Pyogenic brain abscess

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✓Brain abscesses have been one of the most challenging lesions, both for surgeons and internists. From the beginning of the computed tomography (CT) era, the diagnosis and treatment of these entities have become easier and less invasive. The outcomes have become better with the improvement of diagnostic techniques, neurosurgery, and broad-spectrum antibiotics. Atypical bacterial abscesses are more often due to chemotherapy usage in oncology, long life expectancy in patients with human immunodeficiency virus (HIV) infection, and immunosuppression in conjunction with organ transplantation. Surgical treatment options showed no significant difference with respect to mortality levels, but lower morbidity rates were achieved with stereotactically guided aspiration. Decompression with stereotactically guided aspiration, antibiotic therapy based on results of pus culture, and repeated aspirations if indicated from results of periodic CT follow-up scans seem to be the most appropriate treatment modality for brain abscesses. Immunosuppression and comorbidities, initial neurological status, and intraventricular rupture were significant factors influencing the outcomes of patients. The pitfalls and evolution in the diagnosis and treatment of brain abscesses are discussed in this study. (DOI: 10.3171/FOC/2008/24/6/E2)

KEY WORDS • abscess incidence • brain abscess • outcome • stereotaxy • treatment options

IN 1893, Sir William Macewen reported only 1 death in 19 patients suffering from brain abscess.¹⁵ Unfortunately, until the advent of the CT modality, the outcomes in patients with brain abscess were not as satisfactory as in Macewen's series. Use of CT and MR imaging, evolution of microbiological diagnostic techniques, and production of broad-spectrum antibiotics have improved outcomes in the past 20–25 years. The routine use of CT scanning has facilitated the diagnosis of brain abscess and made the patients' follow-up safer.^{12,23,65,80,100} The mortality rate decreased from a range of 22.7–45%^{2,7,17,79,99,104} to 0–20%^{64,92} after the routine use of CT scans. Before the advent of CT scanning, brain abscesses were mostly diagnosed intraoperatively and resected totally.^{65,104} However, easier and safer diagnostic techniques made stereotactic aspiration a favorable treatment option, especially in multiple and non-cortical lesions.^{22,64,73,74} Also, in some cases CT scanning enables safe and successful medical treatment without any surgical intervention.^{6,21,64,65,80,81} Nevertheless, there is no consensus on treatment of brain abscess; the necessity of surgical intervention and the type of surgical procedure are still doubtful.

Demographic Factors

Brain abscesses are seen in ~ 1500–2500 cases/year in

the US, with a higher incidence in developing countries.³⁷ There were more male than female patients; ratios from 1.3:1 to 3.0:1 have been reported.^{18,49,62,88} The patients ranged in age from infants to elderly individuals.^{34,49,62,64,79,88} Roche et al.⁷⁹ reported that most brain abscesses occur in the first 2 decades of life. However, their opinion was based on literature published several decades ago, when intracranial complications of sinus/otitis infections, a common childhood infection, were seen more frequently.^{44,62,66,75,87} Even Roche et al.⁷⁹ found the incidence of brain abscesses in children to be lower than they had expected from earlier reports. However, some authors reported that the incidence in patients < 15 years of age was no more than 15–30%.^{18,41,49,88}

Origins of Abscesses

Cerebral abscess occurs in patients with the following predisposing states: 1) contiguous purulent spread (for example, frontal sinus infection leading to frontal lobe abscess, sphenoid sinus infection leading to cavernous sinus extension, and middle ear/mastoid air cell infection leading to temporal lobe and cerebellar abscess); 2) hematogenous or metastatic spread (for example, pulmonary infections and arteriovenous shunts, congenital heart disease and endocarditis, dental infections, and gastrointestinal infections); 3) head trauma; 4) neurosurgical procedure; and 5) immunosuppression.

According to the earlier literature,^{46,67,81,104} the most common predisposing factor for brain abscesses was direct spread from the middle ear, meninges, mastoid infections,

Abbreviations used in this paper: ADC = apparent diffusion coefficient; CHD = congenital heart disease; CNS = central nervous system; CSF = cerebrospinal fluid; DW = diffusion weighted; MCA = middle cerebral artery.

