow the tablets and hence was advised IV isavuconazole till some improvement occurred.

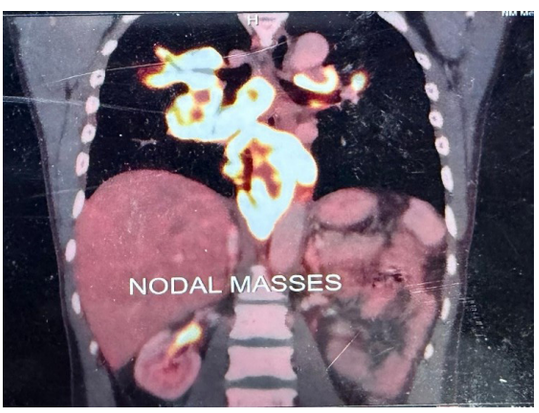

Figure 1: PET CT showing the infiltrating mass

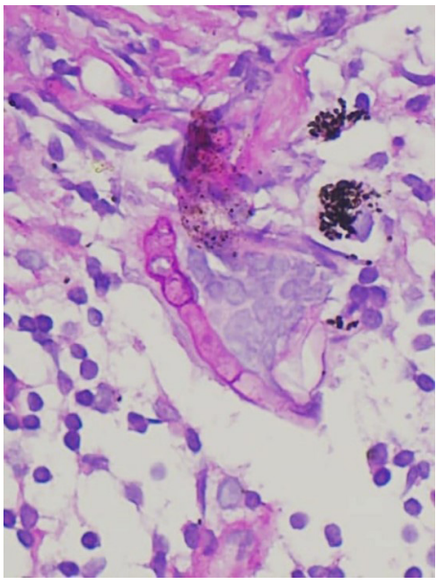

Figure 2: HPE showing septate hyphae.

Discussion

In contrast to acute invasive aspergillosis, tissue necrosis and angioinvasion may be minimal or absent in granulomatous Aspergillosis. The presence of fungal structures within giant cells reflects active phagocytosis and preserved cell-mediated immunity.

Granulomatous aspergillosis should be considered in the differential diagnosis of FDG-avid mediastinal and oesophageal masses, especially in immunocompetent individuals. Histopathological confirmation with presence of granuloma is important to avoid misdiagnosis and ensure timely initiation of antifungal therapy.

Unfortunately in this case the sample was not sent for cultures since index of suspicion for an infection based on the radiologic appearance was low. The case illustrates the fact that "all tumours must be cultured and all abscesses must be biopsied". The choice of the antifungal also merits discussion. Isavuconazole was chosen as there are no breakpoints for voriconazole for *A. flavus* as well as anticipating long duration of therapy where isavuconazole would be better tolerated as compared to voriconazole.

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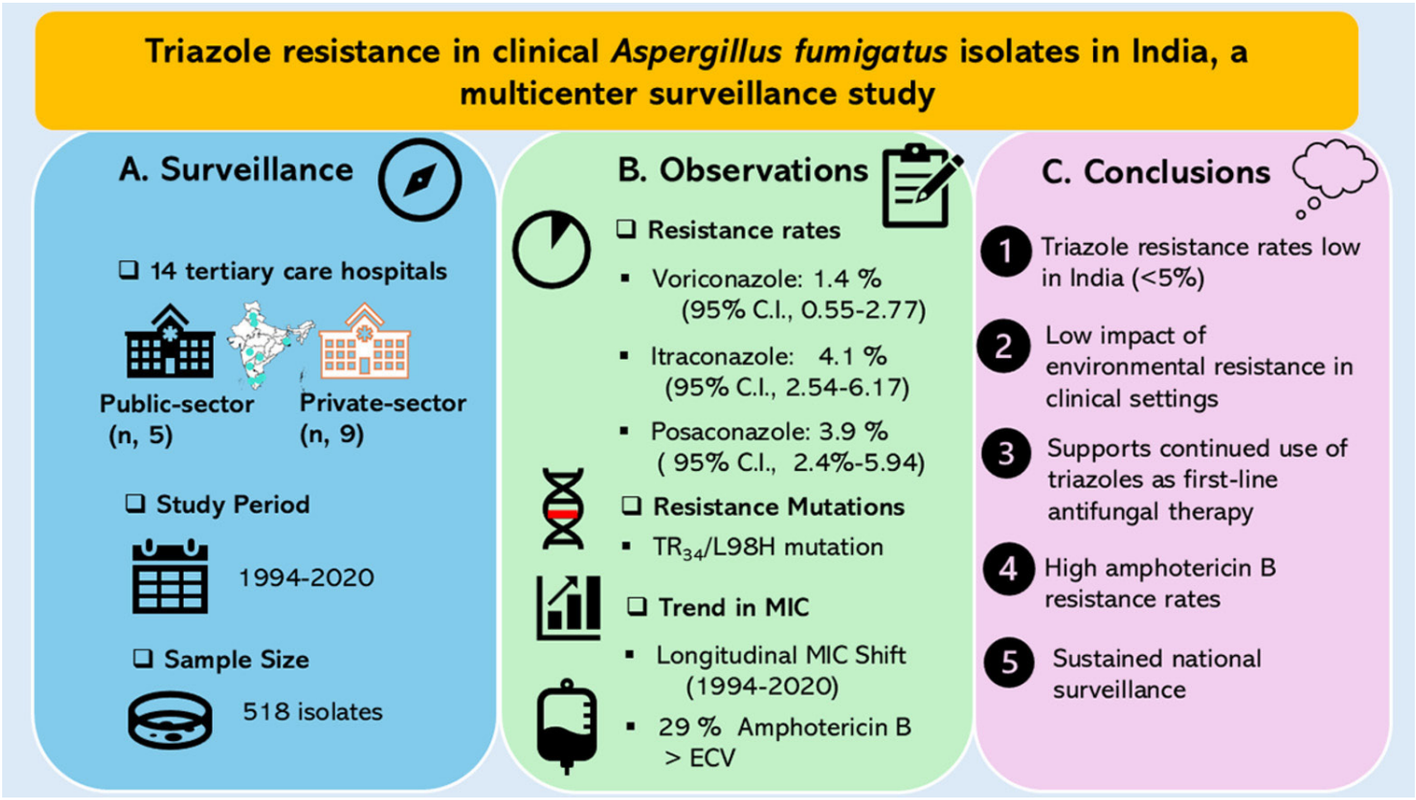

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DELAYED DIAGNOSIS OF COMMUNITY ACQUIRED CANDIDA ENDOCARDITIS IN A CHILD

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Introduction

Candida endocarditis is usually seen in the setting of neonatal candidiasis, cardiac surgery, central line associated candidemia, cancer chemotherapy etc. It is a challenging disease to treat. We present here a case of candida endocarditis in a 3 year old boy where the mode of acquisition was unknown and management was challenging.

