Management of brain abscess: an overview

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✓Recent advances in neuroimaging have resulted in a marked decrease in morbidity and death due to brain abscesses. The advent of computed tomography–guided stereotaxy has reduced morbidity in patients with deep-seated abscesses. Empirical therapy is best avoided in the present era, particularly given the availability of stereotactic techniques for aspiration and confirmation of diagnosis. Despite these advances, management of abscesses in patients with cyanotic heart disease and in immunosuppressed patients remains a formidable challenge. Unusual as well as more recently recognized pathogens are being isolated from abscesses in immunosuppressed patients. The authors provide an overview of the management of brain abscesses, highlighting their experience in managing these lesions in patients with cyanotic heart disease, stereotactic management of brain abscesses, and management of abscesses in immunosuppressed patients. *(DOI: 10.3171/FOC/2008/24/6/E3)*

KEY WORDS • brain abscess • cyanotic heart disease • immunosuppression • stereotaxy

BY DEFINITION, a brain abscess is an intraparenchymal collection of pus. The incidence of brain abscesses is ~ 8% of intracranial masses in developing countries, whereas in the West the incidence is ~ 1–2%.[8,36,54] In this review we present an overview of the diagnosis and treatment options for brain abscesses, with specific reference to patients with cardiogenic brain abscess, the role of stereotaxy in the management of lesions, and management of brain abscesses in immunocompromised patients.

Pathogenesis

Development of a brain abscess requires inoculation of an organism into the brain parenchyma in an area of devitalized brain tissue or in a region with poor microcirculation, and the lesion evolves from an early cerebritis stage to the stage of organization and capsule formation.[9,57] Winn et al.[63] developed a model of experimental brain abscess in rats and demonstrated that abscesses evolve from a stage of cerebritis and massive white matter edema to encapsulation. They observed several similarities between the abscesses in their model and those that occur in humans: 1) abscesses occurred in the white matter or at the junction of gray and white matter, migrating to the ventricle; and 2) the capsule was thickest toward the meninges and thinnest toward the ventricle. The mode of entry of organisms could be by contiguous spread, hematogenous dissemination, or following trauma.[36] The common predisposing causes of a brain abscess are chronic suppurative otitis media, congenital cyanotic heart disease, and paranasal sinusitis.[8,35,39,54,60] Immunosuppression due to disease or therapy is emerging as an important risk factor for development of brain abscess.

Microbiological Spectrum

In the preantibiotic era, the most common organism isolated from a brain abscess was *Staphylococcus aureus*.[36] With the advent of penicillin and improved antibiotic therapy, *Streptococcus* spp have replaced *Staphylococcus* spp as the most common organisms.[18,36] Based on the site of origin, the organisms would be different. Table 1 shows the distribution of organisms depending on the site of origin of infection. De Louvois et al. isolated streptococci from abscesses of all types and at all sites, whereas *Enterobacteriaceae* and *Bacteroides* spp were isolated from otogenic temporal lobe abscesses, which had mixed cultures.[18] *Streptococcus* spp have been most commonly isolated from cardiogenic abscesses.[59] In neonates, the most common organisms are *Proteus* and *Citrobacter* spp. Anaerobes are one of the most common causative organisms in a brain abscess.[17] Polymicrobial infections are common, indicating the importance of using both aerobic and anaerobic cultures in diagnosis.[17,20] Occasionally, intracranial tuberculosis as well as fungal infections can present as an abscess.[16,32,43,44] Therefore, cultures for acid-fast bacilli and fungi should be done in all cases. Uncommon organisms reported include *Listeria monocytogenes*[13] and *Burkholderia pseudomallei*.[31]

Abbreviations used in this paper: CT = computed tomography; MR = magnetic resonance.

TABLE 1

Likely pathogens in brain abscess based on predisposing conditions

Predisposing Condition	Likely Pathogens
otitis media/mastoiditis	streptococci (anaerobic & aerobic), *B. fragilis*, *Enterobacteriaceae* spp
paranasal sinusitis	streptococci, *Bacteroides* spp, *Enterobacteriaceae* spp., *S. aureus*
dental infection	streptococci, *Fusibacterium* spp, *Bacteroides* spp
meningitis	*L. monocytogenes, C. diversus*
cyanotic heart disease	streptococci, *Haemophilus* spp
bacterial endocarditis	*S. viridans, Staphylococcus* spp, enterococci, *Haemophilus* spp
pyogenic lung disease	streptococci, *N. asteroides, Actinomyces* spp, *Bacteroides* spp
T-cell deficiency	*Toxoplasma gondii, Nocardia* spp, *L. monocytogenes*
trauma	*S. aureus, Enterobacteriaceae* spp

