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A

ABSCESS, BRAIN

Brain abscess is a focal pyogenic infection of the brain parenchyma. They constitute less than 2% of intracranial masses and develop mainly in four clinical situations, although 15% to 20% are cryptogenic.

I. *Contiguous spread* (45%–50% of all cases) via direct extension from local neighboring infection sites—frontal or ethmoid sinusitis or dental infection (frontal lobe abscess), middle ear or mastoid air cell infection (temporal lobe and cerebellar abscess), spread by local osteomyelitis or by septic thrombophlebitis of emissary vein.
II. *Hematogenous spread* from distant sites of infection (25%), usually multiple and multiloculated, often in the middle cerebral artery distribution. Common sources of metastatic brain abscesses are pulmonary or abdominopelvic infections, cyanotic heart disease, congenital heart malformations with right-to-left shunts (oral bacterial flora after dental procedures), or bacterial endocarditis.
III. *Trauma* including penetrating head injury or neurosurgical procedures (10%)—compound depressed skull fractures, basal skull fractures with cerebrospinal fluid (CSF) fistulae/leak, and previous craniotomy can lead to brain abscess, sometimes months or years after the acute event. Postneurosurgic abscesses may occur, especially when surgery involves paranasal air sinuses.
IV. *Immunosuppression.* People with acquired immune deficiency syndrome (AIDS) or with other causes of immunosuppression (e.g., neoplasms, steroid use) are susceptible to bacterial infections or infections associated with decreased T-cell immunity such as mycobacteria, fungi, or *Toxoplasmosis*.

Pathogens isolated from abscesses are related to the site of origin, as follows (organisms are listed in order of significance; many abscesses are polymicrobial):

I. Middle ear infection: streptococci (aerobic and anaerobic), *Bacteroides fragilis,* and Enterobacteriaceae (Proteus).
II. Sinusitis: same as middle ear infections, plus *Staphylococcus aureus, Haemophilus* species, and mucormycosis (also seen with orbital cellulitis).
III. Penetrating head trauma: *S. aureus*, streptococci, Enterobacteriaceae, *Clostridium* species, and *Pseudomonas aeruginosa*.
IV. AIDS/immunocompromised: *Toxoplasma, Mycobacterium, Listeria* species infection, *Listeria monocytogenes, Nocardia*, and *Cryptococcus neoformans.*

CLINICAL FEATURES

Clinical features usually resemble those of other space-occupying lesions (focal signs, seizures in 25%–35% of patients) with most symptoms related to

increased intracranial pressure (ICP) (headache, nausea, vomiting, lethargy, and stupor). Fever occurs in only 50% of cases.

HISTOPATHOLOGIC STAGES

Days 1 to 3: Early cerebritis produces a local inflammatory response (usually within white matter or at the gray-white matter junction) around a necrotic center.

Days 4 to 9: Late cerebritis is characterized by increased necrosis and inflammation, with initial fibroblastic formation of the collagen capsule.

Days 10 to 13: Early encapsulation stage shows further development of the collagen capsule, which is typically thinner on the less vascular ventricular side.

Days 14 and later: Late capsular stage shows five distinct histologic layers—the necrotic center, inflammatory cells and fibroblasts, collagen capsule, neovascular layer, and surrounding reactive gliosis and edema.

WORK-UP

I. Blood cultures should be drawn (positive in 15% of cases) and empiric parenteral antibiotic therapy must be initiated before computed tomography (CT) scan or magnetic resonance imaging (MRI). Lumbar puncture may be considered if mass effect is not prominent. However, the diagnostic yield is low and the risk of herniation is greater with abscess than with other mass lesions.

II. CT scans correlate well with the histopathologic stages. In the cerebritis stage, CT without contrast shows the necrotic center as a hypodensity. Ring enhancement begins in the later stages of cerebritis. In capsular stages the capsule becomes visible on CT without contrast as a faint hyperdense ring that produces ring-enhancing lesion with contrast, which is thinner on the ventricular side.

