Consultation with the Specialist

Brain Abscess

D. Douglas Cochrane, MD*

Brain abscess is relatively uncommon in clinical practice in 1999, yet it remains a serious and life-threatening disease among children and adolescents despite technological advances made in the second half of this century. These advances include aggressive treatment of primary infections, detailed understanding of causative organisms, and improved antibiotics and sensitivity testing techniques. Neuroradiologic imaging, specifically computed tomography (CT), now can reveal the infective process before an abscess forms and can demonstrate the effects of both the primary infection and the treatment accurately. To manage the patient who has a brain abscess with minimal morbidity and mortality, aggressive medical and surgical therapies, singly or in combination, are required.

Brain abscess results from seeding of microorganisms into an area of injured cerebral parenchyma by direct spread of infection from soft tissues of the neck and face, sinuses, or cranium or following bacterial implantation resulting from penetrating cranial wounds or operative interventions. Hematogenous seeding from a remote focus also may result in abscess formation. The development of cerebral infection depends on the number of organisms to which the patient is exposed and their virulence, the immunologic competence of the patient, and the timeliness of clinical diagnosis and treatment.

Pathology and Pathogenesis

Brain abscess is a focal, intracerebral infection evolving from an area of cerebritis into a collection of purulent material enveloped in a vascularized capsule. The most common cause of intracerebral abscess formation is direct or indirect spread from infection in paranasal sinuses, middle ear, and teeth in children and teenagers. Frontal, ethmoid, sphenoid, and maxillary sinusitis give rise to abscess formation in the frontal (Fig. 1) and parietal lobes; mastoiditis results in temporal or cerebellar abscess formation. Metastatic spread from remote foci of infection remains an important pathogenic mechanism in children and adults who have congenital cardiac or pulmonary right-to-left shunts as well as those who are immunocompromised. This mechanism commonly results in abscess formation in the parietal or occipital lobes. Fortunately, abscess formation following penetrating brain injury, basal skull fracture, or surgical procedures is uncommon.

Abscesses that occur as a result of sinus, middle ear, or dental infections tend to be solitary and superficial. Septic thrombophlebitis affecting the valueless diploic vessels provides an avenue for bacterial seeding into brain parenchyma. Osteomyelitis with direct erosion through skull and dura often is the source of abscess complicating sinusitis or chronic middle ear infection.

Abscesses complicating pulmonary infection (empyema, bronchiectasis, abscess, or pneumonia), cutaneous infections, osteomyelitis elsewhere in the skeleton, dental abscesses, or bacterial endocarditis tend to be multiple, and their distribution is a reflection of regional cerebral blood flow, often in vascular watersheds. Brainstem and basal ganglia abscess formation are rare in patients who have normal immunity.

Cerebral abscesses may develop in patients who have right-to-left cardiac or pulmonary shunts, especially in the presence of cyanotic congenital heart disease. In both situations, bacteria are not filtered out by the pulmonary vascular bed, which allows systemic spread. Direct arteriovenous shunting in the pulmonary vascular bed also occurs in hereditary hemorrhagic telengiectasia.

Bacterial implantation may complicate compound skull fractures, scalp wounds, and facial sepsis. Retained bone fragments increase the risk of abscess formation more than metallic fragments and projectiles. Abscess formation may complicate anterior cranial fossa or temporal bone fractures, cerebrospinal fluid fistulae, and meningitis. The abscess usually forms at the time of or following the development of meningitis in these patients.

Experimental studies suggest that an abscess forms in an area of preexisting necrosis or injury caused by direct traumatic injury, hemorrhage, or infarction secondary to thrombophlebitis or it may be due to relative hypoxia in watershed areas. Subsequent seeding with organisms sets

**Division of Neurosurgery, Section of Surgery, British Columbia's Children's Hospital; Division of Neurosurgery, Department of Surgery, University of British Columbia, Vancouver, BC, Canada.*