and paranasal sinus. Before the 1980s, CHD (6–50%) and sinus/otitis infections seem to have been the most common factors in brain abscesses in children as well.^{32,41,47,65,95} The evolution in diagnostic techniques, antimicrobial agents, and advances in cardiovascular surgery caused a decrease in the ratio of brain abscesses due to CHD and sinus/otitis infections and an increase in lesions found in patients receiving immunosuppressive therapy due to transplantation procedures, in patients with HIV who had a prolonged life expectancy, and in those receiving chemotherapy for cancer treatment. More abscesses arose after the 1980s in infants and immunosuppressed patients, and were diagnosed at earlier ages (< 6 months).³⁴ Nowadays, hematogenous or metastatic spread has become the most common factor in the formation of brain abscess.³⁷

The organisms that cause brain abscess are typically bacterial in origin. *Peptostreptococcus* and *Streptococcus* spp (especially *S. viridans* and microaerophilic organisms) are mostly identified in patients with cardiac disorders (cyanotic heart disease) and right-to-left shunt bypasses that exclude the normal filtration mechanisms of the pulmonary vascular tree. In CHD, diminished arterial oxygen saturation and increased blood viscosity may cause focal cerebral ischemia and act as a nidus for multiple infections, especially in the gray–white matter junction, often in the MCA distribution.^{26,32,41,47,94,95} At one time CHD was a significant predisposing factor in children's lesions, but there has been a decline in these cases due to advances in cardiac surgery and the use of broad-spectrum antibiotics.

Bacteroides, *Peptostreptococcus*, and *Streptococcus* spp are most commonly identified in brain abscesses caused by contiguous spread. This spread is the result of osteomyelitis in the neighboring air sinus. The risk of a brain abscess developing in an adult with active chronic otitis media is ~ 1/10,000 per year, but in a 30-year-old patient with active infection, the lifetime risk becomes ~ 1/200.^{71,72}

Streptococcus, *S. aureus*, *Pseudomonas*, and *Bacteroides* spp are mostly identified in pulmonary infections (pulmonary abscess, empyema, bronchiectasis). They are located mostly in the MCA distribution and often multiply.

Staphylococcus, *Streptococcus*, *Clostridium*, and *Enterobacter* spp are mostly identified in patients with open head trauma. Gunshot wounds, open depressed skull fractures with foreign bodies in brain parenchyma, and basal skull fracture with CSF fistula cause brain abscesses, generally contiguous with the site of trauma.^{16,18,27,28,34,35,51}

Staphylococcus and *Streptococcus* spp are identified in patients with prior neurosurgical procedures. Wounds that are open > 4 hours are subject to a higher risk of infection. Additional risk factors include implantation of a foreign body such as a shunt or external ventricular drain, high-grade gliomas, and early irradiation after surgical procedures.^{16,100}

Fungal infections, *Toxoplasma*, *Staphylococcus*, *Streptococcus*, and *Pseudomonas* spp are identified in immunocompromised patients with HIV infections, organ transplantation, chemotherapy, or steroid use.¹⁰⁶ Branched hyphal-form fungal infections (for example, aspergillosis) obstruct large- and intermediate-sized vessels, causing cerebral arterial thrombosis and infarction.⁹⁰ Sterile infarcts may be converted to septic infarcts with associated formation of an abscess.^{2,3,25,26,68,90} Abscesses can also result from contiguous spread.²⁵ These lesions are mostly located in the

posterior fossa and lobes of the cerebrum. The mortality rates due to fungal abscesses range from 75 to 100%, despite intensive treatment with amphotericin B.^{26,68,69}

There continues to be a strong representation of anaerobes (30–50%) in patients with brain abscesses. Additionally, atypical bacteria such as *Nocardia* and *Actinomyces* spp may occur in immunocompromised patients. Careful culturing of abscess material obtained at the time of surgery provides the best opportunity to make a microbiological diagnosis. Although positive culture rates have approached 100% in studies with meticulous handling of clinical specimens,⁶⁶ the incidence of negative cultures remains as high as 15–30% in most series,^{19,65,76,98,104} especially in patients in whom antimicrobial therapy is started before operation. Polymerase chain reaction analysis of 16S recombinant DNA and sequencing may identify pathogens to the species level directly from brain abscesses. This approach is rapid and is especially useful in the identification of slow-growing and fastidious organisms.⁹⁷

Lumbar puncture has been considered hazardous in patients with brain abscess.^{19,84} It is usually performed because of a strong suspicion of concomitant meningitis and/or ventriculitis, and yields only 10–30% positive CSF cultures in which organisms similar to those grown in abscess cultures are found.^{19,84,99} Although a significant proportion of the deaths was thought to be caused by lumbar puncture during early work,⁶⁷ a recent study in which multivariate regression was used failed to reveal such a hazard.⁷⁸ Therefore, lumbar puncture could be justified in patients with brain abscess in the absence of increased intracranial pressure and in whom there are clear manifestations of meningitis and/or ventriculitis.

