brain abscess [created by Paul Young 12/11/07]

general

- pyogenic brain abscess is a localised suppurative infection of parenchymal CNS tissue
- differentiating brain abscess from other CNS infections or brain tumours may be challenging as there is significant overlap between the clinical and radiological presentation
- even with modern antibiotic therapy and radiographic techniques, mortality remains as high as 20%

pathophysiology

- a brain abscess begins as a localised area of parenchymal (cerebritis), which evolves to necrosis & frank suppuration
- the initial stage, characterised by vascular congestion, petechial haemorrhage, cerebral oedema and tissue softening is demonstrable by MRI
- as cerebritis progresses, CT findings become abnormal, revealing a capsule like hyperaemic zone surrounding the area of inflammation
- as the abscess matures, a dense capsule is formed. In relatively avascular areas of the brain, capsule formation is delayed. Once it forms, however, the capsule resolves slowly.
- in the preantibiotic era, contagious foci (middle ear, sinuses, mastoids) caused most brain abscesses; however, more commonly now cases are due to distant foci of infection or originate for unknown sites
- with haematogenous spread, abscesses tend to seed along the middle cerebral artery distribution

aetiology

- In brain abscess or subdural empyema, the infecting organism(s) vary with the underlying predisposing cause.
- In the nonimmunosuppressed, most brain abscesses are polymicrobial with microaerophilic cocci, including Streptococcus anginosus/milleri, and anaerobic bacteria predominating. However, where the likely site of origin is the ear, enteric Gram-negative bacilli are commonly involved, while after trauma or surgery, staphylococci predominate.
- In the immunosuppressed, Nocardia species, Toxoplasma and fungi such as Aspergillus or Scedosporium are more likely to occur.

clinical course

- variable signs & symptoms of brain abscess relate to variations in location, size, and rapidity of development. At one extreme, the course may span weeks with few constitutional symptoms. At the other extreme, a previously assymptomatic brain abscess may rupture into the subarachnoid space and cause death within hours
- brain abscess usually progresses subacutely for 7 to 14 days. Classic symptoms include excruciating headache, low grade fever, and focal neurological signs.
- occasionally, a patient has no symptoms referable to the CNS and fever may be absent in as many as 50% of cases
- parameningeal foci spread to brain abscess as inflammatory process erodes through bone and meningeal tissues
- chronic otitis, sinusitis or post-traumatic dural defects with progressive neurological deficit strongly suggests brain abscess
- bacterial pathogens also invade neural tissues via haematogenous spread
- the presence of chronic extrameningeal suppurative foci or illicit iv drug use predisposes to brain abscess; in as many as a third of patients there is no obvious source of infection
- filtration by the pulmonary vasculature protects the brain; cardiac shunts & pulmonary AV fistulae bypass this protection
- CNS complications of brain abscess relate to both tissue inflammation & increased ICP from a space occupying lesion
- non specific complications common to all critically ill patients include aspiration, GI bleeding and thromboembolism
- specific complications include focal neurological deficits, altered mental state or seizures
- when surrounding oedema is excessive, aggressive therapy with corticosteroids is warranted
- if a brain abscess ruptures into the subarachnoid space or into a cerebral ventricle, rapid deterioration in mental state is the rule and mortality is high

imaging

- CT and MRI are both useful in monitoring progress of a brain abscess. An expanding lesion may be aggressively drained or a stable or shrinking abscess can be observed
- CT scanning has some limitations particularly if performed without contrast. It may miss early cerebritis and the cerebellum and brainstem may be poorly seen. In particular, it may miss lesions 1.5cm or smaller as are typically seen in endocarditis

therapy

General
- Aspiration or biopsy is essential to guide antimicrobial therapy.
- Consultation with a clinical microbiologist or an infectious diseases physician in addition to surgical assessment is advised

antimicrobials - general principles:
- choice of antimicrobials should be guided by culture results, given the diversity of pathogens and the need for prolonged therapy (eg 6-8 wks)
- additional pharmacological considerations include CNS penetration and parenteral administration
- empirical therapy should be commenced after aspiration while awaiting culture results and should be guided by likely pathogens

antimicrobials - non immunocompromised patients without prior neurosurgery
- For empirical therapy following aspiration,
use:
benzylpenicillin 2.4 g (child: 60 mg/kg up to 2.4 g) IV, 4-hourly
PLUS
metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 8-hourly
PLUS EITHER
ceftriaxone 4 g (child: 100 mg/kg up to 4 g) IV, daily
or ceftriaxone 2 g (child: 50 mg/kg up to 2 g) IV, 12-hourly
OR
cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly.

antimicrobials - non immunocompromised patients with prior neurosurgery
For postneurosurgical brain abscess, use:
vancomycin 12.5 mg/kg up to 500 mg (child <12 years: 15 mg/kg up to 500 mg) IV, 6-hourly [current evidence for this indication is based on 6hrly dosing]
PLUS EITHER
ceftazidime 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly
OR
meropenem 2 g (child: 40 mg/kg up to 2 g) IV, 8-hourly.

- additional tests for culture negative brain abscess include HIV serology, serum crytococcal antigen, and toxoplasmosis titres

- Modify therapy on the basis of Gram stain and culture results.
- The duration of treatment depends on clinical response and radiological evidence of resolution.

- in selected cases brain abscesses can be treated with antimicrobials alone, particularly when the causative agent is known and the lesion is <2.5cm
- medical management may also be necessary when the lesion is inaccessible or surgical intervention poses unacceptable risk
- steroids should not be routinely used but are often used if oedema is severe

Treatment of the immunocompromised patient
(i) Nocardiosis
- Brain abscess is a common manifestation of disseminated nocardiosis in the immunocompromised.
- For Nocardia asteroides and other species susceptible to sulfonamides, IV or oral trimethoprim+sulfamethoxazole is the usual initial treatment:
trimethoprim+sulfamethoxazole 160+800 mg (child: 4+20 mg/kg up to 160+800 mg) IV or orally, 6-hourly for 3 to 4 weeks
FOLLOWED BY
trimethoprim+sulfamethoxazole 160+800 mg (child: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly for 3 to 6 months.
- Combination therapy with trimethoprim+sulfamethoxazole PLUS amikacin has shown promise as empirical therapy, and in difficult cases that were slow to respond to trimethoprim+sulfamethoxazole alone.
Alternative therapy using drugs such as amoxycillin+clavulanate, meropenem, ceftriaxone, minocycline, amikacin or linezolid have all been reported to be successful in small numbers of cases, particularly for some of the more unusual species.
Ongoing treatment for 6 to 12 months with oral trimethoprim+sulfamethoxazole may be needed
(ii) Toxoplasmosis:
- In AIDS, cerebral infection with Toxoplasma gondii is common. Use:
sulfadiazine 1 to 1.5 g (child: 50 mg/kg up to 1 to 1.5 g) orally or IV, 6-hourly
PLUS
pyrimethamine 50 to 100 mg (child: 2 mg/kg up to 50 to 100 mg) orally, for the first dose, then 25 to 50 mg (child: 1 mg/kg up to 50 mg) orally, daily.
- Duration of therapy is for 3 to 6 weeks depending on clinical response. Relapse is common, so maintenance therapy with half the above dosages is necessary while the patient is immunosuppressed.
- Calcium folinate 15 mg orally daily is usually added to reduce bone marrow suppression, and the white cell and platelet counts must be monitored closely.
- For patients allergic to sulfonamides, substitute for sulfadiazine, clindamycin 600 mg (child: 15 mg/kg up to 600 mg) orally or IV, 6-hourly