Case Report

This 3 year old boy from Rural Maharashtra presented in October 2025 with fever of past 2-3 months duration. This fever was treated with IV and oral antibiotics as well as oral steroids at small nursing homes with no improvement. The past history was significant. He was born of a non-consanguineous marriage and had an uneventful birth and post-natal history. He was hospitalized twice at age 6 months with a bronchopneumonia. After that he had recurrent episodes of cold, cough, fever almost every month for which the child received antibiotics; some CBC's showed low neutrophil counts (25%), but the absolute neutrophil count was never less than 1000. He had a repeat hospitalization at 1.5 years for pneumonia and then continued to have recurrent cold and cough and fever after that till March 2025. He was relatively well from March to August 2025 when he developed fever for which he was admitted and given intravenous antibiotics, steroids and fluids at a rural nursing home. He was discharged after a few days and continued to run fever for which he was treated with oral antibiotics and steroids. After 2 months he was noted to have a murmur and referred to a tertiary care hospital in Pune for further evaluation. An ECHO was done which showed a bicuspid aortic valve with a vegetation and severe aortic regurgitation. Three sets of blood cultures were sent and treatment initiated with ceftriaxone, gentamicin and vancomycin. All three sets of blood cultures grew Candida utilis (MALDITOF ID) which was susceptible to fluconazole, amphotericin B and flucytosine (by Broth microdilution). Treatment was changed to L-AMB and 5 FC. Fever took 10 days to resolve; follow up blood cultures were negative. 5 FC was stopped after 2 weeks due to pancytopenia. The child was discharged after 4 weeks of parenteral therapy on oral fluconazole. A FU 2D ECHO showed no change in the size of the vegetation.

A few days after discharge the child developed fever and presented to the authors hospital. Repeat blood cultures were sent and L-AMB @ 5 mg/kg/day and 5 FC restarted. 2D ECHO showed a large vegetation on aortic valve (Figure 1) . All the three sets of blood cultures grew *C. utilis* which was susceptible to L-AMB and fluconazole but resistant to 5 FC. 5-FC was stopped. In view of history of recurrent infections in past serum immunoglobulins were sent which was negative. HIV serology was negative. The patient was taken up for surgery on day 5 of hospitalization. The child underwent a Ross procedure in which the Pulmonary valve was used to replace the aortic valve and the pulmonary valve was created of contegra pulmonary valve conduit (made of bovine jugular vein). In the immediate post-operative period the child developed shock needing three vasopressors, hyperpyrexia with temperatures exceeding 40ºC which responded to cooling but not paracetamol. In view of this fever a CECT head was done which showed embolus of left internal carotid artery with good collateral circulation. The child also developed a gangrene of the left toe. The valve also grew *C. utilis* of the same susceptibility. Over the next few days the child got better and was off inotropes and regained normal sensorium.

However the fever continued. The blood cultures were sterile. By this time the child had been on L-AMB for 3 weeks. So treatment was changed to anidulafungin @ 3 mg/kg/day. Fever continued. The ECHO showed a well-functioning valve with no vegetation. An USG was done which showed splenic abscess (Figure 2). A search was done for any other focus which showed pyuria of 5 cells/ hpf and grew *Burkholderia cepacia*.

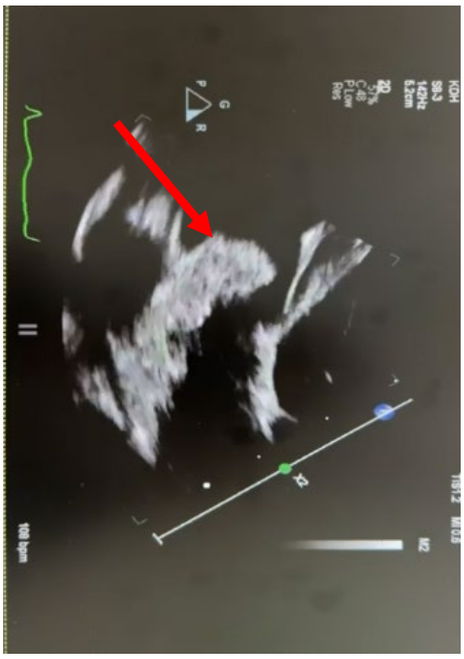

Figure 1: 2D ECHO showing vegetation on the aortic valve

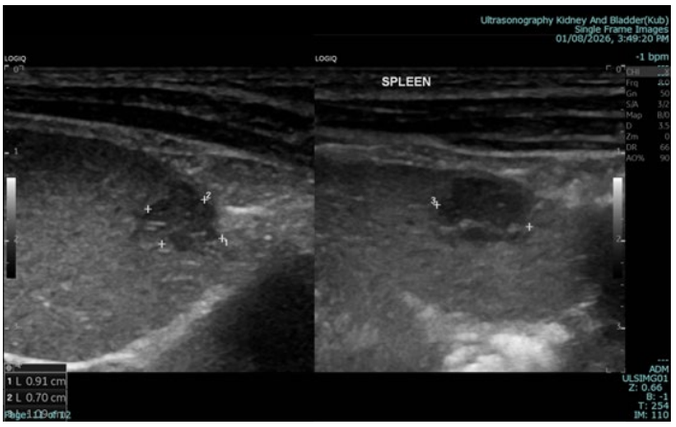

Figure 2: USG showing splenic abscess

IV meropenem was started with which there was no improvement. Repeat USG showed development of new renal abscesses. At this point fluconazole was added @ 12 mg/kg/day following which there was defervescence. The patient was discharged after completing 6 weeks of intravenous antifungals (L-AMB and anidulafungin sequentially) on oral fluconazole. He remained well with a plan to continue oral antifungals for 3-6 months.