III. MRI appearance is bright on diffusion-weighted images (DWIs): T_1 delineates the abscess capsule as hyperintense/isointense and hypointense center and surrounding edema; T_2 demonstrates the hyperintense edema and center and hypointense capsule, enhances with gadolinium.

IV. MR spectroscopy (MRS) can differentiate between abscess, necrotizing tumor, or granuloma. The main finding of MRS in abscesses is elevation of metabolites of bacterial origin, including acetate, lactate, succinate, and amino acids versus necrotic brain tumors with elevated choline and decreased N-acetylaspartate (NAA). The MRS pattern may monitor effectiveness of medical treatment of a brain abscess, showing a decline of the metabolites after a positive response to therapy.

V. Other studies include electroencephalogram (EEG) which may show nonspecific findings such as focal slowing, seizure activity, and evidence of

encephalopathy. Cerebral angiography may show avascular mass and luxury perfusion.

TREATMENT

A combination of broad-spectrum antimicrobials, management of raised ICP, neurosurgical drainage or excision, and eradication of the primary infectious focus is indicated. If CT shows only cerebritis or abscess less than 2.5 cm and the patient is neurologically stable, antibiotics without surgery may suffice. Neurologic deterioration usually mandates surgery.

Excision or aspiration is performed for abscesses greater than 2.5 cm in diameter. Aspiration has become the procedure of choice because it is equally effective and less invasive than excision. Empiric antibiotics should be given based on the expected etiologic agents, presumed route and source of infection, predisposing factors, and adjusted based on the cultures. When the cause is unknown, the patient should receive a third- or fourth-generation cephalosporin, for example, ceftazidime 2 g IV q 8 hr (or ceftriaxone 2 g IV q 12 hr) or penicillin (PCN) G 5 MU IV q 6 hr, and metronidazole 500 mg IV q 6 hr. For paranasal sinus sources, administer PCN and metronidazole. In treatment of posttraumatic cases, administer nafcillin 2 g IV q 2 hr (or vancomycin 1 g IV q 12 hr, if methicillin-resistant *S. aureus* is suspected) and a third-generation cephalosporin such as ceftazidime 2 g IV q 8 hr. Treatment should be given for 6 to 8 weeks, often followed by additional 2 to 6 months of oral therapy or until the resolution of neuroimaging findings. Three to 4 weeks may be adequate in patients treated with surgical drainage. In human immunodeficiency virus (HIV)-positive patients, coverage should be added for toxoplasmosis with pyrimethamine plus sulfadiazine or clindamycin. Mucormycosis is treated with amphotericin B. Antiepileptic drugs may be given for up to 3 months. Routine corticosteroid administration is controversial and should be used only when mental status is significantly depressed and substantial mass effect can be demonstrated on imaging, and therapy should be of short duration.

PROGNOSIS

Mortality rates range from 5% to 15%. Poor prognosis is associated with very young or old age; anaerobic pathogens; large, multiple, deep, cerebellar, or multiloculated abscesses; acute clinical presentation with stupor/coma; intraventricular or subarachnoid rupture; concomitant pulmonary infection or sepsis; and specific organisms (i.e., *Aspergillus* and *Pseudomonas* species, fungal). Long-term sequelae include cognitive deficits (developmental delay in children), seizures, and focal deficits.

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ABSCESS, EPIDURAL

EPIDEMIOLOGY

Spinal epidural abscess (SEA) is an uncommon condition with an estimated incidence of 0.2 to 2.0/10,000 hospital admissions and a peak incidence in the sixth and seventh decades of life. Conditions commonly associated with SEA include diabetes mellitus, intravenous drug misuse, chronic renal failure, alcoholism, and cancer.

ETIOLOGY

The majority of SEAs are thought to result from the hematogenous spread of bacteria usually from a cutaneous or mucosal source with spread to the posterior aspect of the spinal canal. Direct spread from an adjacent source is less common and typically presents within the anterior aspect of the canal. The most common causative organisms are *Staphylococcus aureus* (57%–73%), *Mycobacterium tuberculosis* (25%), other gram-positive cocci (10%), gram-negative organisms 18%, and anaerobes 2%.

