Case Report

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Multiple brain abscesses in a neonate: a rare case report along with review of literature

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Introduction and importance: Brain abscess (BA) is a pyogenic infection of the brain parenchyma caused by various organisms. Multiple BAs are uncommon in neonates, and *Candida albicans* as a causative agent is very rare. If left untreated, BAs are invariably fatal. Early diagnosis, prompt surgical intervention, simultaneous eradication of the primary source, and high-dose intravenous antibiotics decrease the incidence of morbidity and mortality.

Case presentation: A 20-day-old newborn, delivered normally at term with a full APGAR score, presented with a 5-day history of fever, decreased activity, jaundice, and seizures. Imaging identified multiple cerebral cysts, diagnosed as multiple cerebral abscesses. Treatment involved intraoperative USG-guided burr-hole drainage, followed by a 6-week antifungal therapy course. *C. albicans* was found to be the causative organism following microscopic examination and culture of the pus.

Clinical discussion: This literature highlights the rarity of fungal involvement in multiple cerebral abscesses in neonates. Managing such cases is very challenging, as the presentation may mimic bacterial infections. The importance of considering fungi as a causative agent in treatment decisions is crucial.

Conclusion: Multiple BAs of fungal origin are extremely rare. Early detection and management of cases can reduce mortality among neonates.

Keywords: brain abscesses, candida abscesses, candida brain abscess, multiple cerebral abscess, neonates

Introduction

A brain abscess (BA) is defined as a localized area of suppuration that develops within the brain parenchyma after inoculation with a pathogen[1]. Predisposing risk factors include low birth weight, prematurity, immunodeficiency, prolonged intensive care stay and ventilation, extensive use of broad-spectrum antibiotics, and sepsis[2]. The occurrence of multiple BAs in neonates is an uncommon and challenging issue, requiring early diagnosis and prompt surgical removal of pus, simultaneous eradication of the primary source, and high-dose intravenous antibiotics to prevent serious neurological consequences.

HIGHLIGHTS

- A 20-day-old neonate presented with fever, decreased activity, jaundice, and seizures, revealing the uncommon occurrence of multiple cerebral abscesses in neonates.
- *Candida albicans* was identified as the causative agent, highlighting the infrequency of fungal involvement in neonatal cerebral abscess cases.
- Managing neonatal cases of multiple cerebral abscesses poses challenges, given the potential symptom overlap between fungal and bacterial infections.
- Surgical intervention involved Burr-hole drainage with intraoperative ultrasound guidance. A 6-week course of antifungal therapy targeted the *C. albicans* infection.
- Emphasizing the crucial role of early detection in cases of neonatal cerebral abscesses with fungal etiology, aiming to reduce associated mortality.

Fungal etiology is reported in 20% of cases of pediatric BAs with significantly high mortality (almost 80%)[2]. Only a small number of such cases in newborns caused by *Candida albicans* have been reported in the literature, making this condition exceptionally rare[2,3]. Intracranial abscesses caused by fungal infections may present with various clinical syndromes, including basal meningitis, space-occupying lesions, stroke syndromes, hydrocephalus, and spinal infections. Compared to viral, bacterial, or parasitic CNS disorders, symptomatic CNS fungal infection carries higher risks of morbidity and mortality[4]. We report a case

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of multiple cerebral abscesses in a neonate, along with ra review of the literature adhering to SCARE 2023 guidelines[5].

Case presentation

An infant at 20 days of life following normal vaginal delivery was referred to our center with a history of fever for 5 days, up-rolling of the eyes, and decreased activity for 2 days. At birth, he had a full Apgar score. On the second day, the child developed yellowish discoloration of the skin, rapid breathing, excessive crying, poor feeding, and decreased activity and was admitted to the Neonatal Intensive Care Unit (NICU). One episode of seizure occurred on the 14th day of life, which was managed with phenobarbital. At 16 days of life, the baby had developed fever, up-rolling of the eye, lethargy, and decreased feeding. On examination, his respiration rate was 52 per minute, his heart rate was 162 beats per minute, and capillary refill time was less than 3 s with bulging anterior fontanel. Laboratory examination showed a white blood cell count of 17 300/mm^3. Transcranial ultrasonography on the day of admission revealed multiple thick-walled hypoechoic lesions in both cerebral hemispheres suggestive of multiple cerebral abscesses.