Discussion

The first point of discussion is how this child develop CE as he did not have any risk factors for the same. The possibility of inborn error of immunity did arise in view of the multiple infections. However the IEI predisposing to Candida endocarditis is CARD9 deficiency which is also characterized with skin and mucosal candida infections which this child did not have. Hence our hypothesis is that this child developed candidemia following contaminated IV fluids in small hospitals which seeded the bicuspid aortic valve.

The second issue is treatment of CE. The latest global guidelines strongly recommend surgery which is also exemplified in this case. The child relapsed soon after parenteral therapy was stopped. There is no preference between L-AMB with/ without 5-FC and echinocandins (caspofungin) for native valve endocarditis. The unusual feature in this patient was persistent fever even after surgery and trying both drugs L-AMB and echinocandins. This persistent fever was due to deep seated disease in spleen and kidneys which resulted from the prolonged candidemia which this child had before surgery. The guidelines do recommend dual therapy in patients with refractory CE with moderate strength. Dual therapy in this patient fortunately brought about sustained defervescence.

The duration of antifungal therapy is a contentious issue. If surgery is not performed then antifungals need to be continued indefinitely. However if valve replacement is performed then antifungals can be stopped after 12 weeks or on a case by case basis.

Finally, the case also illustrates issues in the delay in diagnosis of endocarditis due to cursory clinical examination and substituting efforts to reach diagnosis by empiric therapy. An early diagnosis would certainly have reduced morbidity in this patient. The importance of infection control while administering fluids and medications cannot be overemphasized.

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EYE DIDN'T SEE THAT COMING: *WICKERHAMOMYCES ANOMALUS* ENDOPHTHALMITIS FOLLOWING CATARACT SURGERY

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Introduction

Delayed postoperative endophthalmitis is an uncommon but vision threatening complication of cataract surgery. While bacteria, Candida species and filamentous fungi are the usual etiological agents, advances in microbiological diagnostics are increasingly identifying uncommon fungal pathogens for which there is limited published guidance on diagnosis and management. We report a case of delayed postoperative endophthalmitis caused by *Wickerhamomyces anomalus*, a rare pathogen, successfully managed with vitrectomy and voriconazole.

Case report

A 64-year-old female with diabetes mellitus and hypertension underwent uncomplicated right eye cataract surgery in December 2025 elsewhere. A few months later, she developed progressive redness of the right eye associated with ocular pain and gradual visual deterioration. She received intravitreal triamcinolone, topical prednisolone and antibacterial eye drops with no improvement. She was then evaluated in the ophthalmology outpatient department of our hospital and diagnosed with possible delayed postoperative endophthalmitis. She subsequently underwent pars plana vitrectomy with intravitreal moxifloxacin and voriconazole.

Figure 1: White-to-cream colored, smooth, glabrous yeast-like colonies on Sabouraud dextrose agar.

Antifungal susceptibility by BMD (Broth Microdilution)

Specimen: Vitreous tap

Organism: Wickerhamomyces anomalus

Antifungal Agent	MIC (ug/ml)	Interpretation
1. Anidulafungin	0.015	IE
2. Micafungin	0.015	IE
3. Caspofungin	0.015	IE
4. Amphotericin B	< 0.12	IE
5. Flucytosine	< 0.06	IE
6. Posaconazole	0.06	IE
7. Voriconazole	0.06	IE
8. Itraconazole	0.06	IE
9. Fluconazole	2	IE

Figure 2: Antifungal susceptibility profile on sensititre-Yeast Y010

Direct microscopy of the vitreous tap demonstrated numerous budding yeast cells on Gram stain and KOH mount, suggestive of fungal endophthalmitis. Fungal culture on Sabouraud dextrose agar yielded white-to-cream colored, smooth, glabrous yeast-like colonies after one week of incubation. (Figure-1) The isolate was identified as *Wickerhamomyces anomalus* by MALDI-TOF mass spectrometry. Antifungal susceptibility testing was performed by broth microdilution where Fluconazole demonstrated a comparatively higher MIC (2 µg/mL). Interpretation was reported as insufficient evidence (IE) due to lack of established clinical breakpoints for this organism. (Figure 2)

The patient was treated with fluconazole initially, later switched to voriconazole following AFST reports. Adequate therapeutic serum drug level (4.36 mg/dL)was achieved. During follow-up ophthalmic examination, the intraocular inflammation significantly regressed with improvement in her vision as well.

Discussion

Wickerhamomyces anomalus (formerly *Pichia anomala, Hansenula anomala, Candida pelliculosa*) is an uncommon opportunistic ascomycetous yeast widely distributed in environmental reservoirs including soil, fruits, plants and bird droppings, while also colonizing the human gastrointestinal tract. Human infections are rare and are predominantly reported as fungemia, neonatal sepsis, catheter-related bloodstream infections, peritonitis and urinary tract infections, while endocarditis and meningitis have been described only sporadically. Ocular disease due to *W. anomalus* is uncommon, with only isolated reports of keratitis and postoperative endophthalmitis.[1]

The source of infection in our patient was most likely perioperative inoculation during cataract surgery, resulting in delayed postoperative endophthalmitis. Diabetes mellitus and advanced age may have further predisposed the patient to infection. This case also highlights the importance of advanced diagnostic techniques in accurately identifying uncommon fungal pathogens as definitive identification of species was achieved using MALDI-TOF mass spectrometry. Moreover, interpretation of susceptibility remains challenging because CLSI and EUCAST have not established clinical breakpoints for *W. anomalus*. Recent multicenter data from India have also demonstrated the emergence of fluconazole non-wild-type isolates associated with ERG11 mutations, efflux pump overexpression and enhanced biofilm formation, suggesting that fluconazole susceptibility may be variable and that treatment should be guided by susceptibility testing whenever available.[3]

Our patient demonstrated an excellent clinical response to vitrectomy and voriconazole. Previous reports of postoperative *W. anomalus* endophthalmitis have similarly highlighted the importance of combined surgical and medical management, with resolution often requiring vitrectomy, targeted antifungal therapy and in some cases, intraocular lens explantation because of suspected biofilm-associated infection.[2]

To our knowledge, only two cases of *W. anomalus* postoperative endophthalmitis have been described worldwide. Our case adds to the limited literature and highlights *W. anomalus* as an emerging cause of postoperative endophthalmitis. A painful red eye with progressive visual loss following cataract surgery should prompt suspicion of endophthalmitis. Fungal cause should be suspected particularly when there is poor response to antibacterial therapy. Early suspicion, prompt microbiological diagnosis, appropriate surgical intervention and targeted antifungal therapy are essential for preserving vision in these rare infections.