CLINICAL FEATURES

The initial manifestations of SEA are often nonspecific and include fever and malaise. The classical diagnostic triad consists of fever, spinal pain, and neurologic deficits. However, over time, an untreated abscess may progress from focal back pain, to radicular pain, to neurologic deficits (motor weakness, sensory changes, and bladder or bowel dysfunction), and then paralysis. Once paralysis develops, it may quickly become irreversible. Thus urgent intervention may be required if progression of weakness or other neurologic findings are detected.

TREATMENT

Surgical decompression and drainage with systemic antibiotic therapy is the treatment of choice. Empirical antimicrobial must be started early and be delivered intravenously in high doses and immediately following the collection of two sets of blood cultures. Appropriate empiric parenteral regimens include: vancomycin (15–20 mg/kg IV every 8–12 hours. Trough levels should be drawn 30 minutes prior to the next dose) for empiric coverage of methicillin resistant Staphylococcus aureus (MRSA) plus either ceftriaxone (2 g IV q 12 hr) or cefepime (2 g IV q 8 hr) or ceftazidime (2 g IV q 8 hr). Treatment should be continued for at least 4 weeks but may be prolonged for 8 weeks or longer if vertebral osteomyelitis is suspected.

PROGNOSIS

Overall prognosis is poor; 5% die due to uncontrolled sepsis or other complications, irreversible paraplegia occurs in 4% to 22%, and residual motor weakness in 37%.

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ACALCULIA

Acalculia refers to an acquired computational disability (as opposed to developmental dyscalculia which occurs in 5% of school-age children and is usually associated with dyslexia). The ability to perform mathematical calculations is complex as it requires not only an arithmetic brain center, but also intact attention, language processing, spatial orientation, memory, body knowledge, and executive function.

Acalculia may be classified as either primary or secondary. Primary acalculia (anarithmetia), an acquired isolated defect in comprehending numerical systems, is rare. Notable secondary types due to other cognitive defects are: aphasic, an inability to read or write numbers, usually occurring with left posterior parietal lesions; spatial, a mental misalignment of numbers usually due to right posterior hemispheric lesions; and frontal, due to impaired attention, perseveration, and executive dysfunction.

Acalculia can be part of Gerstmann syndrome (acalculia, agraphia, right-left disorientation, and finger agnosia) due to left angular gyrus lesions. Common causes of acalculia include epilepsy, metabolic or genetic disorders, focal lesions (e.g., stroke, tumor, trauma, or abscess), or commonly as part of a neurodegenerative disease (e.g., dementia). Rehabilitation is treatment of choice, with variable results. Spontaneous recovery is seen in many stroke and trauma patients.

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ACID-BASE DISTURBANCES

RESPIRATORY ALKALOSIS

This condition is most frequently observed in patients with hepatic cirrhosis, bronchial asthma, salicylate intoxication, hypoxia, sepsis, pneumonia, and acute anxiety (hyperventilation syndrome). Acute respiratory alkalosis constricts cerebral arterioles and decreases cerebral blood flow. Confusion accompanied by a slow electroencephalogram (EEG) may develop. Symptoms of milder respiratory alkalosis include paresthesias, dizziness, cramps as a result of coexistent tetany, hyperreflexia, and muscle weakness. More severe alkalosis (pH 7.52–7.65) in patients with respiratory insufficiency and hypoxia may result in a symptom complex of hypotension, seizures, asterixis, myoclonus, and coma. Treatment is to correct the underlying cause.

RESPIRATORY ACIDOSIS

Acute respiratory acidosis is a condition of low pH and high CO_2 concentration, occurring as a result of impairment of the rate of alveolar ventilation. Causes of acute respiratory acidosis include sedative drugs, brainstem injury, neuromuscular disorders, chest injury, airway obstruction, and acute pulmonary disease. Lethargy and confusion occur as the PCO_2 rises above 55 mm Hg. Seizures, stupor, or coma may occur with levels greater than 70 mm Hg. The serum bicarbonate level is either normal or high, depending on how rapidly the respiratory failure developed. Neurologic manifestations resulting from cerebral vasodilation include headache, increased intracranial pressure, and papilledema. Hyperreflexia or hyporeflexia and myoclonus may also occur.

