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Central nervous system aspergillosis caused by Aspergillus niger after implant cranioplasty in an immunocompetent patient: a case report

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Case Report

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Abstract

Background: Central nervous system aspergillosis (CA) is predominantly seen in immunosuppressed individuals and is associated with poor outcomes. This report describes a rare case of implant associated CA caused by *Aspergillus niger* in an immunocompetent patient following neurosurgery.

Case presentation: A 61-year-old immunocompetent male presented with wound discharge and neurological deficit three years after neurosurgery for a ruptured anterior communicating artery aneurysm. Subsequent surgical interventions included autologous bone and implant cranioplasties. The patient developed a postoperative infection characterized by headache, hemiparesis, and wound discharge. Imaging revealed a peripherally enhancing lesion, and intraoperative findings raised suspicion of fungal infection. Microbiological studies confirmed *Aspergillus niger*. The patient was managed with surgical debridement, implant removal, and targeted antifungal therapy with voriconazole, with careful monitoring of drug levels. Clinical improvement was observed, and reconstructive cranioplasty was successfully performed after six weeks of antifungal therapy.

Conclusion: CA due to *Aspergillus niger*is exceedingly rare in immunocompetent hosts and may occur post-neurosurgery via contiguous spread from the paranasal sinuses. Early recognition combined surgical and antifungal management, and therapeutic drug monitoring are crucial for optimal outcomes.

Introduction

Central nervous system aspergillosis (CA) is a form of invasive aspergillosis that predominantly affects immunosuppressed individuals and is associated with poor outcomes. Clinical manifestations are heterogeneous and may include seizures, focal neurological deficits, or altered mental status.[1,2]The challenges in management include early diagnosis, achieving therapeutic drug levels in the central nervous system (CNS), and surgical debridement when indicated. This report presents a case of CA in an apparently immunocompetent patient who developed implant-associated and central nervous system infection following neurosurgery.

Case description

A 61-year-old male presented with pustular discharge from a wound over the right frontotemporal region. Three years prior, he developed a right frontal hematoma due to rupture of the A1 segment of the anterior communicating artery (ACA) aneurysm, necessitating right frontotemporal decompressive hemicraniectomy that breached the frontal sinus. Cerebral angiography revealed chronic steno-occlusive disease with severe stenosis of the right M1 segment of the middle cerebral artery (MCA) and multiple small vessel clusters originating from the internal carotid artery bifurcation and proximal MCA, raising suspicion for Moya Moya disease. He remained asymptomatic when he underwent right-sided autologous bone cranioplasty one year later. Subsequently, he developed a sunken flap, and an implant

cranioplasty was performed after removal of the bone flap, two months prior to presentation to our hospital. All previous surgeries were done elsewhere. (Fig. 1)

Two weeks later, the patient developed a new-onset headache accompanied by worsening left hemiparesis. Caregivers observed protrusion of one of the screws and discharge from the postoperative wound, which was managed conservatively at another facility with oral cefuroxime and repeated dressings. Upon admission to this center, the patient was afebrile, haemodynamically stable, drowsy but oriented (Glasgow Coma Scale score E3V5M6), and exhibited reduced motor power (3/5) in the left arm and leg.

Computed tomography (CT) scan of the brain performed at this center revealed pneumocephalus underlying the flap. A heterogeneous soft tissue lesion with air foci and a peripherally enhancing collection was observed in the right temporal region (Fig. 2). The patient subsequently underwent re-exploration of the cranioplasty wound with debridement and removal of the implant. Frontal sinus granulation tissue was removed and exteriorised

Intraoperatively, unhealthy granulation tissue with blackish pigmented deposits was observed beneath the artificial bone flap, raising suspicion of a fungal infection. However, bacterial infections, residual collections and foreign body reactions were also kept as differentials. To rule out, tissue specimens were submitted for aerobic bacterial culture, anaerobic culture, fungal culture, and microbiological evaluation. Histopathological examination was not performed (Fig. 3).