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AN UNUSUAL PRESENTATION OF DISSEMINATED HISTOPLASMOSIS WITH BILATERAL ADRENAL AND MUCOCUTANEOUS INVOLVEMENT

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Introduction

Histoplasmosis is a systemic mycosis caused by the thermally dimorphic fungus *Histoplasma capsulatum*, acquired through inhalation of

aerosolized spores from contaminated soil. In India, it is endemic in the Gangetic plains, though increasing cases are being reported from non-endemic regions. Although infection is usually asymptomatic or self-limiting, progressive disseminated histoplasmosis (PDH) is a severe manifestation that occurs predominantly in immunocompromised individuals and may involve multiple organ systems, including the bone marrow, gastrointestinal tract, skin, lymph nodes, and adrenal glands. Adrenal involvement is reported frequently in disseminated cases, while concurrent bilateral adrenal and mucocutaneous involvement is uncommon. We report a rare case of disseminated histoplasmosis with bilateral adrenal and mucocutaneous involvement, initially misdiagnosed as Behcet's disease, underscoring the importance of considering histoplasmosis.

Case Presentation

A 60-year-old male resident of Solan, Himachal Pradesh, a farmer by occupation, presented to a tertiary hospital with a history of high-grade fever, oral lesions, and skin lesions for 2 months. He also reported decreased appetite and disturbed sleep for 2 months. He had a history of epistaxis one-year prior, bilateral hearing loss for the past 10 years, and urinary urgency with polyuria for one year, managed with silodosin. He was a chronic smoker with a smoking history of 35 pack-years. The patient was diagnosed with Behçet's disease at a private clinic and treated initially with prednisolone, followed by tofacitinib. On general examination, the patient was conscious, oriented, and afebrile, with normal vitals. Pallor, bilateral pitting pedal oedema, and cervical and axillary lymphadenopathy were present. On local examination, multiple umbilicated papules were present over the left angle of the mouth, left side of the neck, and fingers, along with multiple papulonodular lesions involving the palate and tongue (Figure 1). Systemic examination was unremarkable.

Initial laboratory investigations revealed anaemia (haemoglobin, 10.4 g/dL), leukopenia (TLC 2680), lymphopenia (10.4%), monocytosis (16.7%), hyponatremia (130 mmol/L), and hypokalaemia (3.14 mmol/L). Inflammatory markers were elevated, including C-reactive protein (62.84 mg/L), lactate dehydrogenase (274 U/L), D-dimer (664

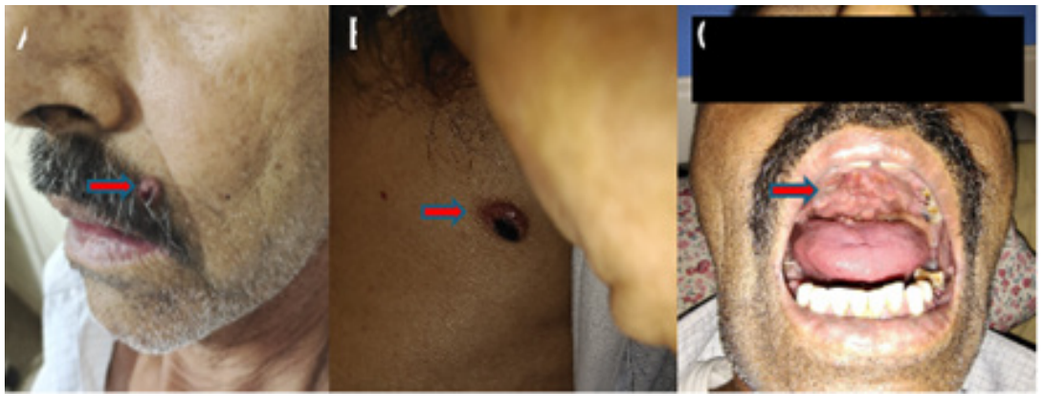

Figure 1: Papulonodular lesions over the face (A), chest (B), and palate (C)

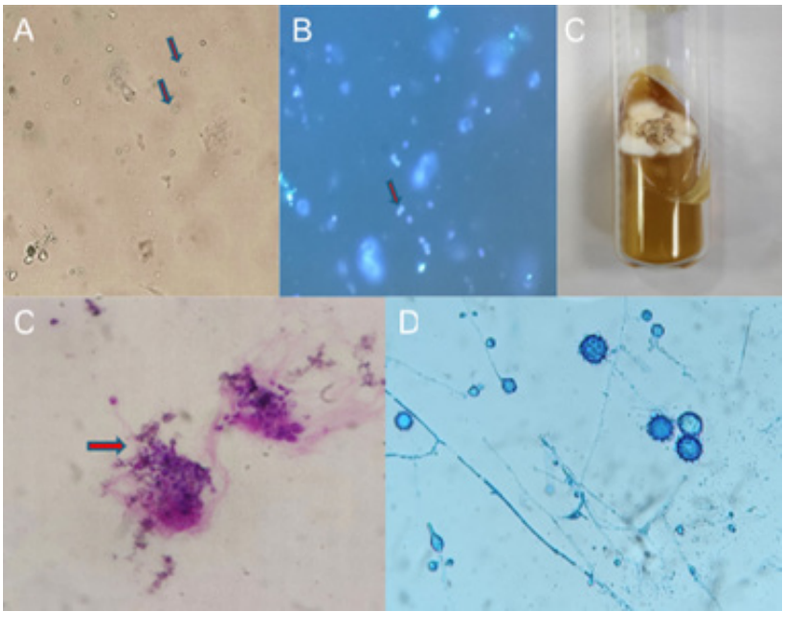

Figure 2: (A) KOH mount (400x) and calcofluor white stain under a fluorescent microscope (400x) showing small, oval yeast cells with narrow-based budding; (B) Giemsa stain (400x) showing intracellular yeast cells; (C) culture on Sabouraud dextrose agar after 3 weeks showing white to buff-coloured colonies, (D) lactophenol cotton blue (LCB) mount of slide culture demonstrating hyaline, septate hyphae with conidiophores arising at right angles and tuberculate, thick-walled, round, hyalinemacroconidia with finger-like surface projections.