Pathogenesis of Brain Abscesses

Brain abscesses develop in response to a parenchymal infection with pyogenic bacteria, which begins as a localized area of cerebritis and evolves into a suppurative lesion surrounded by a well-vascularized fibrotic capsule. Staging of brain abscesses in humans has been based on findings obtained during CT scans or MR imaging sessions. The early stage or early cerebritis occurs from Days 1 to 3 and is typified by neutrophil accumulation, tissue necrosis, and edema. Microglial and astrocyte activation is also evident at this stage and persists throughout abscess development. The intermediate, or late cerebritis stage, occurs from Days 4 to 9 and is associated with a predominant macrophage and lymphocyte infiltrate. The final or capsule stage occurs from Day 10 onward and is associated with the formation of a well-vascularized abscess wall, in effect sequestering the lesion and protecting the surrounding normal brain parenchyma from additional damage. Early capsule formation develops from Days 10 to 13 and tends to be thinner on the medial or ventricular side of the abscess and prone to rupture in this direction. After Day 14, late capsule formation develops, with gliotic, collagenous, and granulation layers.¹²

In addition to limiting the extent of infection, the immune response that is an essential part of abscess formation also destroys surrounding normal brain tissue. This is supported by findings in experimental models, in which lesion sites are greatly exaggerated compared to the local-

FIG. 1. Schematic showing how pyogenic bacteria such as *S. aureus* induce a localized suppurative lesion typified by direct damage to brain parenchyma and subsequent tissue necrosis. Bacterial recognition of peptidoglycan (PGN) from the cell wall by Toll-like receptor 2 (TLR2) leads to the activation of resident astrocytes and microglia; the elaboration of numerous proinflammatory cytokines and chemokines leading to increased blood–brain barrier (BBB) permeability; and the entry of macromolecules such as albumin and immunoglobulin G (IgG) into the brain parenchyma. In addition, cytokines induce the expression of adhesion molecules (intercellular adhesion molecule [ICAM] and vascular cell adhesion molecule [VCAM]), which facilitate the extravasation of peripheral immune cells such as neutrophils, macrophages, and T cells into the evolving abscess. Newly recruited peripheral immune cells can be activated by both bacteria and cytokines released by activated glia. IL = interleukin; MCP = monocyte chemoattractant protein; MIP = macrophage inflammatory protein; RANTES = regulated on activation, normal T cell expressed and secreted; TNF = tumor necrosis factor.

ized nature of bacterial growth, reminiscent of an overactive immune response.⁵² This phenomenon is also observed in human brain abscess, in which lesions can encompass a large portion of brain tissue, often spreading well beyond the initial focus of infection. Therefore, controlling the intensity and/or duration of the antibacterial immune response in the brain may allow for effective elimination of bacteria while minimizing damage to surrounding brain tissue (Fig. 1).

As mentioned earlier, lesion sites in both experimental models and in human brain abscesses are greatly exaggerated compared to the localized nature of bacterial growth,

reminiscent of an overactive immune response. To account for the enlarged region of affected tissue involvement associated with brain abscesses compared to the relatively focal nature of the initial insult, Kielian et al.⁵⁴ have proposed that proinflammatory mediator production following *S. aureus* infection persists, effectively augmenting damage to surrounding normal brain parenchyma. Specifically, the continued release of proinflammatory mediators by activated glia and infiltrating peripheral immune cells may act through a positive feedback loop to potentiate the subsequent recruitment and activation of newly recruited inflammatory cells and glia.⁵³ This would effectively perpetuate

the antibacterial inflammatory response through a vicious pathological circle culminating in extensive collateral damage to normal brain tissue.