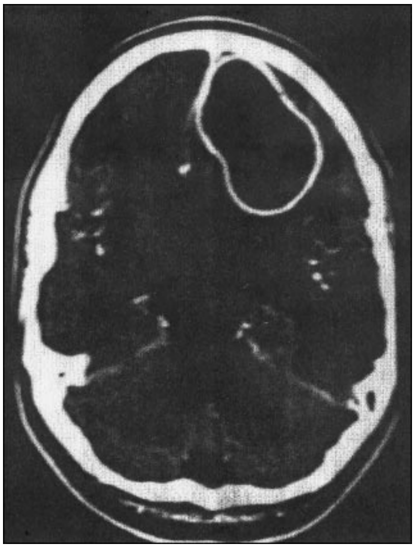

FIGURE 1. Computed tomography with contrast enhancement of a frontal lobe abscess that developed as a complication of sinusitis in a 12-year-old girl.

the stage for the development of septic cerebritis within the white matter. Cerebritis is characterized by an acute inflammatory response, vascular dilatation, diapedesis, microthrombosis, and rupture of small vessels. Edema and infiltration by polymorphonuclear lymphocytes with a surrounding microglial response occur. The center of the lesion then undergoes liquefaction.

By 10 to 13 days, early encapsulation is seen in experimental brain abscesses. Central necrosis is bounded by a peripheral zone of inflammatory cells, neovascularization, and fibroblasts. The latter cells produce a dense collagenous capsule, which is surrounded by edema and reactive gliosis. The capsule is thinnest adjacent to the ventricle and thicker on the side of the more luxuriantly vascularized cortex.

The nature of the offending organism may influence the development of the capsule. *Bacteroides* sp excrete a collagenase that inhibits capsule formation, resulting in the development of small daughter abscesses. Propagation of edema is aided by bacterial production of hyaluronidase and heparinase.

Patients succumb to brain abscesses because of increased intracranial pressure and brain herniation from the volume of pus and surrounding edema. Although it occurs less commonly, rupture of an abscess, either into the ventricular system (pyocephalus) or through the cortex into the subarachnoid space, can result in acute deterioration and death.

Bacteriology (Table)

The spectrum of organisms cultured from brain abscesses has changed in the latter part of this century. This is a reflection of improved bacteriologic isolation techniques, aggressive treatment of primary infections, and a decreased incidence of nonmissile compound brain wounds. In most series, the incidence of *Staphylococcus aureus* has decreased and that of anaerobes has increased.

Anaerobic organisms isolated from brain abscess pus include *Bacteroides, Peptostreptococcus, Fusobacterium, Veillonella, Propionibacterium*, and *Actinomyces*. Aerobic organisms include *Staphylococcus, Streptococcus, Enterobacteriaceae*, and *Haemophilus*. In at least one third of brain abscesses, the pus will culture multiple organisms. This is particularly common in otitic abscesses. No growth is reported from up to 30% of properly handled specimens.

The bacteriologic diagnosis often suggests the originating infection. *S aureus* abscess formation occurs most commonly following compound skull fracture. Gram-negative organisms, including *Bacteroides* and *Haemophilus*, generally are isolated from otogenic abscesses. Most brain abscesses that complicate paranasal sinus infection will culture aerobic or anaerobic streptococci or both.

Fungal brain abscesses develop most commonly in patients who have impaired host defenses, particularly those who have acquired immunodeficiency syndrome or who are immunologically suppressed following organ transplantation. *Candida, Aspergillus, Nocardia,* and *Cryptococcus* are the fungal organisms isolated most commonly. Pathogenic fungi, acquired either through inhalation or implantation, can result in brain abscess formation and generally involve *Histoplasma, Coccidiodes*, and *Blastomyces*.

Brain abscess formation in the neonate (Figs. 2, 3, and 4) usually is caused by *Proteus* sp. Individual case reports and series also have reported *Salmonella, Serratia, Enterobacter*, and *Staphylococcus* as causative organisms. Meningitis caused by *Citrobacter, Proteus, Serratia*, or *Enterobacter* is complicated by abscess formation in a high percentage of patients.