MRI was done, which showed multiple variable-sized cystic lesions in bilateral frontal, parietal, temporal, and occipital lobes with rim enhancement in the postcontrast images (Fig. 1). The largest lesion on the right side measured ~1.5 × 1.3 cm and that on the left side measured ~1.8 × 1.0 cm. Intraoperative ultrasound-guided burr-hole drainage of abscesses was done. Examination on direct microscopy of the specimen did not show any pathogens. The pus specimen was inoculated onto routine culture media (MacConkey agar, blood agar, and chocolate agar) and additionally onto brain heart infusion broth and an automated Bac/ALERT system. Growth in all culture procedures after 48 h of aerobic incubation at 37°C was indicative of *C. albicans*, thus eliminating the possibility of the fungal isolate being a contaminant in the laboratory. Findings of the colony morphology,

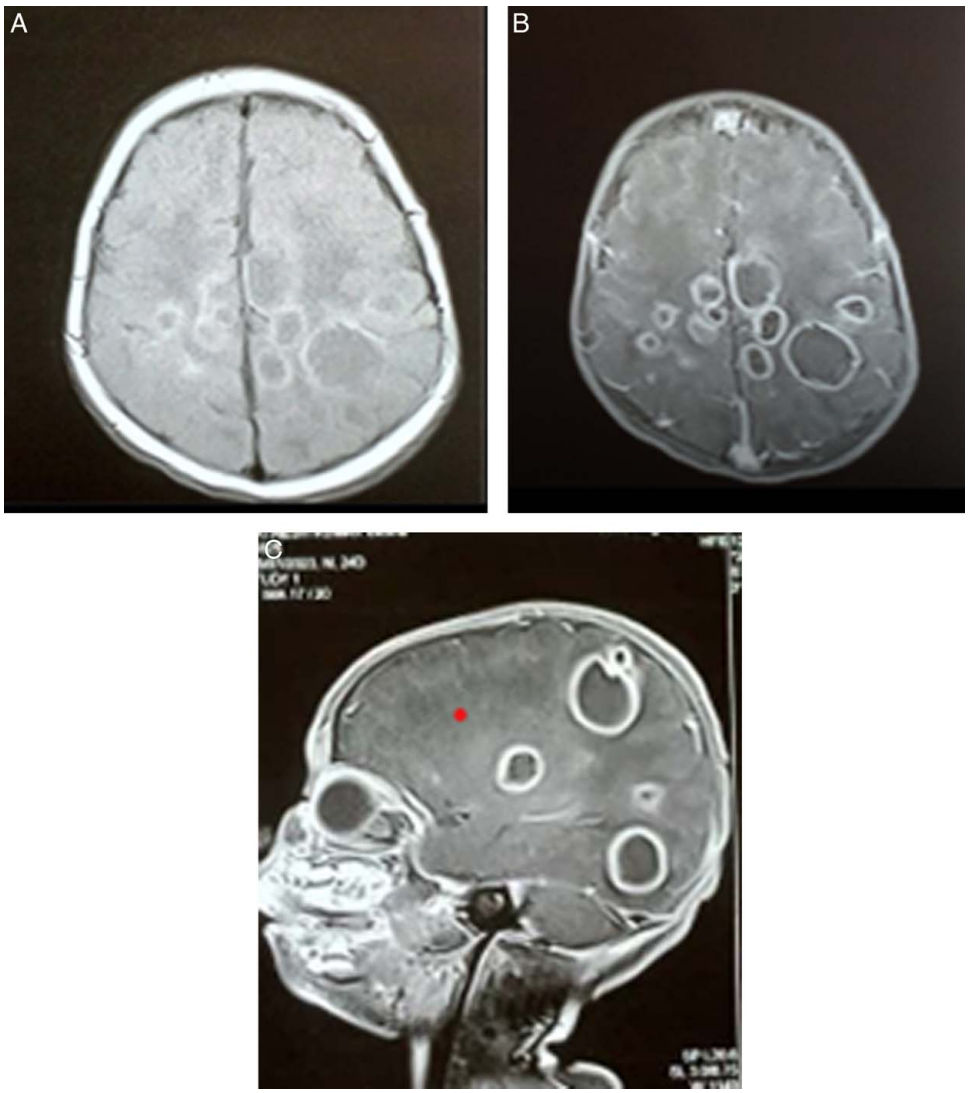

Figure 1. Noncontrast axial T1 MRI (A) and post-gadolinium Axial (B) and sagittal (C) MRI showing multiple rims enhancing lesions in the bilateral cerebral hemispheres in b frontal, parietal, temporal and occipital lobes. The largest lesion on the right side (arrow) measured ~1.5 cm × 1.3 cm.