Recent studies support persistent immune activation associated with experimental brain abscesses, in which elevated levels of interleukin-1 β , tumor necrosis factor- α , and macrophage inflammatory protein-2 have been detected between 14 and 21 days after *S. aureus* exposure.⁵⁴ Concomitant with prolonged proinflammatory mediator expression, *S. aureus* infection was found to induce a chronic disruption of the blood-brain barrier, which correlated with the continued presence of peripheral immune cell infiltrates and glial activation.^{53,54} Collectively, these findings suggest that intervention with antiinflammatory compounds subsequent to sufficient bacterial neutralization may be an effective strategy to minimize damage to surrounding brain parenchyma during the course of brain abscess development, leading to improvements in cognition and neurological outcomes.⁵⁴ The responses of microglia and astrocytes to *S. aureus* have been elucidated in terms of proinflammatory mediator expression, and in general have been found to be qualitatively similar to those observed following lipopolysaccharide exposure.⁴ Although studies with primary microglia and astrocytes from Toll-like receptor 2 knockout mice reveal an important role for this receptor in mediating *S. aureus*-dependent activation, it is clear that additional receptors are also involved in glial responses to this bacterium.⁵⁴ This functional redundancy is not surprising because these pathogens have the potential for devastating consequences in tissue such as the CNS, which has limited regenerative capacity. The implications of glial cell activation in the context of brain abscess are probably several. First, parenchymal microglia and astrocytes may be involved in the initial recruitment of professional bactericidal phagocytes into the CNS through their elaboration of chemokines and proinflammatory cytokines. Second, microglia exhibit *S. aureus* bactericidal activity in vitro, suggesting that they may also participate in the initial containment of bacterial replication in the CNS. However, their bactericidal activity in vitro is not comparable to that of neutrophils or macrophages, suggesting that this activity may not be a major effector mechanism for microglia during acute infection. Third, activated microglia have the potential to influence the type and extent of antibacterial adaptive immune responses through their upregulation of major histocompatibility complex class II and costimulatory molecule expression. Finally, if glial activation persists in the context of ongoing inflammation, the continued release of proinflammatory mediators could damage surrounding normal brain parenchyma.

Clinical Presentation

There are no pathognomonic clinical signs; most patients present with clinical signs that depend on the location or mass effect of the lesion: headache, nausea, emesis, fever, alteration in consciousness, seizures, and motor weakness are the most common symptoms.¹⁶ These symptoms are more rapidly progressive, however, with respect to tumoral lesions. Fever is not uniformly seen, and only 30–55% of patients have a fever > 38.5°C.⁴¹ Seizures are a presenting sign in 16–50% of patients.^{16,18,34,103} Focal neurological def-

icits are seen in 40–60% of patients, depending on the location of the lesion.^{16,18,41,103} Papilledema is rare in patients < 2 years of age. Patent sutures and low ability to limit the infection and cranial enlargement can occur. Nevertheless, the triad of symptoms of brain abscess (headache, fever, and neurological deficit) can be seen in only 15–30% of patients.^{16,103} If the lesion is located in the brainstem, mostly in the pons (2%), cranial nerve palsies, motor weakness, and many different symptoms may be present and deterioration tends to be more rapid.

Diagnosis

Imaging features of a brain abscess depend on the stage at the time of imaging as well as the source of infection.¹⁴ Brain abscess development can be divided into 4 stages: 1) early cerebritis (1–4 days); 2) late cerebritis (4–10 days); 3) early capsule formation (11–14 days); and 4) late capsule formation (> 14 days).³⁹ The majority of abscesses demonstrate considerable surrounding edema, which generally presents during the late cerebritis or early capsule formation stage, secondary to mass effect. Hematogenous abscesses, which can be seen in the setting of endocarditis, cardiac shunts, or pulmonary vascular malformations, are usually multiple, identified at the gray-white junction, and located in the MCA territory.

In the earlier phases, a CT scan performed without addition of contrast may show only low-attenuation abnormalities with mass effect. In later phases, a complete peripheral ring may be seen. On CT scans obtained after administration of contrast material, uniform ring enhancement is virtually always present in later phases. In early phases the capsule will be difficult to visualize via conventional techniques, and double contrast CT often is helpful in defining encapsulation of abscess. Metastatic tumors, high-grade gliomas, cerebral infarction, resolving cerebral contusion or hematoma, lymphoma, toxoplasmosis, demyelinating disease, and radiation necrosis must be kept in mind as the differential diagnosis for brain abscesses appearing as ring-enhancing lesions.^{1,82} The advanced techniques in neuroradiology have facilitated the diagnosis of multiple brain abscesses. The incidence of multiple brain abscesses, which was reported as 1.8–17% of patients^{16,65,67,81,104} in the pre-CT era, is 23–50% in modern-day cases.^{16,18,21,34,98,103}