Clinical Aspects

The clinical presentation of brain abscess varies with the size of the abscess, its location, the multiplicity of lesions, the virulence of the organism, and the patient's host defenses and age. Symptoms and signs may be categorized as follows:

- Systemic toxicity from the primary infection, complicating meningitis, or ventriculitis
- Raised intracranial pressure due to the edema and the mass effect of the abscess
- Focal neurologic dysfunction related to the location of the abscess

Toxic symptoms usually are mild early in the course and commonly are attributed to the primary infection. Fever, if present, is minimal, and body temperature may be subnormal in the face of an established abscess. In up to one third of patients, there are no overt signs of sepsis and no clinical clues to the causative infection.

The symptoms caused by increased intracranial pressure usually dominate the clinical presentation. Headache is most common and occurs early in the course. Unfortunately, there is nothing specific about a headache due to increased intracranial pressure from an abscess. Initially, it may be localized, becoming generalized as intracranial pressure rises with edema formation and the increased mass of the abscess. As with any headache due to increased intracranial pressure, the pain may be throbbing and worsen with changes in posture or Valsalva maneuver. Pain associated with cerebellar abscess usually is occipital in location, while frontal lobe abscesses are characterized by headache anteriorly over the cranium. Drowsiness, confusion, and vomiting occur during the acute

TABLE. Bacterial Etiology and Suggested Initial Antibiotic Choices for Brain Abscess*

UNDERLYING CONDITION	SITE OF ABSCESS	USUAL ORGANISMS	INITIAL ANTIBIOTIC CHOICE
Otorhinologic disease			
Paranasal sinuses	Frontal lobe	Aerobic and anaerobic *Streptococcus* *Staphylococcus aureus* *Haemophilus* sp *Bacteroides* sp *Fusobacterium* sp	Penicillin + metronidazole **or** Cefotaxime + metronidazole **or** Penicillinase-resistant synthetic penicillin + third-generation cephalosporin + metronidazole
Chronic otitis media, mastoiditis	Temporal lobe, cerebellum	Aerobic and anaerobic *Streptococcus* *Enterobacteriaceae* *Bacteroides* sp (including *B fragilis*) *Pseudomonas aeruginosa*	Penicillin + metronidazole + ceftazidine
Head injury	Subjacent to site of injury	*S aureus* *Clostridium* sp *Enterobacteriaceae*	Penicillinase-resistant synthetic penicillin + third-generation cephalosporin (cefotaxime)
Postoperative infection	At operative site	*S aureus* *S epidermidis* *Enterobacteriaceae*	Penicillinase-resistant penicillin + third-generation cephalosporin
Metastatic spread	Multiple lesions, commonly middle cerebral artery territory	Endocarditis *S aureus* *S viridans* Urinary tract *Enterobacteriaceae* *Pseudomonas* Intra-abdominal *Streptococcus* *Enterobacteriaceae* Anaerobes Pulmonary *Streptococcus* *Actinomyces* *Fusobacterium*	Penicillinase-resistant penicillin + third-generation cephalosporin + metronidazole
Cryptogenic infection	Single or multiple	Unknown	Penicillinase-resistant synthetic penicillin + third-generation cephalosporin + metronidazole

If a Gram-positive organism has the potential for resistance to beta-lactam antibiotics or if allergy to beta-lactam antibiotics is suspected, substitute vancomycin for penicillin or penicillinase-resistant synthetic penicillin. Third-generation cephalosporins include cefotaxime and ceftriaxone. Use ceftazidine if** P aeruginosa **is suspected in the setting of chronic otitis media.

phase, leading to slowing in mentation, drowsiness, and coma. Papilledema is not a consistent finding.

Focal neurologic disturbances reflect the location of the abscess. Frontal lobe abscesses are characterized by the development of apathy, memory deficits, personality change, and mental slowing. Hemiparesis occurs with lesions in the postfrontal region or as a consequence of uncal herniation. Temporal lobe abscesses are characterized by a contralateral homonymous upper quadrantopia and a mild hemiparesis that usually