Direct microscopic examination using a 10% potassium hydroxide (KOH) preparation demonstrated branching, septate fungal hyphae at ×400 magnification. Tissue inoculated onto Sabouraud Dextrose Agar and incubated at 35°C yielded fungal growth within 72 hours of debridement. Colonies were initially white and velvety, becoming dense, black, and powdery with a narrow white peripheral margin upon further incubation, while the reverse remained cream colored. Lactophenol cotton blue mount (LPCB) demonstrated hyaline, septate hyphae with acute-angle (approximately 45°) branching, long, smooth, thick-walled conidiophores arising from distinct foot cells and terminating in large globose vesicles. The conidial heads were biseriate and completely radiate, consistent with *Aspergillus niger* (Figs. 4 and 5). Identification was further supported by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI Biotyper; Bruker Daltonics, Bremen, Germany) using the Bruker MBT Filamentous Fungi Library, which identified the isolate as *Aspergillus niger* with a score of 1.96.

Antifungal susceptibility testing was performed using the broth microdilution reference method and interpreted according to the EUCAST Antifungal Clinical Breakpoint Tables and Epidemiological Cut-Off Values (Version 12.1, 2026). The voriconazole minimum inhibitory concentration (MIC) was 2 µg/mL (Table 1). Based on the susceptibility profile and clinical scenario, oral voriconazole therapy was initiated with a loading dose of 6 mg/kg every 12 hours on Day 1, followed by 4 mg/kg twice daily. Voriconazole trough levels sent on the fifth day were elevated; therefore, the dosage was reduced accordingly. Repeat cranioplasty with a flap was postponed for several weeks due to the high risk of reinfection in the presence of fungal infection. A serum voriconazole trough level obtained after one week was 11.6

µg/mL, exceeding the recommended therapeutic range (2–6 µg/mL). The dosage of voriconazole was decreased to 300 mg daily in divided doses. However, the patient developed headache, nausea, vomiting, and loss of appetite with fluctuating consciousness due to sunken flap syndrome. These clinical events adversely affected oral drug absorption, resulting in subtherapeutic voriconazole exposure and necessitating conversion to intravenous voriconazole (200 mg twice daily).

Table 1
Antifungal susceptibility profile
Minimum inhibitory concentrations (MICs) of antifungal agents against the isolated Aspergillus *niger* strain obtained from bone tissue. Performed using Broth Microdilution Method

Antifungal agent	MIC (µg/mL)
Anidulafungin	0.016
Amphotericin B	0.5
Isavuconazole	2
Voriconazole	2
Posaconazole	0.25

Reconstructive cranioplasty with a polyetheretherketone (PEEK) bone flap was successfully performed after six weeks of antifungal therapy. The patient demonstrated clinical improvement and is currently receiving oral voriconazole 200 mg twice daily. The duration of treatment will be determined based on clinical and radiological response.

Discussion

CA is a rare and often fatal condition. Although immunosuppressed patients are more predisposed to this infection, cases have also been reported in immunocompetent individuals. In a systematic review by Meena et al, the reported mortality was 45.1%. Corticosteroid use was the most common risk factor, followed by malignancy. A history of trauma or surgery was noted in 4.7% of cases.[3] Hematogenous dissemination from extra-cerebral sites or contiguous extension of infection from paranasal sinuses or ear are commonly implicated mechanisms of fungal spread. Head injury or neurosurgery can precipitate localized spread from paranasal sinuses or ear, leading to invasive infection.

Among Aspergillus species, Aspergillus *fumigatus* was the predominant cause of CA, as reported by Meena et al and in the French CEREALS cohort. Aspergillus *niger* was reported in only 2.6% of cases. In cases related to contiguous spread or neurosurgery, Aspergillus flavus was the exclusive pathogen in the French CEREALS cohort.4 Cases caused by Aspergillus flavus were mostly reported from tropical regions, and the majority occurred in immunocompetent hosts.[5] In the present case, Aspergillus *niger*

was isolated from an immunocompetent host, most likely due to contiguous spread from the frontal sinus.

Cultures remain the gold standard for diagnosis, while additional tests such as MALDI TOF and Internal Transcribed Spacer (ITS) sequencing are used to identify the fungus at the species level. Newer methods, including metagenomic next generation sequencing (mNGS), may also facilitate rapid diagnosis and identification of the fungus.[6]

Management of CA is often challenging. The use of antifungal agents capable of penetrating the blood-brain barrier and achieving therapeutic concentrations in brain tissue is essential. Voriconazole has been used effectively in these conditions due to favorable pharmacokinetic and pharmacodynamic properties, making it a first-line agent.[7,8] Adjunctive surgical intervention is also recommended whenever feasible, particularly in cases with contiguous involvement from paranasal sinuses.[8] Isavuconazole is another promising treatment option and has demonstrated similar mortality rates compared with voriconazole.[9] The optimal duration of CA management remains undefined.