ng/mL), and ferritin (1288 ng/mL), with low serum iron (40.5 µg/dL). Serum ACTH was elevated (136 pg/mL), while serum cortisol was within the normal range (488 nmol/L). Lymphocyte subset analysis showed absolute lymphopenia with reduced CD4+ (210/µL) and CD19+ B-cell (24/µL) counts. Serological tests for HIV, HBV and HCV were non-reactive.

CECT abdomen and pelvis revealed bilateral heterogeneously enhancing adrenal masses (right: 6.6 × 5.6 cm; left: 6.5 × 4.4 cm), multiple enlarged para-aortic lymph nodes, and a simple interpolar renal cortical cyst. Positron FDG PET demonstrated hypermetabolic lesions involving the nasopharynx, bilateral buccal mucosa, palatine tonsils, bilateral carinal lymph nodes, bilateral partially necrotic adrenal masses, and the prostate with the left seminal vesicle.

Bone marrow showed a hypercellular marrow with trilineage hematopoiesis and infrequent hemophagocytosis (M: E 1.9:1, NE: E 2.5:1), without infiltration or malignancy. Bone marrow and blood cultures were sterile. Samples, including a skin biopsy, a palatal biopsy, and a fine-needle aspiration of the right cervical lymph node, were sent for microbiological and histopathological investigations. The KOH mount showed small, oval yeast cells with narrow-based budding (Figure 2a). Histopathology of the skin and palatal biopsies using Periodic acid–Schiff (PAS) and Grocott stain revealed a dense histiocytic collection with lymphomononuclear cells, the histiocytes being loaded with numerous 2–4 µm yeast forms consistent with histoplasmosis. Fine needle aspiration (FNA) from the right cervical lymph node was cellular, showing macrophages containing numerous intracellular and a few extracellular, uniform, small (2–4 µm) oval yeast forms with eccentric nuclei and occasional narrow-based budding in a necroinflammatory background. Fungal culture on Sabouraud dextrose agar after 3 weeks of incubation, at 25˚C, showed slow-growing, white to buff-coloured colonies on the obverse and yellowish-brown pigmentation on the reverse (Figure 2c). Slide culture after 3 weeks of incubation at 37˚C demonstrated hyaline, septate hyphae with conidiophores arising at right angles, and tuberculate, thick-walled, round, hyaline macroconidia with finger-like surface projections (Figure 2d). The isolate was confirmed as *Histoplasma capsulatum* by sequencing of the ITS regions (unpublished data).

The patient was diagnosed with disseminated histoplasmosis involving the oral cavity, skin, chest wall, lymph nodes, and adrenal glands and started on amphotericin B deoxycholate for 14 days, followed by oral itraconazole 200 mg twice daily. He became afebrile, and the oral, cutaneous, and chest wall lesions showed gradual regression. He was discharged in a hemodynamically stable condition, with oral itraconazole planned for 1 year and clinical follow-up every 3 months.

Discussion

We present a case of disseminated histoplasmosis with mucocutaneous and adrenal involvement in a patient from Himachal Pradesh, initially misdiagnosed and treated with immunosuppressants, underscoring the importance of considering fungal infections in the differential diagnosis.

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INVASIVE PULMONARY ASPERGILLOSIS OR PULMONARY MUCORMYCOSIS OR BOTH?

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Background

Both invasive pulmonary aspergillosis (IPA) and pulmonary mucormycosis (PM) are angio-invasive mycelial infections with differences in the extent and nature of this process. Both infections share risk factors including hematologic malignancy, stem cell/solid organ transplant, and prolonged neutropenia. However, poorly controlled diabetes mellitus is more strongly associated with mucormycosis, while prior influenza infection are more suggestive of aspergillosis. Notably, Mucorales species are intrinsically resistant to voriconazole, so breakthrough infection on voriconazole prophylaxis should raise suspicion for mucormycosis. Chest pain and haemoptysis are more commonly described clinical features in PM. IPA especially in neutropenic hosts is characterized by the halo-sign which indicates angioinvasion and subsequent hemorrhage around nodules. PM is a more aggressive and causes extensive vascular invasion and thrombosis, with rapid tissue necrosis giving characteristic reverse halo sign (RHS). Differentiating PM from IPA relies on an integrated approach combining clinical risk factors, CT imaging features, biomarkers, histopathology, and molecular diagnostics. This differentiation can sometimes be tricky as this case illustrates.

Case History

A 68 years old male farmer with diabetes presented with fever, cough, and bodyache for last 2 weeks and breathlessness for last one week. He described progressively worsening cough, breathlessness, heaviness in left upper chest with scanty haemoptysis for last 3 days. Patient was transferred to Ahmedabad with clinical deterioration for further treatment. His available laboratory features were Hb: 9.9 gm/dL, WBC count of 16380 mm^3 with 92% PMN, 5% lymphos, platelets: 488000, ESR: 76, CRP was raised - 8 X ULN, LFT/RFT: WNL, HbA1c: 11.0, (269 mg/dL), S. Acetone: <3. CT Thorax (figure 1a) showed opacities in both hilar