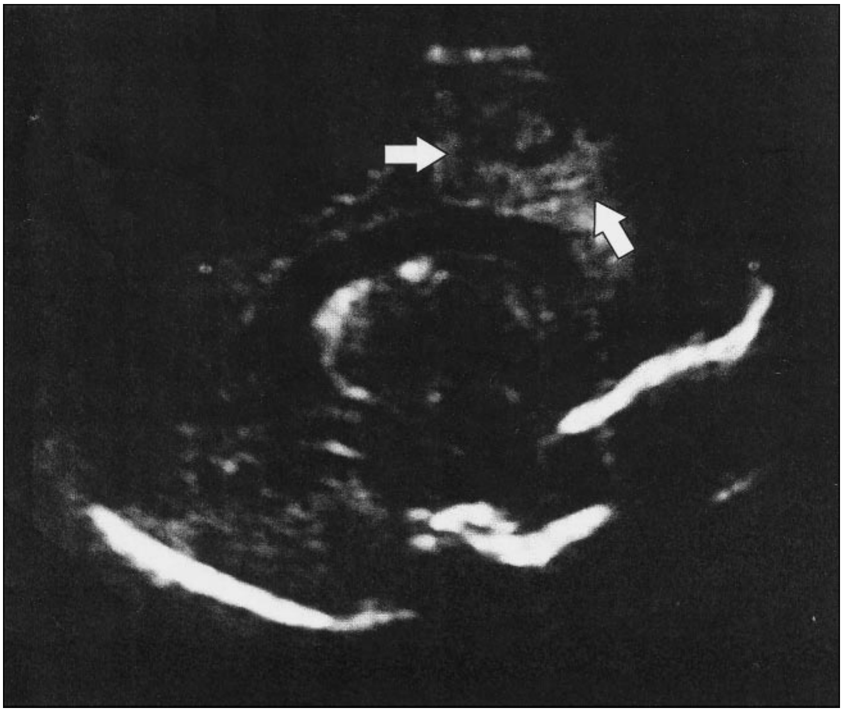

FIGURE 2. *Cranial ultrasonography of late cerebritis, early abscess stage in a neonate (arrows).*

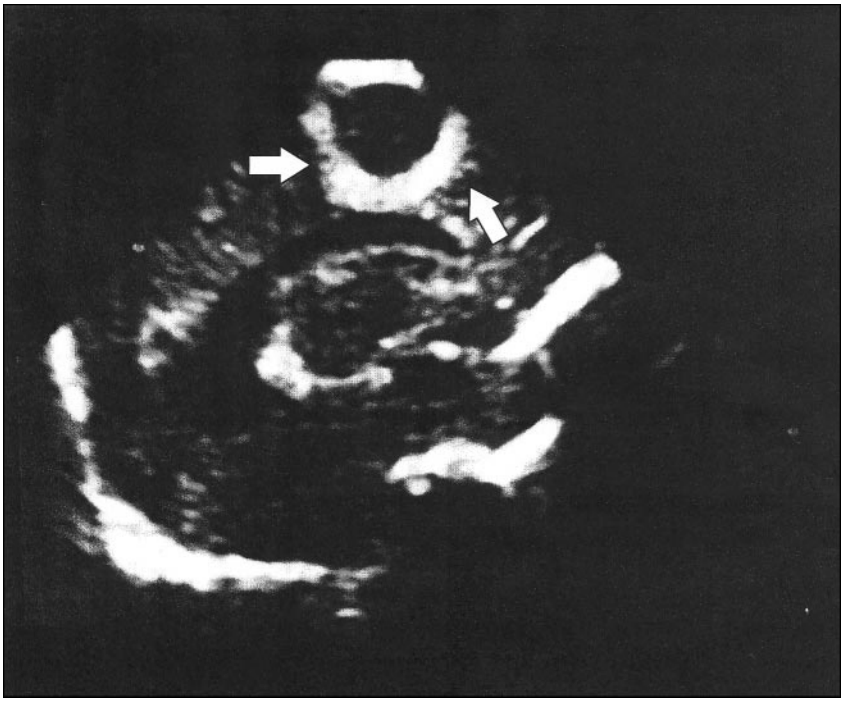

FIGURE 3. *Cranial ultrasonography 1 week later of the echogenic abscess wall in the same patient as in Fig. 2 (arrows).*