Clinical Presentation

Brain abscess occurs in the younger age groups-usually in the first three decades of life.[8,46,54,58] The most common presentation is that of headache and vomiting due to raised intracranial pressure. Seizures have been reported in up to 50% of cases.[4,8,54] Focal neurological deficits related to the site of the abscess may be present, depending on the size of the lesion. Altered sensorium with nuchal rigidity may occur in cases of increased mass effect resulting in herniation, or in cases of intraventricular rupture of brain abscess.[54,57]

Diagnosis

A lumbar puncture is contraindicated in patients with a suspected brain abscess because it can result in transtentorial or transforaminal herniation and subsequent death.[61] Moreover, analysis of cerebrospinal fluid does not aid in diagnosis of an unruptured brain abscess. A CT scan of the brain obtained after administration of contrast material shows evidence of a ring-enhancing lesion in a well-defined abscess (Fig. 1) and features of cerebral edema in the stage of cerebritis. The rim of a brain abscess is usually thinner than that seen with neoplastic lesions (Fig. 2).[8] It aids in determining the location of the abscess, its size, number, mass effect, and shifts, and the presence of intraventricular rupture.[2,8,11,31] It also provides information with regard to the cause; the paranasal sinuses and mastoids are also imaged concomitantly. Although MR imaging obtained with diffusion weighting may be more sensitive in the differentiation of an abscess from other cystic brain lesions as well as in detection of the cerebritis stage, it may not be useful in an acutely ill patient and we do not recommend routine MR imaging for diagnosis in patients with a suspected brain abscess.[8,36] In children with an open anterior fontanelle, an ultrasonogram can be used to diagnose an abscess.

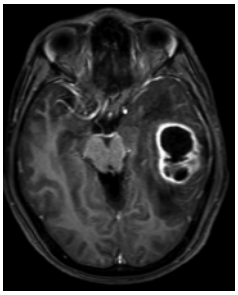

FIG. 1. Axial Gd-enhanced MR image obtained in a 22-year-old man showing a large, multiloculated, ring-enhancing lesion with a thick wall in the left temporal lobe. The patient had a history of chronic discharge from his left ear and underwent cortical mastoidectomy. He developed headache 2 days after the procedure, at which time this MR image was obtained. He underwent craniotomy and excision of the abscess, followed by antibiotic therapy. Culture of the pus showed *P. mirabilis*.

FIG. 2. Axial contrast-enhanced CT scan obtained in a 33-year-old man who was inconsistent in taking his medications for tuberculous lymphadenitis. The scan demonstrates a hypodense right-sided parietal lesion with a thin enhancing capsule. The patient presented with altered sensorium and right hemiparesis of 1-day duration. He underwent excision of the abscess followed by intravenously administered antibiotics. Pus cultures showed nonhemolytic and anaerobic streptococci. Histopathological investigation of the abscess wall showed evidence of an organizing abscess with occasional granulomas, suggesting synchronous tuberculous and pyogenic infection.

The definitive microbiological diagnosis is made by submission of the pus from the abscess for testing with aerobic and anaerobic cultures. Because fungal and tuberculous diseases can present as a brain abscess, pus should be submitted for both acid-fast bacilli and fungal cultures.[2,16,43,44] Pus from a brain abscess should be submitted for immediate microbiological studies because a delay could lead to negative cultures.[17,18] Screening investigations should be done in all cases to determine the source of the infection.

Treatment

Treatment of a brain abscess involves aspiration of the pus or excision of the abscess, followed by parenteral antibiotic therapy.[1,2,8,36,42,49,54,60] Empirical medical therapy is best avoided and should be reserved for patients in whom a bacteriological diagnosis has been obtained from a systemic source or who are extremely ill; that is, too ill to undergo any form of intervention.[2,40,51] Small abscesses and lesions in the cerebritis stage respond well to medical therapy alone.[59] Multiple abscesses are best treated with aspiration of the largest one, followed by antibiotic therapy, which may be required for a longer duration of up to 3–6 months.[7,11,16] Most recent articles recommend aspiration followed by appropriate antibiotic therapy based on sensitivity of the causative organisms.[8,54] Weekly or biweekly CT scans to monitor the size of the abscess are, however, mandatory following aspiration, and repeated aspirations may be required.[54,63] The recommended duration of parenteral antibiotic therapy is 6–8 weeks following aspiration.