The MR imaging findings also depend on the stage of the infection. In the early phase, lesions revealed on MR images can have a low signal on T1-weighted and a high signal on T2-weighted images, with patchy enhancement. In later phases, the low signal on T1-weighted images becomes better demarcated, with a high signal on T2-weighted images, both in the cavity and surrounding parenchyma. The abscess cavity shows a hyperintense rim on T1-weighted images obtained without contrast and a hypointense rim on T2-weighted images.⁴⁰ As on CT scanning, MR imaging usually demonstrates a ring of enhancement surrounding the abscess.⁹¹ Abscesses tend to grow toward the white matter, away from the better-vascularized gray matter, with thinning of the medial wall.⁵⁰ However, the enhancing-ring sign is nonspecific and must be evaluated in the context of the clinical history. Thickness, irregularity, and nodularity of the enhancing ring are suggestive of

FIG. 2. Sagittal T1-weighted MR images obtained in different patients after administration of contrast material, demonstrating ring-enhancing cystic lesions. *Left:* Admission MR image revealing a thin, homogeneous, well-circumscribed cystic lesion with mild perilesional edema. The pathological examination revealed a cystic pilocytic astrocytoma. *Right:* Admission MR image demonstrating a thick, heterogeneous (thicker on the cortical, thinner on the ventricular side), well-circumscribed lesion with extensive perilesional edema and contrast enhancement due to vasculitis and cerebritis of the surrounding parenchyma. The pathological and microbiological examinations revealed pyogenic brain abscess.

tumor (the majority of cases), or possibly fungal infection (Fig. 2).⁴⁰ On DW images, restricted diffusion (bright signal) may be seen; this helps to differentiate abscesses from necrotic neoplasms, which are not usually restricted,^{20,39} although not all abscesses follow this rule. Fungal and tuberculous abscesses may have elevated diffusivity and low signal on DW imaging.⁴⁰

Several studies demonstrate the utility of DW imaging in differentiating between necrotic or cystic lesions and brain abscesses.^{20,39} Brain abscesses demonstrate increased signal on the trace images and reduced ADC, whereas necrotic neoplasms demonstrate decreased signal on the trace image and high ADC values. Initially, DW imaging was thought to be helpful in differentiation of toxoplasmosis from lymphoma.

In 1 study an ADC threshold of 0.8 was proposed, where ADC ratios < 0.8 would favor lymphoma over toxoplasmosis; however, that study showed a significant overlap in ADC values in toxoplasmosis and lymphoma.⁸⁶ The authors concluded that in the majority of patients, ADC ratios are not definitive in making the distinction between toxoplasmosis and lymphoma. Nevertheless, DW imaging has a high sensitivity for detection of early acute ischemic changes in cortical and deep white matter that can occur in cases of infectious vasculitis. The brain abscess cavity shows regions of increased fractional anisotropy values, with restricted mean diffusivity compared with other cystic intracranial lesions. This information may prevent misinterpretation of the diffusion tensor imaging information as white matter fiber bundle abnormalities associated with mass lesions.³⁸ Intracerebral abscesses are characterized by specific resonances on MR spectroscopy that are not detected in normal or in sterile diseased human tissue. The MR spectroscopy modality has been shown to be specifi-

cally useful in differentiating between brain abscesses and other cystic lesions,¹³ which is information that can be used to expedite implementation of the appropriate antimicrobial therapy. Metabolic substances, such as succinate (2.4 ppm), acetate (1.9 ppm), alanine (1.5 ppm), amino acids (0.9 ppm), and lactate (1.3 ppm), can all be present in untreated bacterial abscesses or soon after the initiation of treatment.⁵⁷

Treatment

There are 3 treatment options for brain abscesses: 1) medical; 2) aspiration (freehand, stereotactically or neuroendoscopically guided); or 3) total excision. In choosing the appropriate treatment option, the following factors must be considered: Karnofsky performance scale score; primary infection; predisposing state; and the number, size, location, and stage of the abscess. Modern-day therapy of brain abscesses generally includes a combined surgical and medical approach.⁶⁴

Medical Management

Antibiotics play a critical role in the management of brain abscesses. The characteristics of the agent (such as penetration into the brain) and the prior use of intrathecal or interstitial therapy must be known before the treatment. To choose the appropriate antibiotic, the microorganism or underlying illness must be identified.³⁶ If the patient is not in sepsis or critical condition, antibiotic therapy should be postponed until culture material is obtained. Mampalam and Rosenblum⁶⁵ reported an eightfold greater number of sterile cultures in patients receiving preoperative antibiotics. Xiao et al.¹⁰³ reported that cultures of intracerebral