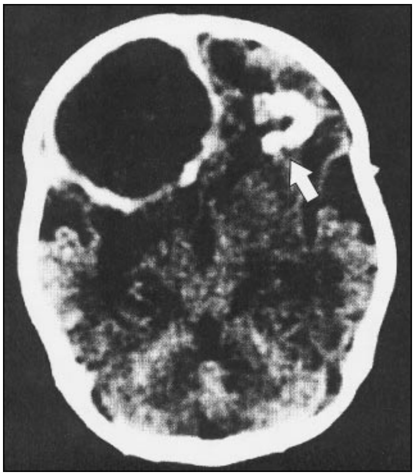

FIGURE 4. *Computed tomography without contrast enhancement of a neonatal brain abscess with calcification in the abscess wall. More densely calcified smaller abscesses are visible in the opposite frontal lobe (arrow).*

is maximal in the face. If the dominant hemisphere is affected, nominal dysphasia is characteristic. Cerebellar abscesses classically exhibit nystagmus with the slow phase to the side of the lesion, defective conjugate eye movements to that side, ataxia, and hypotonia. Seizures occur in at least 25% to 50% of patients, may be focal or generalized, and may occur at any time during the course of the disease.

Classically, abscess formation evolves through three clinical phases. The initial phase is characterized by transient malaise, fever, and headache. At this stage, headache usually is not severe. An acute onset of extremely severe headache suggests either meningitis or subarachnoid hemorrhage. Occasionally, seizures occur following symptoms attributable to the primary infection. Subsequently, there is a latent phase during which time the patient seems relatively well. Thereafter, worsening headache and vomiting occur, culminating in the terminal phase that is characterized by focal neurologic deficits and cerebral herniation.

The rapidity with which symptoms develop can vary substantially. Most patients are symptomatic within 1 week of the onset of abscess formation, particularly if they have normal host defenses. Those who are immunocompromised may have a more insidious progression. Chronic abscesses, particularly those complicating cranial injury, can present years after the insult.

The presentation of brain abscess in infancy reflects increased intracranial pressure, with bulging fontanelle, vomiting, irritability, and an enlarging head circumference. Seizures are common.

Brain abscess remains a serious complication of cyanotic congenital heart disease in middle childhood (4 to 7 y), most commonly in association with tetralogy of Fallot or transposition of the great vessels.

Laboratory Diagnosis

Little in the laboratory investigation of patients who have brain abscesses is specific to the diagnosis except for culture of the purulent material and antibiotic sensitivity of the responsible organism. The peripheral white blood count may be mildly elevated, as may the erythrocyte sedimentation rate due to cerebritis, abscess formation, or the primary infective process. Changes in cerebrospinal fluid (CSF) are not specific and should not be sought prior to neuroimaging. An elevated CSF protein level, with mildly elevated white blood cell count ($<200/mm^3$), hypoglycorrhachia, negative Gram stain, and sterile culture, suggest a brain abscess or parameningeal infection. The finding of organisms in the CSF infers either pyocephalus due to rupture of an abscess into the ventricular system or complicating meningitis.

Culturing of purulent material obtained at the time of surgical drainage provides the best opportunity for microbiologic diagnosis. Proper handling of the specimen and appropriate aerobic and anaerobic culture techniques result in positive cultures in the majority of cases. Gram staining of the pus can guide therapy in the face of a negative culture.

Neuroimaging

Of all of the technologic improvements in the last half century, CT of the brain has been the most responsible for a better understanding of abscess formation. Early cerebritis is characterized by an ill-defined, low-density change within the parenchyma. Enhancement occurs following administration of contrast material. Later in the evolution, imaging will show the classic ring-enhancing lesion with surrounding edema (Fig. 1). Ring enhancement may correlate with capsule formation. Capsule formation can be differentiated from enhancing cerebritis by using delayed (30 to 60 min) scanning following administration of contrast. Enhancement within the ring lesion suggests that the lesion reflects cerebritis. In addition, multiple loculations and multiple abscesses can be revealed. Calcification is common in abscesses in neonates.

Magnetic resonance imaging (MRI) scans have typical characteristics on T1-weighted (central hypointensity surrounded by a ring of enhancement after gadolinium administration) and T2-weighted (hyperintense area of pus, surrounded by hypointense capsule, enveloped within surrounding edema) images. Although resolution of soft tissue is better than on CT, MRI does not add significant information in guiding management.