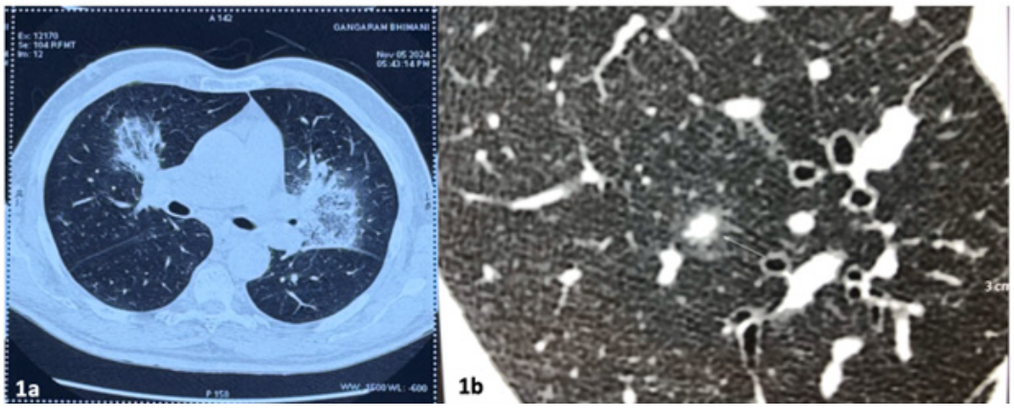

Figure 1: 1a CT scan plain study showing RHS, 1b dense nodule with halo (magnified image)

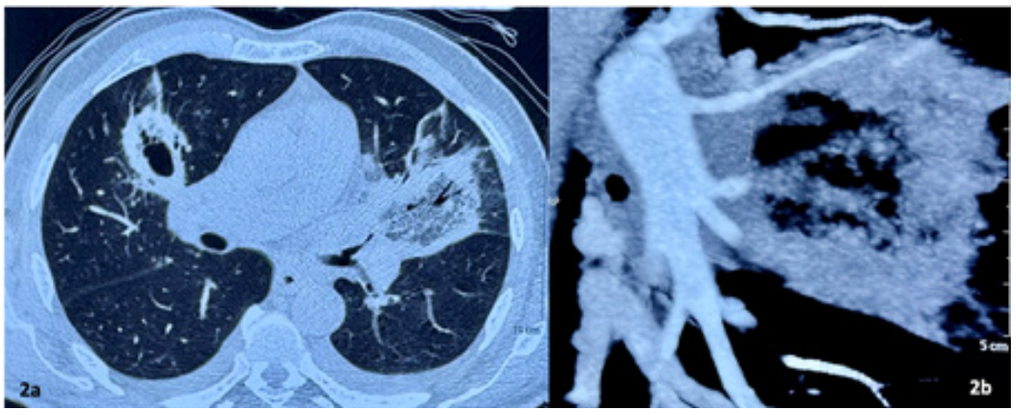

Figure 2a: Follow up CT thorax showing cavity (right) and RHS (left), 2b Vessel occlusion sign (white arrow)

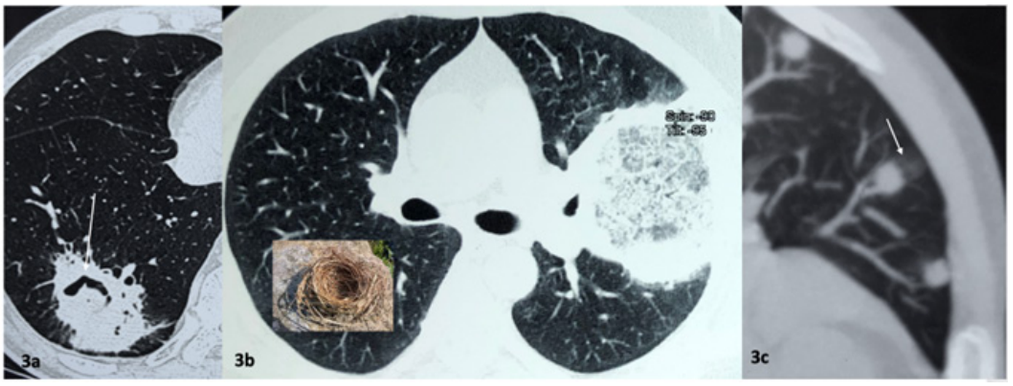

Figure 3: Radiological features of IPA and PM, 3a. air crescent sign, white arrow, 3b. bird nest sign and 3c nodule with halo.

region left > right side with RHS Also present was a small dense nodule with halo (Figure 1b).

Sputum examination was sent as patient was expectorating good amount of sputum with haemoptysis. Sputum examination revealed 25-30 pus cells, KOH: no fungal elements, Fungal and bacterial culture remained sterile at 48 hours and sputum galactomannan was 4.63. A clinical diagnosis of probable IPA in uncontrolled diabetics was entertained.

Voriconazole was added to antibiotics. Patient started feeling better, & was off oxygen after 3rd hospitalization day and shifted to the room. His cough and haemoptysis were steadily improving. Patient then described sudden worsening of left sided chest pain at midnight on 5th hospitalization day. His cardiac work up was negative for coronary artery disease. CT thorax with CT pulmonary angiography was performed. CT showed increase in size of RHS on the left and cavity on the right lung field (Figure 2a). CT pulmonary angiography showed vessel occlusion sign (VOS) (Figure 2b).

Patient's repeat induced sputum examination after 3% saline nebulization showed broad aseptate fungal hyphae on direct microscopic examination, Mucorales PCR positive and culture grew *R. arrhizus*. Patient's antifungal therapy was revised to L-AmB and tablet posaconazole in standard dosage.