The patient was treated with oral voriconazole, and surgery with reimplantation of the flap was performed six weeks later. Voriconazole trough levels were 4.16 µg/mL two weeks before surgery. Intraoperative cultures obtained from tissue samples were negative.

Challenges included fluctuating voriconazole levels due to sunken flap syndrome and non-availability of molecular sequencing methods.

Limitations

Case report of a single case and limited details of earlier surgeries performed elsewhere.

Conclusions

CA caused by Aspergillus *niger* is rare in immunocompetent hosts. Infection typically occurs via contiguous spread from the sinuses following surgery or trauma. Combined surgical and medical management is often necessary.

Declarations

Ethics approval and consent to participate

Ethical approval for publication of this case report was obtained from the Ethics Committee of Aditya Birla Memorial Hospital, Pune, India (Approval No. ABMH/EC/4/26). All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the Declaration of Helsinki and its later amendments. Written informed consent was obtained from the patient's next of kin for participation and publication of the clinical data.

Consent for publication

Written informed consent for publication of the clinical details and accompanying images was obtained from the patient's next of kin.

Competing interests

The authors declare no competing interests.

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Author Contribution

Viplov Vaidya: Conceptualisation, Data curation, Methodology, Writing - original draft;Rakesh Ranjan: Supervision, Writing - review & editing;Sagar Chandrakar: Investigation, Writing - review & editing;Nivedita Khaire: Investigation, Data curation;Sohini Arora: Investigation, Data curation

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Figures

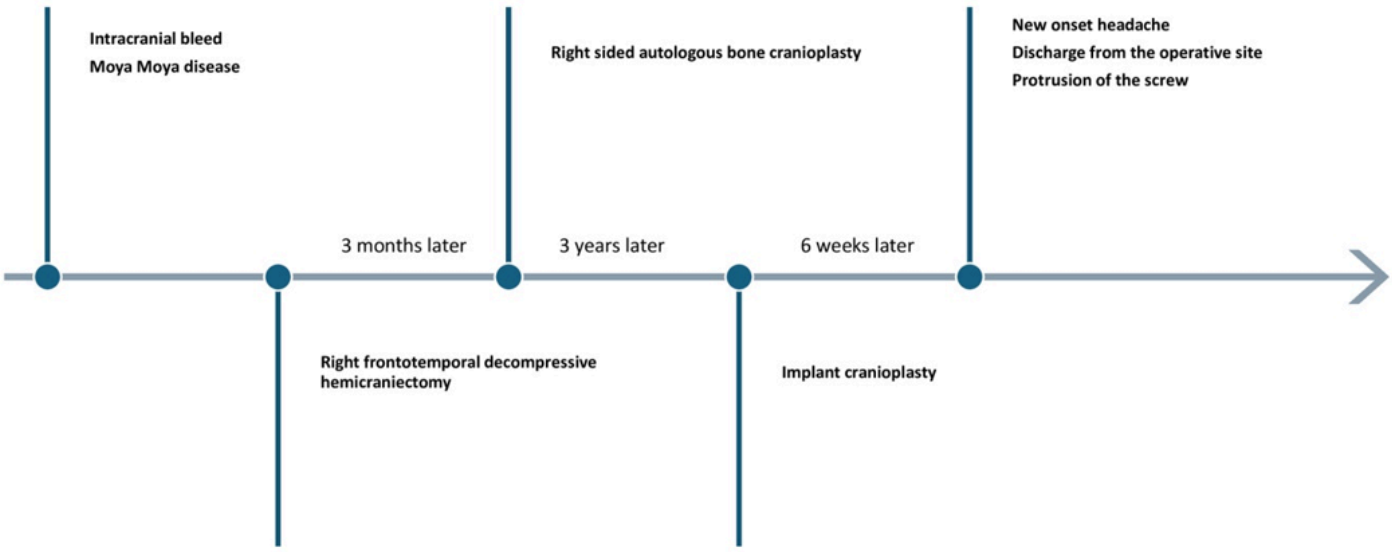


Figure 1

Timeline of the clinical presentation



Figure 2

Computed tomography (CT) findings

Axial contrast enhanced CT images of the brain demonstrating heterogeneous peripherally enhancing small collection with few air foci within, in the right inferior temporal region convexity along the lower margin of the postoperative site(left). Pneumocephalus underlying the cranioplasty flap with inward concavity of the scalp flap and subjacent cerebral parenchymal indentation suggesting sunken flap syndrome (right).