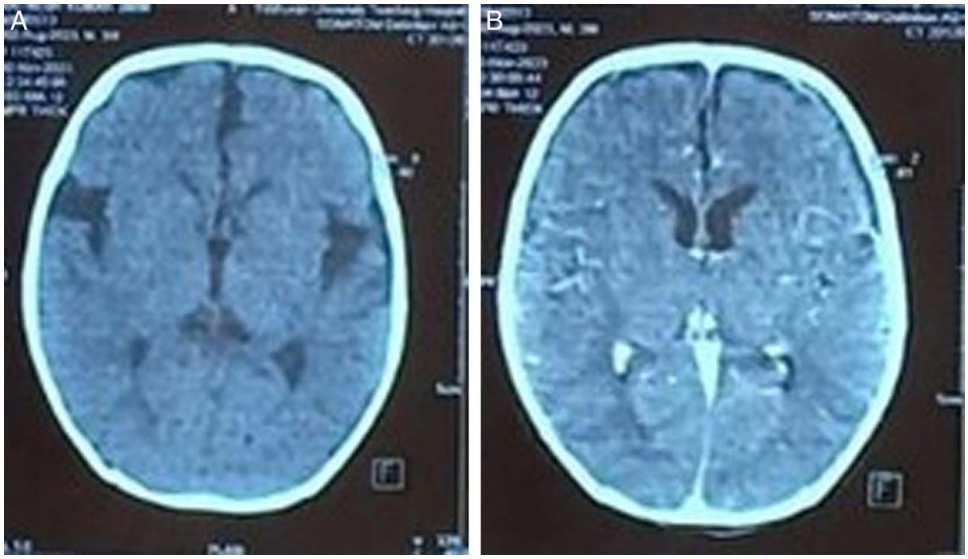

Figure 2. Contrast-enhanced computed tomography scan in 6 weeks after surgery revealing near complete resolution of the abscesses. CECT head done after 6 weeks of management showing near complete resolution of abscess which was present earlier in frontal temporal and occipital lobe reinforcing our management for brain abscess.

Gram stain microscopy, and germ tube test of the significant growth from each culture procedure confirmed the fungal isolate as *C. albicans* (Fig. 2).

The neonate was medically managed with Amphotericin B for 6 weeks. Follow-up contrast-enhanced computed tomography (CECT) performed 3 weeks postsurgery demonstrated a gradual shrinking of abscess cavities, indicating a positive response to antifungal therapy. A subsequent CECT 6 weeks after abscess drainage revealed complete resolution of the abscesses. Presently, 5 months postdischarge, the infant is in good health, feeding well, and exhibiting normal growth and development.

Discussion

A BAs is a focal intracerebral infection characterized by the collection of pus in a well-defined capsule. The most common causative agents are often bacteria such as Streptococcus species, Staphylococcus, and Enterobacteriaceae[6,7]. Global data in pediatric BAs reports fungal etiology in 20% of cases, with a very high mortality rate (almost 80%). Indian data shows a prevalence of less than 1%[2]. In our country, sufficient data are lacking. Fungi causing BAs are an uncommon occurrence, with *C. albicans* being the most prevalent among them[3]. The organism is frequently found in the gut and is present in 40–60% of healthy adults in the gastrointestinal tract and mouth[6]. It is usually a commensal organism, but it can become pathogenic in immunocompromised individuals under conditions such as prematurity, congenital heart disease, neutropenia, HIV infection, the use of broad-spectrum antibiotics and steroid therapy, extended endotracheal intubation, central venous catheters, and parenteral nutrition[2,8]. Studies have shown that *C. albicans* can pass through the blood-brain barrier without damaging the integrity of endothelial cells; meanwhile, the blood-brain barrier is insufficient. As a result, neonates are prone to have multiple abscesses[9,10]. However, it is a rare causative agent for BAs in neonates[11,12]. It is rare for a child under 6 months old to show multiple BAs in all four lobes of the brain, even when they have a BAs. And in such cases, the likelihood of severe illness and death is typically high. BAs, a rare complication of neonatal meningitis, is seen in 1.3–4% of cases[13]. Our patient presents with symptoms resembling sepsis, with the presence of multiple BAs involving all lobes of the cerebrum.