Discussion

This patient had uncontrolled diabetes mellitus as a risk factors for PM. Clinical features of chest pain and hemoptysis also favoured PM. The imaging finding of RHS and large consolidations again were in favour of PM. The patient did have a dense nodule with halo which can point to IPA but the same can be seen even with PM. However this nodule is very

Table 1: CT Imaging Features helpful in differentiating IPA vs PM

Reverse halo sign (RHS): An area of ground-glass opacity surrounded by a rim of consolidation — significantly more common in PM (OR 6.73) and the strongest radiologic predictor
Lesion size ≥ 4 cm: Large consolidative lesions favor PM (OR 3.61)
Absence of airway-invasive pattern: Airway-invasive lesions (tree-in-bud, centrilobular nodules) favour IPA rather than PM
The halo sign (ground-glass opacity surrounding a nodule (Figure 3c), is more classically associated with early IPA in neutropenic patients, though it can also be seen in PM
Consolidation as the dominant pattern: More common in PM (OR 5.56), whereas IPA more often presents with nodular lesions.
Pleural effusions and >10 nodules are more suggestive of PM
The bird's nest sign (Figure 3b) is seen in up to a third of PM cases versus only ~3% of IPA
Abscess formation on CT is more associated with PM
The air crescent sign occurs in later stages of IPA during neutrophil recovery and is uncommon in PM (Figure 3a)
Contiguous spread: Mass or consolidation traversing tissue planes to invade adjacent structures (chest wall, diaphragm, pleura, spleen) suggests the aggressive behaviour of mucormycosis
Rapid progression: Serial imaging showing rapid enlargement of consolidative lesions with clinical deterioration is characteristic of PM
Jang HM describe a point-based CT scoring system (RHS = 17 points, lesion ≥ 4 cm = 11 points, airway invasion = −12 points; score > 8 favors PM) achieved 70.6% sensitivity and 78.3% specificity for differentiating PM from IPA

tiny as compared to the consolidation with RHS since both the images are not of the same scale. Table 1 lists the radiologic features of IPA and PM. Now the patient had an elevated sputum GM of 4.6 which would make one suspect IPA, but it should be remembered that specificity of sputum GM (75%) is lower than BAL GM (95%). The positive predictive value is also likely to be low if the pre-test probability of IPA like in this case is low. A coinfection could be another explanation. In such a setting where one cannot accurately identify the invasive mould infection or where dual infection is suspected, it is prudent to start with treatment that would be effective against both mucorales and aspergillus viz. L-AMB with without posaconazole/ isavuconazole.

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CLEARING THE WAY TO CURATIVE TRANSPLANT: NON-RESOLVING CONSOLIDATION IN A CHILD WITH REFRACTORY JMML

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Introduction

Juvenile myelomonocytic leukemia (JMML) is a rare pediatric myelodysplastic/myeloproliferative neoplasm overlap disease that can be aggressive and also present with leukemic infiltration into organs including liver, spleen and lungs. Allo-HSCT (hematopoietic stem cell transplant) with myeloablative conditioning is the only curative option. We present a case of refractory JMML listed for HSCT who had persistent lung consolidation. Lung biopsy revealed an invasive fungal infection and he required aggressive medical/surgical management which enabled a successful haploidentical HSCT.

Case Report

A five-year-old boy with refractory JMML with PTPN11 and NF1 mutations had persistent disease and required salvage chemotherapy followed by maintenance with azacytidine, cytarabine and trametinib while being prepared for haploidentical HSCT. He was on voriconazole prophylaxis during his chemotherapy.

During prolonged chemotherapy-induced pancytopenia, he developed carbapenem resistant *E. coli* sepsis followed by severe parainfluenza pneumonia with bilateral pulmonary consolidation requiring high-flow nasal oxygen support. Although the acute respiratory illness gradually improved, child continued to have repeated fevers over the next 4 weeks. Serial high resolution CT chest (HRCT) scans demonstrated persistent dense consolidation involving the left lower lobe (Figure 1)

with only minimal radiological regression over several weeks despite broad-spectrum antimicrobial therapy including oral posaconazole with therapeutic drug monitoring (trough level 1.3mg/l). Flexible bronchoscopy with bronchoalveolar lavage (BAL) failed to establish a diagnosis, as bacterial, fungal and mycobacterial cultures, fungal biomarkers, Xpert MTB Ultra, Nocardia stain and cytology were negative.

Differential diagnoses considered for the persistent pulmonary consolidation included persistent bacterial pneumonia, organizing pneumonia following parainfluenza infection, invasive fungal infection (including aspergillosis and mucormycosis), leukemic pulmonary infiltration secondary to refractory JMML, and less likely chemotherapy-related pneumonitis.

In view of the persistent radiological abnormalities and the inability to exclude either invasive fungal disease or leukemic infiltration, a CT-guided core biopsy of the left lower lobe was undertaken. Histopathological examination demonstrated extensive necrotic tissue containing broad aseptate fungal hyphae with angioinvasion, consistent with invasive pulmonary mucormycosis. Fungal cultures remained negative, and serum β-D-glucan and galactomannan was also negative, consistent with the known limitations of this biomarker in Mucorales infections.

Liposomal amphotericin B 5mg/kg IV once daily was initiated immediately. The patient was reviewed jointly by pediatric hematology, infectious diseases and pediatric surgery. Despite two weeks of intravenous liposomal amphotericin B, repeat CT imaging demonstrated persistent localized consolidation with interval development of additional ground-glass opacities, suggesting inadequate disease control.

Following multidisciplinary tumor board discussion on the management options, it was concluded that active invasive pulmonary infection posed an unacceptable risk during post-transplant immunosuppression. Hence, definitive surgical resection was recommended.

The child underwent left thoracotomy with lower lobectomy and post operative CT scan is shown in Figure 2. Histopathological examination of the resected specimen revealed invasive mucormycosis involving the left lower lobe and pleural tissue, demonstrating broad degenerated aseptate fungal hyphae within necrotic lung tissue (Figure 3a and 3b). Fungal, bacterial and mycobacterial cultures were negative.

Postoperatively, liposomal amphotericin B was continued, and serial imaging demonstrated expected postoperative changes without evidence of progressive fungal disease. Following satisfactory clinical and radiological control of infection, the child successfully underwent TCR αβ haploidentical HSCT from his father. Amphotericin B was continued throughout the period of the transplant. The course during transplant remained uneventful. Post-transplant child is on prophylactic posaconazole. Early post-transplant evaluation demonstrated complete donor chimerism, and there has been no evidence of recurrent pulmonary mucormycosis during early follow-up at D+30 (Figure 4).