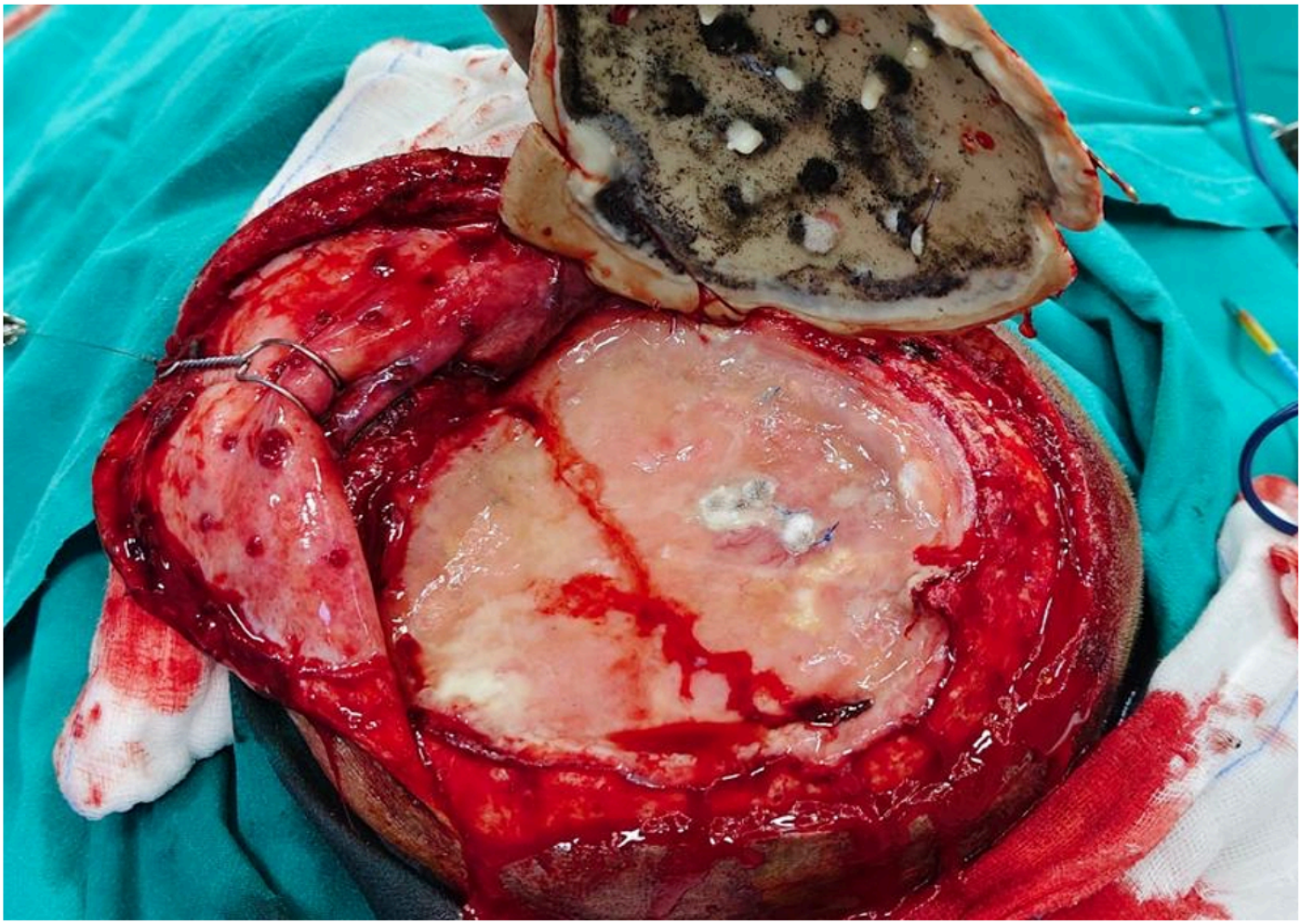


Figure 3

Intraoperative findings
Intraoperative photograph demonstrating re-exploration of the right frontotemporal cranioplasty wound. The explanted craniopolasty implant shows extensive irregular blackish discoloration with multiple adherent whitish deposits/ colonies on its undersurface. The underlying operative field demonstrated inflamed, hyperaemic soft tissues with abnormal granulation tissues overlying the calvarial defect.