Craniotomy and excision is usually reserved for abscesses that enlarge after 2 weeks of antibiotic therapy or that fail to shrink after 3–4 weeks of antibiotics.[2,8,23,40,54,57] Craniotomy is also recommended for multiloculated abscesses and larger lesions with significant mass effect that are superficial and located in noneloquent regions of the brain. We also recommend excision of abscesses in the cerebellum, where recurrent pus collection following aspiration can lead to precipitous neurological worsening.[61] There are certain advantages to excision of a brain abscess in an otherwise neurologically intact patient. The risk of repeated collection of pus is almost completely eliminated, and hence the expense involved in repeated imaging is saved. The duration of hospitalization is also reduced. Furthermore, in patients with an otogenic brain abscess, the disease in the middle ear can also be surgically treated at the same sitting or soon thereafter.[32] This also reduces the likelihood of recurrence of the abscess.

The antibiotics of choice are crystalline penicillin, chloramphenicol, and metronidazole, followed by definitive therapy based on the sensitivity pattern of the causative organisms.[8,11,26,59] There is a recent trend toward the use of third-generation cephalosporins and avoidance of chloramphenicol.[8,59] If staphylococci are suspected, an antistaphylococcal penicillin should be used, with vancomycin being the alternative in cases of antibiotic resistance or patient intolerance to penicillin.[59] The source of the infection should be treated surgically or medically to prevent recurrence of the abscess.[33]

Outcome

The cure rate for single or multiple abscesses reported in the literature is ~ 90% with surgical and medical therapy.[8,36,40,54] With the advent of the CT modality in the 1970s, there was a marked decrease in the morbidity and death due to brain abscesses, and this was a result of earlier diagnosis.[8,11,19,25,51,57,64] The mortality rate has decreased by nearly one third from that found in the pre-CT era.[57] Patients with nocardial and listerial brain abscesses have a threefold higher rate of mortality compared to those who die of other causes.[13,35,41] Intraventricular rupture of brain abscesses and a poor Glasgow Coma Scale score at presentation have been associated with worse outcomes.[40,57] Long-term sequelae include cognitive dysfunction and delayed onset of seizures as well as focal neurological deficits.

Cyanotic Heart Disease and Brain Abscess

Patients with congenital cyanotic heart disease (with a right-to-left shunt) are at risk for developing a brain abscess.[3,4,8,14,20,22,29,37,39,49,57] Cyanotic heart disease accounts for 12.8–69.4% of all cases of brain abscesses with identified risk factors in several series, with the incidence being higher in children.[1,3,24,39,49] In most series of patients from developed countries, cyanotic heart disease is the most commonly identified risk factor for development of brain abscess in immunocompetent patients. The incidence of brain abscess in patients with cyanotic heart disease has been reported to range between 5 and 18.7%.[57] Tetralogy of Fallot is the most common cardiac anomaly associated with brain abscess.[12,23,57] Transposition of great vessels, tricuspid atresia, pulmonary stenosis, and double-outlet right ventricle have also been reported as predisposing factors.[12,56,57] Most of these abscesses are supratentorial in location.[23,49,56] Because most of these patients present only with headache, the threshold for performing a CT scan in a patient with cyanotic heart disease should be low.

In patients with cyanotic heart disease, there is a right-to-left shunt of venous blood in the heart, bypassing the pulmonary circulation. Thus, bacteria in the bloodstream are not filtered through the pulmonary circulation, where they would normally be removed by phagocytosis. Patients with cyanotic heart disease could have low-perfusion areas in the brain due to chronic severe hypoxemia and metabolic acidosis as well as increased viscosity of blood due to secondary polycythemia. These low-perfusion areas commonly occur in the junction of gray and white matter, and they are prone to seeding by microorganisms that may be present in the bloodstream.[28,56] The hematogenous mode of spread accounts for the subcortical location as well as the multiple number of abscesses often encountered in these patients.[7,12,22,57]