Primary candidiasis of the brain is rare; usually, it is secondary to hematogenous dissemination. Systemic fungal disease in a neonate is usually due to Candida species, particularly *C. albicans*, though only 4% of neonates with Candida sepsis develop BAs[2]. We did not detect the growth of Candida organisms by culturing blood samples from our patient. The presentation of multiple BAs in neonates is quite nonspecific and includes fever, irritability, bulging fontanel, a rapid rise in head circumference with wide separation of sutures, vomiting, seizures, and poor feeding[13,14]. In our study, the neonate presented with sepsis-like symptoms of fever for 5 days, poor appetite, and decreased responsiveness, which were initially managed at the local center hospital by administration of antibiotic therapy through peripheral lines. As the medication failed to elicit a response, the child was transferred to our hospital, where radiological imaging revealed the presence of multiple BAs. In infants exhibiting altered sensorium, heightened intracranial tension, and recent onset of focal neurological deficits, the possibility of an intracerebral abscess should be taken into consideration. Detecting focal neurological deficits in early infancy can be challenging, making nonspecific signs like fever, decreased response, and refusal to feed as the primary indicators of intracranial pathology, as observed in this instance.

To confirm the diagnosis of multiple cerebral abscesses, necessary investigations include routine tests such as complete blood count (CBC) with differential and platelet count, erythrocyte sedimentation rate (ESR), serum C-reactive protein (CRP), serologic tests, blood cultures (at least 2, preferably before antibiotic therapy), lumbar puncture (LP), neuroimaging (Ultrasound, CT, and MRI), and surgical aspiration[15]. In our

study, the blood count showed an increased leukocyte count with no decrease in platelet count. Serology results were negative, and blood cultures did not show the growth of organisms. Routine CSF collection is often discouraged in circumstances where an abscess is suspected due to the perception of low yield and significant risk[16]. Lumbar puncture was not performed in our case as the patient's family declined it due to the perceived risks outweighing the benefits of diagnosis. Neuroimaging, usually a CT scan with contrast, is essential for diagnosing a BAs. The typical finding on CT scan or MRI is a hypodense lesion with contrast-enhancing ring. CT facilitates early detection, precise localization, accurate characterization, determination of the number, size, and staging of the abscesses. MRI characteristics can effectively identify pyogenic abscesses with considerable accuracy[17]. In our case, MRI was obtained, showing multiple variable-sized cystic lesions in bilateral frontal, parietal, temporal, and occipital lobes with rim enhancement in the postcontrast images (Fig. 1). The largest lesion on the right side measured ~1.5 × 1.3 cm, and on the left side, ~1.8 × 1.0 cm.

BAs usually require drainage in addition to appropriate microbial therapy, so early neurosurgical consultation is recommended. The two main surgical methods of treatment include burr-hole aspiration and craniotomy excision of the abscess. In a study conducted by Ali *et al*., it was found that patients undergoing craniotomy showed a longer hospital stay, but the overall difference between the two groups was not statistically significant. Craniotomy was associated with a higher cure rate and lower recurrence compared to the burr-hole group[18]. In another case study, burr-hole aspiration is considered the preferred approach for treating neonatal BAs, and craniotomy is only advised for multiloculated abscesses[2,19]. Our patient was a neonate, and a prolonged surgical operation could be difficult to perform, so burr-hole drainage of the abscess on the right side was performed under intraoperative ultrasound guidance, which showed a good outcome for the patient. After the surgical resection of the abscess, the pus was sent for culture and antimicrobial susceptibility testing. Subsequently, the child showed improvement in their feeding and sleeping patterns. Following culture, it was found that *C. albicans* was the responsible pathogen for the multiple cerebral abscesses. As listed here, bacteria are the prevalent group of organisms, while fungi are infrequent. Although both present with similar symptoms, their treatment approaches differ. It is crucial to consider fungi as potential causative organisms, as failure to diagnose and treat promptly may result in elevated morbidity and mortality rates.

The duration of antifungal therapy, typically 6–8 weeks, is determined by the organism and its response to treatment[20]. The mainstay of medical therapy for candidal BAs is an amphotericin B preparation plus 5-flucytosine. While the efficacy of fluconazole in treating Candida BAs has not been extensively evaluated, a case report involving a premature infant with *C. albicans* BAs showed a decrease in abscess size after the addition of fluconazole to amphotericin B plus 5-flucytosine[4,21]. Our case was managed medically through the administration of Amphotericin B for 6 weeks, which demonstrated a good response during follow-up. The abscess cavities gradually shrank with postoperative intensive intravenous Amphotericin B. Postoperative contrast-enhanced computed tomography after 3 weeks of initial surgery revealed significant resolution of the abscesses (Fig. 3). After successful antifungal treatment for almost 6 weeks, the infant was discharged in good condition with oral antifungal fluconazole for an extended period.