Chronic respiratory acidosis generally occurs in patients with chronic obstructive pulmonary disease (COPD), restrictive lung disease (e.g., severe kyphoscoliosis), or extreme obesity (Pickwickian syndrome). It is most often symptomatic with acute exacerbations of disease. Compensatory polycythemia often results from chronic hypercapnic states. Hypoventilation or Pickwickian syndrome may manifest as excessive daytime somnolence.

Therapy of respiratory acidosis involves ventilatory support and treating the underlying disorder. The possibility of sedative or narcotic drug ingestion must be suspected in otherwise healthy patients who suddenly develop acute respiratory depression.

METABOLIC ALKALOSIS

Metabolic alkalosis may result from either excessive ingestion of base or excessive loss of acid. Causes of hypokalemic metabolic alkalosis include Cushing syndrome, vomiting or gastric drainage, diuretic therapy, and primary aldosteronism. Neurologic manifestations include paresthesias, cramps (due to tetany), muscle weakness (due to associated hypokalemia), and hyporeflexia. Severe metabolic alkalosis produces a blunted, confused state rather than stupor or coma and may result in cardiac arrhythmias and severe compensatory hypoventilation.

Treatment depends on the underlying cause.

METABOLIC ACIDOSIS

Metabolic acidosis occurs when a decrease in plasma bicarbonate level lowers pH. Cardinal features are hyperventilation and, when severe, *Kussmaul* respirations. In chronic metabolic acidosis, hyperventilation may be difficult to detect on clinical examination. The most common causes of metabolic acidosis sufficient to produce coma and hyperpnea include uremia, diabetes, lactic acidosis, and ingestion of acidic poisons. Ketoacidosis occasionally develops in severe alcoholics after prolonged drinking episodes. In diabetics treated with oral hypoglycemic agents, lactic acidosis and diabetic ketoacidosis must be considered.

The presence of neurologic symptoms depends on various factors, including the type of systemic metabolic defect, whether the fall in systemic pH

affects the pH of the brain and cerebrospinal fluid (CSF), the rate at which acidosis develops, and the specific anion causing the metabolic disorder. All forms of metabolic acidosis produce hyperpnea as the first neurologic symptom. Other manifestations include lethargy, drowsiness, confusion, and mild, diffuse skeletal muscle hypertonus. Extensor plantar responses occur at a later stage. Stupor, coma, or seizures generally develop only preterminally. Because metabolic acidosis is a manifestation of a variety of different diseases, the treatment varies depending on the underlying process and on the acuteness and severity of the acidosis.

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ADEM DISEASE

ACUTE DISSEMINATED ENCEPHALOMYELITIS

Acute disseminated encephalomyelitis (ADEM) is a monophasic multifocal demyelinating disorder of the CNS, often following infection or vaccination. ADEM is more frequent in children; however, it may occur at any age. The most frequent preceding infections are flulike illnesses, nonspecific upper respiratory tract infections, and gastroenteritis. Although viral etiologies are most common, it can also follow a bacterial infections and, in rare cases, parasitic infections. Postvaccination ADEM is seen in approximately 10% of cases and is most common after measles, mumps, and rubella.

CLINICAL PRESENTATION

Initial presentation may include meningoencephalitis, fever, encephalopathy, seizures, headache, and meningismus. Focal motor or sensory deficits, ataxia, cranial neuropathies, or brain stem pathology may also be seen.

A more severe presentation known as acute hemorrhagic encephalomyelitis may develop.

DIAGNOSIS

MRI

MRI shows multifocal demyelinating lesions in CNS white matter, with increased signal in T2-weighted and FLAIR images. Lesions may be large, with poorly defined margins, and are often asymmetric. Lesions may enhance with contrast depending on the time of onset. Lesions that are hypointense on T1 argue against the diagnosis.

CSF

Lymphocytic pleocytosis and elevated protein are commonly seen; however, CSF studies can be normal.