Streptococcus milleri was the most common organism isolated from the abscess in patients with cyanotic heart disease in one series.[3] *Staphylococcus*, other *Streptococcus* spp, and *Haemophilus* have also been isolated.[57] The isolation of gram-positive cocci is higher than that of gram-negative bacilli. With the advent of broad-spectrum antibiotic therapy, sterile cultures are being reported more often. Multiple organisms have also been isolated in some patients.[17,57]

Patients with cyanotic heart disease have compromised

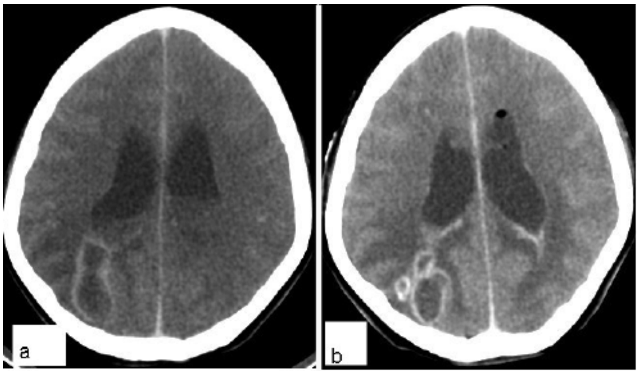

FIG. 3. Axial contrast-enhanced CT scans obtained in a 17-year-old girl with tetralogy of Fallot who presented with fever that had lasted for 4 days and altered sensorium with right hemiparesis of 1-day duration. a: A right parietal subcortical ring-enhancing lesion abutting the ventricle wall is demonstrated. b: A CT scan obtained 10 days after antibiotic therapy, revealing persistence of the abscess with enhancement along both lateral ventricle walls, indicating ventriculitis. The patient was treated with external ventricular drainage and intravenous antibiotics for 1 month, after which a right ventriculoperitoneal shunt was inserted. The cerebrospinal fluid culture had shown peptostreptococci. She was asymptomatic after 1 year and could undergo surgery for her cardiac anomaly.

cardiopulmonary systems and exhibit a variety of coagulation defects, rendering them poor candidates for general anesthesia. Moreover, these abscesses are often deep seated in location, in proximity to the ventricular system (Fig. 3), and they are often multiple. The treatment of choice in these patients is thus aspiration of the abscess through a bur hole or twist-drill craniostomy performed after induction of local anesthesia.[1,22,49,57] Any coagulopathy, if present, should be corrected before the surgical intervention. In one series, the mortality rate following craniotomy and excision was as high as 71%.[27] Prusty[49] has reported that even with aspiration, nearly 17% of patients can develop cyanotic spells that could lead to life-threatening complications.

The recommended antibiotic therapy is penicillin with chloramphenicol,[8,22] although there has been a shift toward third-generation cephalosporins in recent years. Takeshita et al.[57] have suggested that intravenous antibiotics be administered for 6 weeks in these patients, with regular CT scans obtained to monitor the size of the abscess. Repeated aspirations may be required. Craniotomy should be restricted to patients with abscesses resistant to antibiotic therapy.[23,49,56,57]

The advent of CT scans and their use in the management of these abscesses has resulted in a fourfold decrease in the mortality rate in patients with brain abscesses secondary to cyanotic heart disease; from 40–60% in the pre-CT era to ~ 10%. This could be attributed to early detection, availability of image guidance for aspiration (particularly in small lesions), and better radiological follow-up during the course of the antibiotic therapy.[1,8,14,45,51,52,57] Intraventricular rupture of brain abscess has been reported to be a poor prognostic factor in these patients.[56,57] In our experience,[45,52] the advent of stereotaxy has aided in avoiding empirical therapy in patients with brain lesions, particularly so in patients with brain abscesses secondary to cyanotic heart disease. Stereotactic intervention can also help in obtaining a histological diagnosis of lesions mimicking a brain abscess in these patients. One of our patients with cyanotic heart disease and a ring-enhancing lesion in the brainstem was treated empirically at another institution with antibiotic therapy, with no clinical or radiological response. A stereotactic biopsy of the brainstem lesion revealed a tuberculoma, which responded to antituberculous drugs.[45]