Radionucleotide brain scans have been used to localize abscesses. Thallium- and indium III-labeled leukocyte scans may be useful to differentiate abscess from tumor.

Differential Diagnosis

The differential diagnosis for brain abscess should include intracranial abscess formation in the extradural or subdural spaces as well as septic thrombophlebitis. An extradural abscess usually is not large enough to cause severely increased intracranial pressure or focal signs, although it may be associated with localized headache, fever, and scalp swelling (Potts puffy tumor). Subdural empyema is characterized by rapidly progressive, severe headache; hemiparesis; and cerebral herniation. Bacterial meningitis is seen in patients who are acutely sick, often without focal signs (other than cranial nerve palsies or extensor plantar responses). The headache of meningitis frequently is more acute in onset and more severe than that due to brain abscess. Ventriculitis secondary to rupture of a paraventricular abscess into the ventricular system results in a catastrophic clinical deterioration. Patients are suddenly desperately ill and comatose with severe neck rigidity, high fever, irregular pulse, and respiration.

Treatment

Successful treatment of a brain abscess requires a multidisciplinary approach that includes input from specialists in infectious disease, neuroradiology, neurosurgery, and pediatrics. A team effort allows for early recognition of parenchymal infection, precise localization and drainage of purulent material, appropriate administration of antibiotics, monitoring of the therapeutic response, control of seizures, and rehabilitation as needed.

ANTIMICROBIAL THERAPY

The microbial spectrum of brain abscess varies with the primary site of infection (Table). If this is known, the initial choice of antibiotics can be directed to the most likely organisms. For abscesses arising as a result of sinusitis in which streptococci are the most likely organisms, penicillin or cefotaxime and metronidazole provide basic coverage. Because chronic otitis media or mastoiditis often is associated with *Pseudomonas aeruginosa* and *Enterobacteriaceae*, antibiotics to treat abscesses secondary to these infections should include penicillin, metronidazole, and a third-generation cephalosporin. Metastatic abscesses require a regimen based on the likely site of primary infection.

S aureus commonly is isolated in abscess following trauma. Compound wounds, in particular those contaminated with soil, may contain facultative Gram-negative organisms or *Clostridium* sp. In these situations, a penicillinase-resistant penicillin and a third-generation cephalosporin provide initial coverage. Postoperative brain abscess is rare and usually due to *S aureus* or *S epidermidis*. Vancomycin should be considered because of the resistance of nosocomial organisms to penicillinase-resistant penicillins.

The optimal duration of antibiotic therapy is not known, although 6 to 8 weeks of intravenous therapy has been recommended. In some situations, a shorter course may be sufficient. Depending on the organisms cultured, their sensitivity to the prescribed antibiotic regimen, and the response to therapy, some authors recommend an additional 2 to 3 months of oral antimicrobial therapy to prevent recurrence.

In the adult literature, there is

evidence that brain abscess can be treated with empiric antibiotic regimens without surgical intervention. Generally this applies to cerebritis and abscesses smaller than 2 cm in diameter. If nonoperative treatment is being implemented, neuroimaging should be performed frequently, and a response to therapy should be seen within 2 weeks of the initiation of antibiotic treatment.

SURGICAL INTERVENTION

The role of surgical intervention is to:

- Provide a specimen of purulent material for bacteriologic analysis and antibiotic sensitivity testing;
- Remove purulent material, thereby lowering intracranial pressure and decreasing the mass effect of the abscess;
- Decompress and irrigate the ventricular system and debride the abscess in the event of its rupture into the ventricular system.

The abscess can be aspirated by using a variety of techniques. Freehand CT or ultrasonographically guided aspiration assists with the accurate placement of a drainage needle or catheter in most superficial cerebral abscesses. Deeply seated abscesses can be reached safely by using framed or frameless stereotaxic techniques. Repeated aspirations may be needed as the infection is brought under control. Formal craniotomy and excision of the abscess is required less frequently now than in the past because of the effectiveness of antibiotics and the ability to confirm the response to therapy with CT. Excision is indicated for recurrent bacterial abscesses that do not respond to antibiotic treatment and drainage and in situations in which the diagnosis or the bacteriology remains in doubt (*Nocardia* or fungal abscesses).