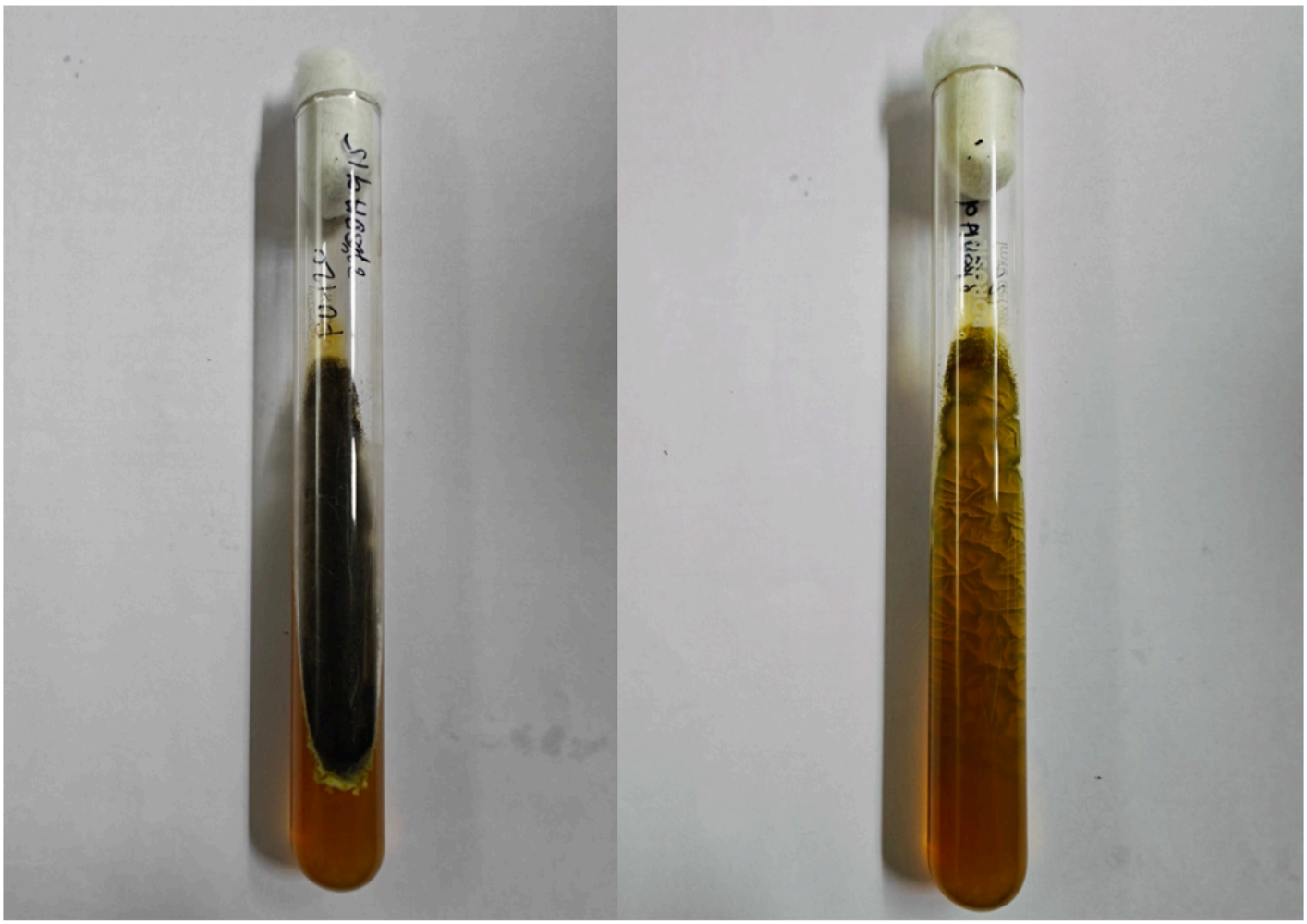


Figure 4

Macroscopic fungal growth Sabouraud dextrose agar (SDA)

Obverse (left): Dense black, filamentous fungal growth on SDA.
Reverse (right): Yellowish-brown pigmentation of the colony on the revers side, consistent with *Aspergillus niger*.