Delays in treatment due to misdiagnosis and increasing drug resistance contribute to an overall death rate for multiple BAs due to candida ranging from 35 to 80%. However, prompt treatment results in a significant decrease in mortality[2]. Early diagnosis includes CSF examination and culture, routine examination, blood culture, and neuroimaging. Additionally, the detection rate of pathogenic microorganisms is extremely low after infection, making timely and appropriate treatment difficult. Among CSF cultivation-confirmed pediatric patients with Candida cerebral abscess, 25% showed normal results during routine CSF tests and biochemical examinations. Therefore, normal CSF is not sufficient to rule out the occurrence of a BAs[10]. Diffusion-weighted imaging (DWI) MRI is useful for early detection and management. Abscesses in their early stage or small abscesses manifest as hyperintense signal nodules on T1WI, whereas larger abscesses or those with central liquefaction/necrosis manifest as ring-shaped nodules and enhancement effects. In other words, abscesses at different pathological stages exhibit different imaging features, aiding in early detection and staging. Early diagnosis of suspected cases of BAs and prompt empirical antibiotic therapy should be initiated immediately in every case, even at the cerebritis stage[22].

In previous studies, potential predictors of poor outcomes in children with BAs, aside from younger age and multiple lesions, include lower levels of consciousness at admission, development

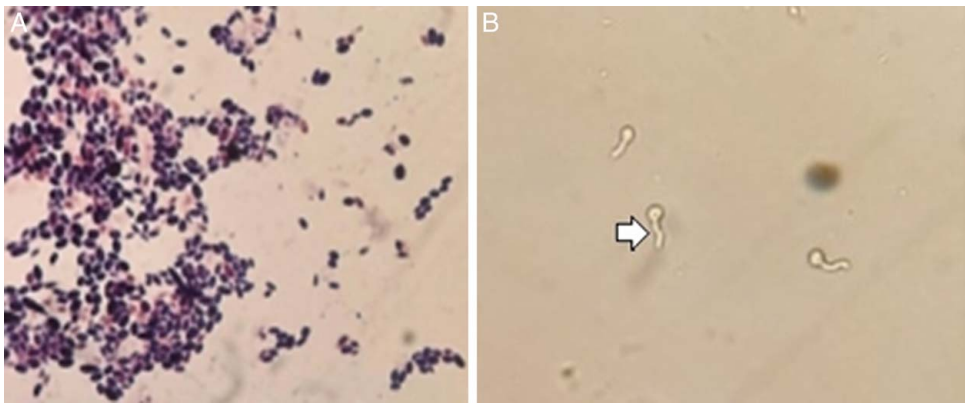

Figure 3. Photomicrograph showing Gram-positive budding yeast cells (A) and formation of germ tube by Candida albicans (B).

of meningitis, delayed initiation of antimicrobial therapy following diagnosis, lesions localized near ventricles or large in size, and lack of surgical aspiration[23]. In our study, the neonate presented with lethargy, irritability, and poor feeding without signs of meningitis. Investigations revealed multiple lesions. After discussion with a multidisciplinary team, empirical antibiotic therapy was initiated, but it did not yield a satisfactory response, ultimately leading to surgical management through burr-hole drainage and a 6-week course of antifungal therapy. Hence, early detection and management are imperative for favorable outcomes. Our case report is the first documented instance of multiple cerebral abscesses in a neonate reported from Nepal. While there may have been similar cases in the past, none have been reported in the medical literature. The patient presented late to our center, which is not uncommon in low-resource settings like Nepal. Late presentation can significantly impact treatment outcomes and increase the risk of complications.

Conclusion

Multiple BAs of fungal origin are exceedingly rare. They often share overlapping features with bacterial abscesses in terms of presentation and imaging characteristics, posing challenges in management as bacterial and fungal BAs require different treatment approaches. Our case represents the first reported pediatric case of multiple fungal abscesses in a neonate successfully managed in our center. This case underscores the importance of considering fungal organisms as potential causes of BAs and highlights the significance of adhering to basic principles such as early drainage, isolating the organism, and providing appropriate treatment based on microbiological isolate findings.

Ethical approval

Not applicable. Our institution does not require ethical approval for reporting individual case report or case series.

Consent

Written informed consent was obtained from the patient's parents for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contributions

A.M., B.K.G., and M.Y.: wrote the original manuscript, and reviewed, and edited the original manuscript; B.T., J.R., S.B.T., S. K.Y., D.Y., and M.R.S.: reviewed and edited the original manuscript.

Conflicts of interest disclosure

The authors have no conflict of interest to declare.

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Guarantor

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Data availability statement

All the required information is within the manuscript itself.

Provenance and peer review

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