material remained sterile for 39 (34%) of their 115 surgical patients. Of the 76 patients whose cultures were positive, in 68 (89%) a single pathogen was identified and in 8 (11%) 2 pathogens were found. If the predisposing state is hematogenous spread or the patients have symptoms of systemic infection, blood cultures can be useful in identifying the microorganism. Tseng and Tseng⁹⁸ performed blood cultures in 49 of 122 patients who had a clinical presentation of systemic infection (fever and leukocytosis). Only 13 of those patients had blood cultures that grew bacteria (positive rate, 26.5%); 7 of them had the same pathogen in both blood and brain abscess cultures. Blood culture is the least invasive, cheapest, and fastest way to identify the pathogenic microorganism. Despite low rates of positive findings, blood cultures must be taken in every patient in whom a brain abscess is suspected and who has symptoms of systemic infection.

Medical management alone can be considered if the patients are poor candidates for surgical intervention according to the following criteria: if the lesions are multiple; < 1.5 cm in diameter; located in eloquent areas; or if there are any concomitant infections like meningitis or endophthalmitis. The most important objection is to empirical treatment with no microbiological identification; another microorganism may be responsible for the abscess. At least one aspiration procedure would be very useful in identification of the microorganism, if the patient has no coagulopathy.

Medical treatment alone is more successful if the treatment is begun during the cerebritis stage, if the lesion is < 1.5 cm in diameter, if the duration of symptoms is < 2 weeks, and if the patient shows clinical improvement within the 1st week.⁸⁰

Systemic antibiotics were given for 6 weeks, although some centers now prescribe 2 weeks of intravenously administered antibiotics followed by up to 4 weeks of oral antimicrobial therapy.^{33,65,80} If no microorganism can be identified, broad-spectrum therapy for 6–8 weeks may be warranted.^{29,64} Despite appropriate treatment, 5–10% recurrence rates were reported in brain abscesses, which can be caused by early discontinuation of the treatment.¹⁶ Jamjoom⁴⁵ reported a series in which the duration of antibiotic therapy was based not on a specific time but rather on normalization of C-reactive protein levels. Additionally, elevated C-reactive protein levels can be used in the differential diagnosis of brain abscess from other ring-enhancing lesions.⁴³ Three of 26 patients had persistently elevated C-reactive protein levels and were found to have a recurrence of the abscess. There were no recurrences in patients in whom the levels returned to normal. Kutlay et al.⁵⁶ reported that parenteral antibiotics and hyperbaric oxygen therapy were administered for a total of 4 weeks in 13 patients, even in patients without a bacteriological diagnosis. Overall, initial surgery failed in 2 patients (15.3%). Two abscesses that recurred were again aspirated 6 and 9 days, respectively, after the first procedure. However, long-term radiological evaluation has failed to show a recurrence of abscesses in any of these cases after a mean follow-up period of 9.5 months. The main difference between their study and others reported in the literature is the reduced duration of antibiotic therapy.^{5,21,65,80} Nowadays, with easy radiological follow-up of the brain abscess and broad-spectrum an-

tibiotics, practitioners tend to choose medical treatment, especially if the pathogen can be diagnosed based on cultures of blood, CSF, or direct aspiration. Leys et al.⁶⁰ reported on 56 patients who were nonrandomly selected for medical treatment, simple aspiration, or excision of their brain abscess and found no statistically significant difference. In fact, brain abscesses cause too much physiological stress for patients, and surgical stress should not be added if it is not necessary.

Corticosteroids can be used, but they have side effects, and their use in the treatment of vasogenic edema due to brain abscess is still being debated. The negative effect of dexamethasone on capsule formation was shown in an experimental study.⁷⁷ Black et al.⁸ made the same comment about the effect of corticosteroids. However, Schroeder et al.⁸⁵ reported that corticosteroids do not stop the formation of the capsule, and that they only act as a retarding force. Mampalam and Rosenblum⁶⁵ reported a higher mortality rate in the patients treated with corticosteroids, but these patients were in poor neurological condition initially and had decreasing levels of consciousness. These authors recommended corticosteroid usage in patients with significant perilesional edema that was diagnosed radiologically. Sandrock et al.⁸³ reported a retrospective study of 26 patients that demonstrated no detrimental effect on outcome when corticosteroids were used in patients with intracranial abscesses. It should be kept in mind that steroids may decrease the contrast enhancement of the abscess capsule in the early stages of infection and that this can be a false indicator of radiological improvement, or it may even delay diagnosis.²⁴

Surgical Management

Throughout the history of neurosurgery, the treatment of brain abscesses has been a challenge. Nonsurgical empirical treatment of suspected small brain abscesses with antibiotics has been advocated.^{10,29} Rational management of intracranial mass lesions requires establishment of a positive diagnosis before implementation of therapeutic measures. Indeed, patients presenting with rapidly progressive neurological deficits that are attributable to the mass effect of the neuroradiologically verified brain abscess are strong candidates for urgent decompression, both for neurosurgeons and internists.