ADJUVANT THERAPY

Corticosteriods

Corticosteriods are indicated only to control life-threatening intracranial hypertension that is associated with the risk of herniation. Steroids interfere with the inflammatory response, impairing formation of granulation tissue, resulting in a thinner capsule, lower concentrations of some antibiotics within the purulent material, and impaired clearance of some organisms.

Anticonvulsants

Seizures occur in 25% to 50% of patients during their acute illness and during long-term follow-up in at least this percentage. Prophylactic anticonvulsants are recommended by some authors and should be started in all patients upon their first seizure. The duration of anticonvulsant therapy must be individualized and can be guided by electroencephalographic (EEG) studies in the post-treatment phase. Most authors recommend at least 3 months of prophylaxis if no seizures have occurred. If the patient has suffered seizures, therapy should be continued indefinitely or until results of the EEG are normal.

Prognosis

The mortality associated with brain abscess in older series approached 32%. Recently, this number has decreased to less than 10%, reflecting earlier, more accurate diagnosis and appropriate antibiotic treatment. Focal residual deficits may persist, depending on the location of the abscess and whether complicating meningitis or herniation has occurred. Seizures occur in 40% to 50% of patients following treatment.

Brain abscess remains a serious and life-threatening disease among children and adolescents. Those who have sinusitis, mastoiditis, or cyanotic congenital heart disease and experience increasing headache should be investigated with CT on an urgent basis. Worsening neurologic function following compound head injury or operation should raise the index of suspicion for brain abscess formation. Examination of CSF is not indicated in these clinical situations. Aggressive multidisciplinary treatment involving infectious disease specialists, neuroradiologists, pediatricians, and neurosurgeons is required to minimize morbidity and mortality and maximize the potential for cure.

SUGGESTED READING

Canale DJ. William Macewen and the treatment of brain abscess: revisited after one hundred years. *J Neurosurg.* 1996;84:133–142

Mathisen GE, Johnson JP. Brain abscess. *CID.* 1997;25:763–781

Osenbach RK, Loftus CM. Diagnosis and management of brain abscess. *Neurosurg Clin North Am.* 1992;3:403–420

Takeshita M, Kagawa M, Yato S, et al. Current treatment of brain abscess in patients with congenital cyanotic heart disease. *Neurosurgery.* 1997;41:1270–1278

PIR QUIZ

Quiz also available online at www.pedsinreview.org.

14. Brain abscess is caused *most* commonly by:
    - A. Generalized immunodeficiency.
    - B. Left-to-right cardiac shunts.
    - C. Penetrating brain injury.
    - D. Right-to-left cardiac shunts.
    - E. Sinus, middle ear, and tooth disease.

15. A previously healthy 10-year-old boy presents with a severe frontal headache, fever, and drowsiness, preceded by a 2-week history of thick nasal discharge and cough. The pain is worsened by coughing and lying down. On physical examination, the patient appears confused. Slight nuchal rigidity is apparent. The optic discs are not blurred. Thick nasal discharge is present. No other abnormalities are detected. The most appropriate *initial* diagnostic step would be to order:
    - A. Intracranial computed tomography.
    - B. Lumbar puncture.
    - C. Plain films of paranasal sinuses.
    - D. Plain films of sella turcica.
    - E. Thallium leukocyte brain scan.

Match each of the following settings for brain abscess with the the *most* likely corresponding bacterial pathogen listed.

16. Compound skull fracture.

17. Dental abscess.

18. Organ transplantation.

19. Paranasal sinusitis.

20. Prematurity.
    - A. *Bacteroides*.
    - B. *Cryptococcus*.
    - C. *Proteus*.
    - D. *Staphylococcus*.
    - E. *Streptococcus*.

POINT OF CLARIFICATION

Water Heater Temperatures

In the article on Pediatric Burns (*Pediatr Rev*. 1999;20:117–124), the temperature settings for water heaters should read: Water heaters in the individual house should be set between 49°C and 55°C (120°F and 130°F). The statements in the article regarding higher temperatures were in reference to apartment houses, where higher water temperatures are often difficult to reduce.