Role of Stereotaxy in Management of Brain Abscess

Sharma et al.[54] have highlighted the role of minimally invasive procedures like stereotactic aspiration or lavage with endoscopic stereotactic evacuation in the treatment of abscesses, even if the lesions are multiloculated. Several authors have recorded the utility of stereotactic techniques in the management of brain abscesses.[6,11,25,34,38,43,47,53,55,61,62] There are several advantages of stereotactic aspiration. Only stereotactic aspiration is appropriate for small, deep-seated abscesses or those located in eloquent regions of the brain, because it provides a direct and rapid access to the abscess through a predetermined route. Therefore, it is ideal for management of abscesses in the thalamus, basal ganglia, or brainstem.[21,38,45,48,52] Stereotactic aspiration also avoids the so-called leukotomy effect that can occur with a freehand aspiration technique. Finally, a biopsy of the wall of the abscess can also be obtained at the same time as the aspiration to confirm the diagnosis in case there is any doubt. Sometimes though, the penetration of a thick abscess wall with the blunt-tipped stereotactic probes can be difficult, and one may fail to enter the abscess. Impedance monitoring can avoid the "false-negative" result.[50]

Kondziolka et al.[30] have reported the use of a technique for drainage of abscesses for which a stereotactically guided catheter is placed in the cavity of abscesses > 3 cm. In their experience, factors associated with initial treatment failure following stereotactic aspiration include inadequate aspiration, lack of catheter drainage of larger abscesses, chronic immunosuppression, and insufficient antibiotic therapy. In almost three fourths of their patients, the lesions were successfully managed with a single stereotactic procedure. Itakura et al.[27] have reported good or excellent outcomes in > 90% of patients in whom external drainage of abscesses is in place for an average of ~ 2 weeks following stereotactic aspiration.

Management of Brain Abscesses in the Immunocompromised Patient

Immunosuppression can predispose patients to the development of brain abscesses. Cunha[15] has reviewed the pathogenesis of central nervous system infections in immunocompromised patients. Compromised hosts with impaired T-lymphocyte or macrophage function are prone to developing infections with intracellular pathogens such as fungi (particularly *Aspergillus* spp) and bacteria like *Nocardia* spp. Brain abscesses caused by *Aspergillus* and *Nocardia* spp have been reported in immunosuppressed patients (Fig. 4).[10,16,35,41,43,44] Immunosuppression can result from illnesses like systemic or hematological malignancy or infections like human immunodeficiency virus, or it may

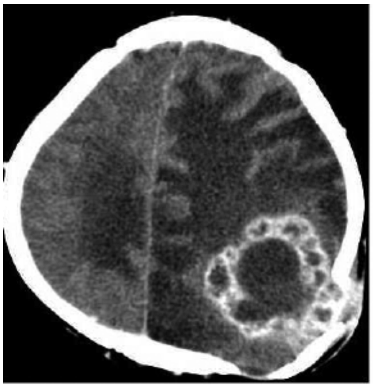

FIG. 4. Axial contrast-enhanced CT scan obtained in a 12-year-old boy who presented with recurrent partial motor seizures and progressive loss of vision bilaterally, showing a ring-enhancing left-sided parietal lesion with multiple conglomerate smaller lesions adjacent to it. Note the extensive edema adjacent to the lesion and mass effect in the form of elevation of the craniotomy bone flap overlying it. The patient was receiving long-term steroid therapy for recurrent nephrotic syndrome, and his disease had been managed initially in another hospital with repeated aspiration of pus through a craniotomy over the past 9 months, along with prolonged courses of antibiotics. The pus had been sterile on routine cultures. Repeated exploration and excision of the abscess was performed, at which time the culture showed *A. fumigatus*. The patient is currently undergoing antifungal therapy.

be iatrogenic and due to long-term steroid medication, chemotherapy for malignancies, or immunosuppressive agents used in patients undergoing organ transplants. These patients are prone to the development of brain abscesses secondary to organisms that may not be seen in immunocompetent individuals, and because of this, empirical therapy in these patients should be avoided. Attention should be directed to obtaining a microbiological diagnosis so that appropriate antibiotic therapy can be initiated without delay. The imaging features of the abscess on CT or MR imaging studies do not help in arriving at a diagnosis of its cause. It is also important to subject the pus obtained from the abscess to microbiological examination for fungal elements and acid-fast bacilli besides the routine aerobic and anaerobic cultures. Arunkumar et al.[2] reported a series of 5 renal transplant recipients who developed brain abscesses secondary to chronic immunosuppression and whose lesions were managed with CT-guided stereotactic techniques. Each of their patients had a different causative organism, emphasizing the need for specific microbiological diagnosis in every immunocompromised patient with a brain abscess.

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