Various types of operative procedures have been used for the treatment of brain abscess. The choice of procedure has been the subject of many debates.^{70,90,102} Craniotomy, which was much advocated in the earlier era when neither antibiotics nor CT scanning was available, is now rarely used. Aspiration, repeated as necessary or with drainage, has widely replaced attempts at complete excision. Nevertheless, an open surgical procedure is still preferred to management of the brain abscess with a combination of medical treatment and surgical evacuation, in the following circumstances: if there is evidence of increased intracranial pressure due to significant mass effect of the brain abscess; if there are difficulties in diagnosis; if the abscess is the result of a traumatic injury that has introduced foreign materials; if the lesion is located in the posterior fossa; and if there is any presumption of fungal infection. Even decompression with a craniotomy or craniectomy will be helpful for patients in poor neurological condition.

Because a diagnosis based only on clinical and neuroradiological findings can be erroneous, nonsurgical therapeutic decisions should not be made without a positive diagnosis of the pathogen. Stereotactic management of brain abscess, which allows both confirmation of the diagnosis and institution of therapy by aspiration of lesion contents and identification of the offending organism, has become widespread since the introduction of CT-guided stereotaxy.^{5,22,63,64,89,90,93} A review of the recent literature shows several series of brain abscesses primarily treated with stereotactic techniques. Stapleton et al.,⁹² reviewing their series of 11 patients, concluded that stereotactic aspiration should be considered the treatment of choice in all but the most superficial and the largest cerebral abscesses. Kondziolka et al.⁵⁵ related the failure of stereotactic treatment of brain abscesses in a series of 29 cases, because of either inadequate aspiration, lack of catheter drainage, long-term immunosuppression, or insufficient antibiotic therapy. Longatti et al.⁶¹ reported on 4 patients harboring cerebral abscesses who underwent surgery in which the neuroendoscopic technique with freehand stereotaxy was used. They aspirated the pus and washed the cavity with antibiotics. Both Hellwig et al.⁴² and Kamikawa and colleagues⁴⁸ reported their experiences with a flexible scope (freehand or stereotactically guided), whereas Fritsch and Manwaring³⁰ opted for a rigid one in a pediatric series. Longatti et al. reported the usefulness of flexible endoscopes in certain crucial surgical actions, such as aspirating and inspecting the abscess in all spatial directions or coping with a firm and elastic membrane that requires scissors or other instruments for its perforation.^{42,61} Hellwig et al. maintained that drainage catheters need not be inserted inside the abscess after endoscopy (to be used for antibiotic infusion and further aspiration during the following days), whereas Fritsch and Manwaring reported placing catheters in all cases. Longatti et al. avoided drain insertion in 1 patient only, and no second operation was needed because no residual abscesses with a space-occupying effect occurred; conversely, Hellwig et al. performed subsequent operations in 4 of their patients. Longatti et al. reported that no significant difference could be found in the length of hospital stay, number of postoperative CT scans, and duration of the antibiotic therapy between traditional and endoscopic stereotactically guided aspiration.

Intraoperative sampling of abscess material and smear preparations for microscopic analysis and identification of the organisms in brain abscess is fraught with pitfalls. First, abscess-related necrosis must be differentiated from tumor necrosis. Small or large areas of coagulation necrosis are frequently seen in glioblastomas. Sometimes the necrotic area of a tumor is taken over by a massive infiltration of polymorphonuclear leukocytes that change the necrotic area into a liquefactive one, leading to the erroneous diagnosis of a brain abscess. On the other hand, perilesional gliosis of an abscess may be so marked as to mimic a low-grade astrocytoma. Although in a nonneoplastic proliferation of reactive astrocytes the cellularity is usually lower and individual cells are very regular, it is not uncommon to encounter predominantly cellular areas of proliferating astrocytes with pleomorphic and hyperchromatic nuclei.⁵ Barlas et al. categorized brain abscesses as cerebritis (Stage I) when scarce polymorphonuclear leukocytes and perivas-

cular erythrocytes were detected and encapsulation (Stage II) when frank pus, polymorphonuclear leukocyte crowding, necrosis, granulation tissue, and dense reactive gliosis were found; this provided a better and simplified understanding of the pathological features and more effective pathological–radiological correlation. On the other hand, advanced neuroradiological techniques can be used for the differential diagnosis of these lesions.