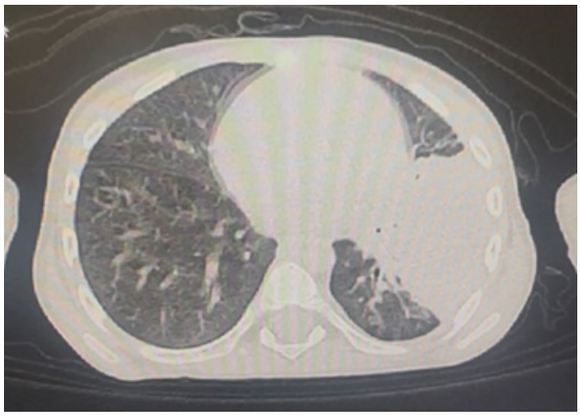

Figure 1: Left lower lobe consolidation at diagnosis

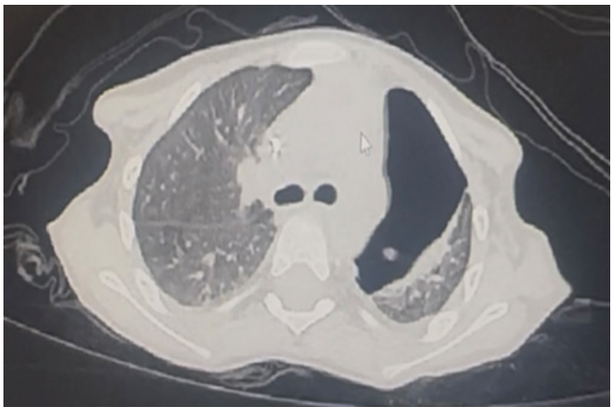

Figure 2: Post lobectomy CT

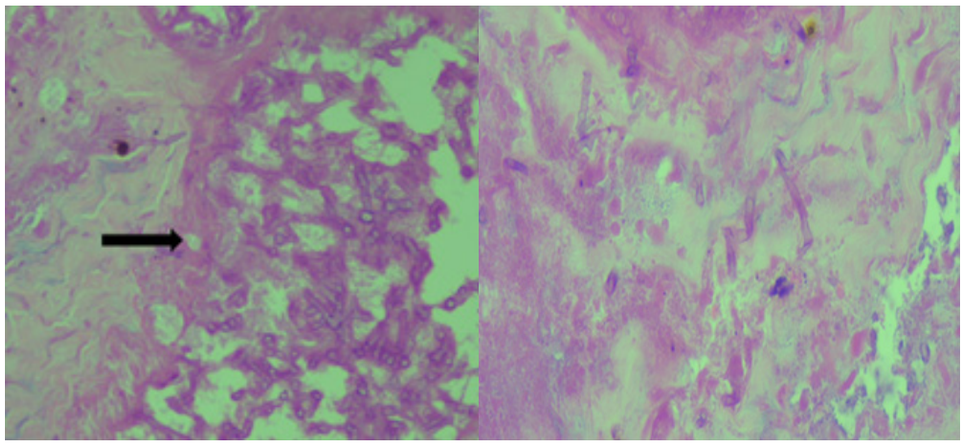

Figure 3a and 3b: Necrotic tissue with few broad aseptate fungal hyphae, favour invasive mucormycosis

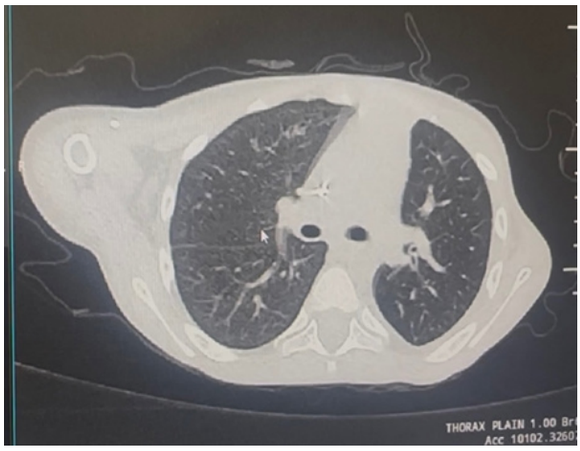

Figure 4: Post HSCT follow up

Discussion

Pulmonary mucormycosis is among the most devastating invasive fungal infections encountered in patients with hematological malignancies. Early diagnosis is difficult and medical therapy alone is frequently insufficient. Despite advances in antifungal therapy, mortality remains high owing to delayed diagnosis, angio-invasive disease and limited penetration of antifungal agents into necrotic tissue. Based on a literature review of mucormycosis in pediatric hematological malignancies, infection related mortality was 36% in all cases and 66% in those with disseminated disease. Seventy percent patients required surgery. Recent literature cites that survival improved modestly after 2015, correlating with earlier antifungal use, surgical intervention, and immune recovery. Combined medical plus surgical therapy significantly reduces risk of death compared to medical therapy alone. The challenge becomes even greater in patients awaiting hematopoietic stem cell transplantation (HSCT), where inadequately controlled fungal infection may delay HSCT leading to progression of the underlying malignancy.

Persistent pulmonary consolidation despite clinical improvement should prompt a systematic evaluation. Although bronchoscopy with BAL is often the initial diagnostic investigation, its yield may be low especially in pulmonary mucormycosis. When imaging abnormalities persist despite inconclusive BAL findings, clinicians should have a low threshold for obtaining tissue biopsy, particularly in children with hematological malignancies where the differential diagnosis includes resistant infection, leukemic pulmonary infiltration and drug-induced lung injury.

Unlike Candida and Aspergillus, Mucorales lack significant β-(1⟶3)-D-glucan within their cell wall, making serum β-D-glucan assays unreliable. Consequently, histopathology remains the diagnostic gold standard, while cultures may remain negative despite invasive disease.

This case highlights the importance of combined medical and surgical therapy. Angioinvasion results in vascular thrombosis and extensive tissue necrosis, limiting antifungal penetration into infected tissue. Although liposomal amphotericin B remains the cornerstone of treatment, persistent localized disease despite appropriate antifungal therapy should prompt consideration of surgical resection whenever feasible. In our patient, lobectomy achieved definitive source control and enabled safe progression to transplantation.

Successful management required close multidisciplinary collaboration between pediatric hematology, infectious diseases, radiology and pediatric surgery. Rather than considering invasive fungal infection as an absolute contraindication to HSCT, aggressive infection control allowed curative transplantation without evidence of recurrent fungal disease during early follow-up. In refractory JMML, HSCT is the only curative option to eliminate the risk of recurrence of invasive mucormycosis.

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