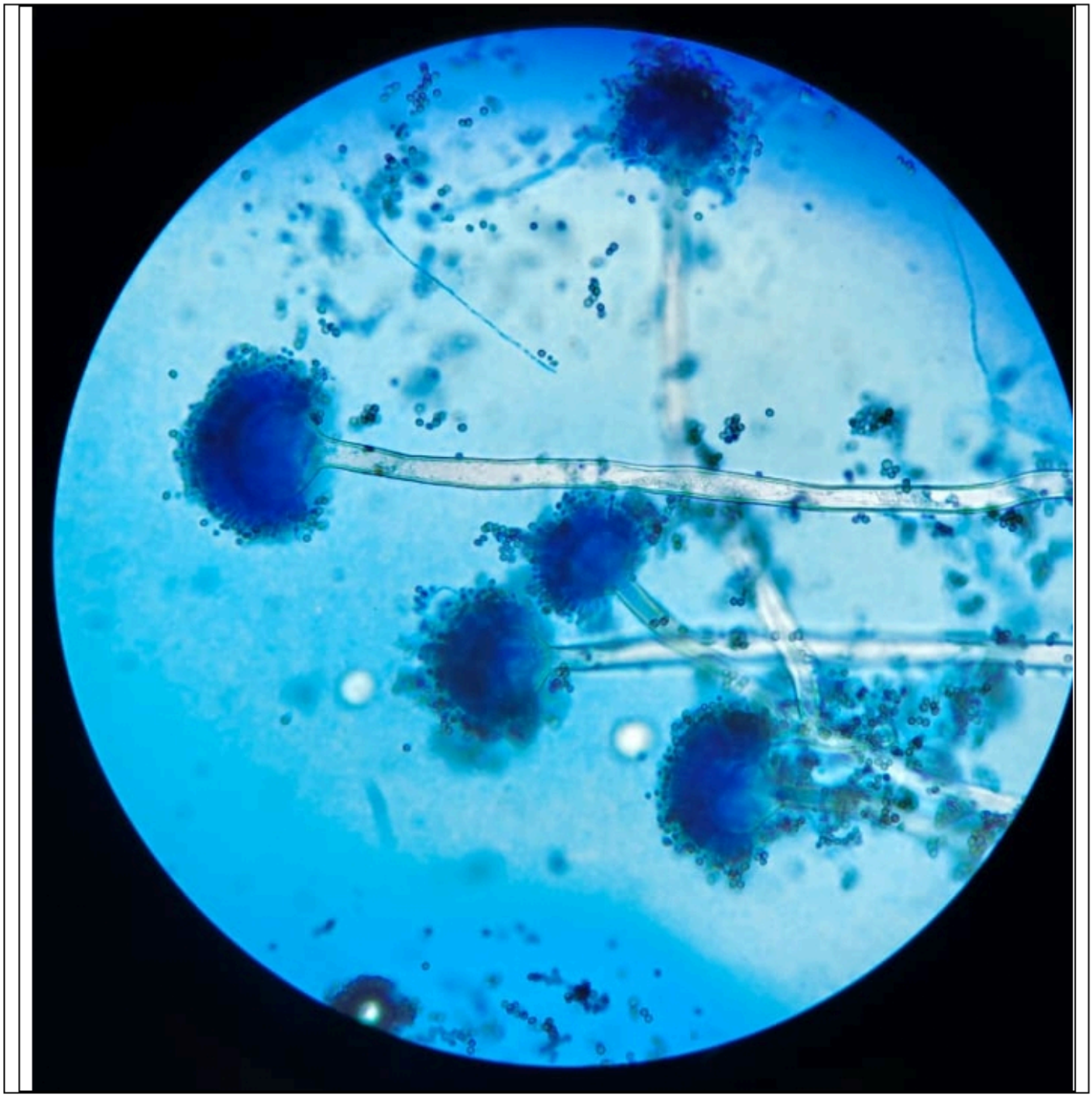


Figure 5

Microscopic morphology in LPCB Mount

Microscopy (lactophenol cotton blue stain) demonstrating broad, septate hyphae with characteristic conidiophores, globose vesicles, and radiating chains of darkly pigmented conidia, consistent with Aspergillus species.