In lesions that are deep seated, multiloculated, and close to the ventricle wall, a reduction of 1 mm in the distance between the ventricle and brain abscesses will increase the rupture rate by 10%.⁵⁹ Although a combination of intrathecal and intravenous antimicrobial treatment has been recommended in intraventricular rupture, the therapeutic strategy in this special group of patients remains controversial.¹¹ Other therapeutic regimens have been recommended, including the following: 1) urgent craniotomy with rapid evacuation of the abscess;¹⁰⁵ 2) emergency evacuation with lavage of the ventricles and ventriculostomy placement accompanied by the administration of intraventricular antibiotics;⁹ and 3) a 5-component therapeutic regimen, including open craniotomy with debridement of the abscess cavity, lavage of the ventricular system, intravenous administration of antibiotics for 6 weeks, intraventricular administration of gentamicin twice daily for 6 weeks, and intraventricular drainage for 6 weeks.¹⁰⁷

Outcome

The mortality rate ranged from 40 to 60% in the pre-CT era and was reduced to 10% from the beginning of the CT era to 2000.^{94,96,104} After 2000, the mortality rate was reported to be between 17 and 32%.^{49,58,62,78,79} This discrepancy may be mainly due to the drastic changes in epidemiology taking place nowadays. Compared to the previous reports, the incidence of brain abscesses caused by sinus/otitis infection decreased, whereas those associated with immunodeficiency increased markedly. It is challenging to cure patients who are receiving chemotherapy for cancer or immunosuppressive therapy for organ transplantation, or who have HIV infection. Xiao et al.¹⁰³ reported 2.8-fold risk of poor outcome in immunocompromised patients. Other comorbidities like diabetes mellitus or cirrhosis are also factors negatively influencing the outcome.

A much poorer prognosis was reported for patients presenting with lower Glasgow Coma Scale scores.^{90,94,103} Xiao et al. reported that 13 (62%) of the 21 patients with initial Glasgow Coma Scale scores < 9 either died or fell into a vegetative state. Intraventricular rupture is a devastating and often fatal complication of brain abscess and is associated with a high death rate.^{88,105} Death was reported in 109 (84.5%) of 129 patients in a review of the literature published between 1950 and 1993.¹⁰⁷ In another recent study from Japan,⁹⁴ the overall mortality rate was 38.7% (12 of 31 patients). Lee et al.⁵⁹ reported a series of 62 patients in which 30 (48%) had a poor outcome (severe disabilities, vegetative state, and death) due to intraventricular rupture of the brain abscess. The pretreatment neurological status of the patient is the most influential independent factor related with the outcome.

It is not uncommon for survivors to suffer neurological sequelae including hemiparesis, seizure, and cognitive dys-

function.^{16,31,65} Seizure is a long-term risk in 30–50% of patients suffering from brain abscesses.^{16,18,74} The latency period can be as long as 5 years, but is shorter in older patients.⁷⁴ Especially in any tumoral lesion in which antiepileptic treatment is initiated after an attack, antiepileptic prophylaxis must be initiated immediately and continued for at least 1 year due to the high risk of subsequent seizures in patients with brain abscesses. The treatment can be discontinued if no significant epileptogenic activity can be shown on electroencephalograms. The management of the abscess is one of the most important factors both in seizure and neurological outcome. Cansever et al.¹⁶ reported that, after surgical removal of abscesses, more focal neurological deficits (5.2% compared with 0%) and seizures (47.7% compared with 31.2%) were seen in comparison with stereotactic aspiration. The location of the abscess had no effect on predisposition to seizure. However, the hypodense areas surrounding the cavity of the abscess were wider in surgically treated patients. These areas were thought to be the damaged brain parenchyma that was causing neurological deficits and epileptic activities.

Rates of recurrence are estimated to be 10–50%. The period of surveillance should be continued for at least 1 year. The resolution of the surrounding edema and loss of the enhancing rim must be documented in this period, which can take up to 6 months.¹⁰¹ If the patients show no neurological deterioration, imaging can be obtained at 1-week intervals with and without addition of contrast in the first 6 weeks. Lesions that do not show any regression should be aspirated again. Surgical therapy may be preferred for patients with neurological deterioration and/or radiologically unresolved lesions.

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