Brain abscess is relatively uncommon problem in general practice yet it is important to be aware of the problem and consider it as one of the differential diagnoses in an individual who presents with symptoms of raised intracranial pressure (especially if there are predisposing factors). Brain abscess is a potentially life-threatening illness and the treatment is almost always involves surgical intervention along with medical therapy. It is therefore essential to know when to suspect a brain abscess, when to refer and how to manage a patient before referral to a center with neurosurgical facilities. Appropriate treatment results in a cure in more than 90% of cases.

Two case descriptions are given below. Try to answer the questions before you proceed to an overview on the diagnosis and management of brain abscess.

Case descriptions

1. An eight year old girl was brought to the outpatient department with progressively worsening headache associated with vomiting for three weeks. She had recurrent cyanotic spells since the age of three years. On examination, her GCS score was 15/15 and she had left hemiparesis (grade 4 power in upper and lower limbs). There was central cyanosis. She had been treated elsewhere with multiple parenteral antibiotics for 2 weeks. A CT scan of the brain with contrast is shown in Fig. 1.

2. A twenty five year old lady with systemic lupus erythematosus (SLE) who had been on oral steroids for three years complained of headache and vomiting for 2 weeks with episodes of blurred vision and one episode of generalized tonic-clonic seizure. MRI of brain with gadolinium was done (Fig. 2) and she was started on anti-tuberculous medications empirically elsewhere. Her symptoms continued to worsen.

Questions

What will you suspect as the cause of headache in each of these scenarios and why?

How would you approach this patient to arrive at a diagnosis and then to treat the illness?

See the end of the article for a brief discussion of these cases.
**Definition and overview**

Pyogenic brain abscess is a focal collection of pus in the brain parenchyma. It is a focal suppurative process which begins as a localized area of inflammation (cerebritis) within an area of devitalized brain tissue with poor microcirculation which then develops into a collection of pus with a well formed capsule.

In developing countries the incidence of brain abscess is about 8% of all intracranial tumours while it is lower in developed countries. Improvement in living conditions and widespread use of antibiotics have not reduced the incidence because of the rise in the incidence of infection among immunocompromised individuals. Almost every person with a brain abscess died in the pre-antibiotic era. The advent of antibiotics and CT imaging have ensured early diagnosis and reduced mortality rates significantly. Most patients in the present era are cured with medical and surgical therapy.

**Pathogenesis of brain abscess**

Brain abscess develops when microorganisms are introduced into brain parenchyma. The routes of entry of micro-organisms are as follows.

1. **Contiguous spread** occurs in about 40% of abscesses, with spread from middle ear infection (acute or chronic suppurative otitis media), infection in paranasal sinuses (usually frontal and sphenoid) and mastoiditis. Middle ear infections are a common source and tend to result in abscesses in the temporal lobe and cerebellum.

2. **Haematogeneous spread** occurs through the bloodstream from infectious focus at a distant site. Eg. Pulmonary infection (bronchiectasis, pneumonia, empyema), infective bacterial endocarditis, dental infection, osteomyelitis, acute diverticulitis. These metastatic abscesses are usually small and multiple. They are most common in the middle cerebral arterial territory. Spread of middle ear infection through septic thrombophlebitis of the sigmoid and transverse sinuses can also occur.

3. **Direct inoculation from outside** – About 10% of abscesses are caused by spread of organisms introduced from outside (infected compound skull fracture, bullet injury, intracranial surgery).

4. In about 10-37% of abscesses, the source of infection is not determined.

**Children with congenital cyanotic heart disease and individuals who are immunocompromised due to HIV infection or long term corticosteroid therapy are particularly predisposed to developing brain abscess.**

After inoculation of brain tissue, brain abscesses evolve from a stage of ill-defined cerebritis and oedema to gradual development of a capsule.

**Micro-organisms that cause brain abscess**

The organisms that cause brain abscess vary according to the predisposing condition (Table 1) and by age. The most common organisms that cause brain abscess are streptococci that are usually anaerobic or microaerophilic. In several cases there are multiple causative organisms. Mycobacterium tuberculosis or fungal infection can also result in brain abscess formation. Hence it is important to send pus for aerobic, anaerobic, fungal and acid-fast bacilli cultures.

<table>
<thead>
<tr>
<th>Predisposing condition</th>
<th>Likely pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>otitis media/mastoiditis</td>
<td>streptococci (anaerobic &amp; aerobic), <em>B. fragilis</em>, <em>Enterobacteriaceae</em> spp</td>
</tr>
<tr>
<td>paranasal sinusitis</td>
<td>streptococci, <em>Bacteroides</em> spp, <em>Enterobacteriaceae</em> spp, <em>S. aureus</em></td>
</tr>
<tr>
<td>dental infections</td>
<td>streptococci, <em>Fusibacterium</em> spp, <em>Bacteroides</em> spp</td>
</tr>
<tr>
<td>meningitis</td>
<td><em>L. monocytogenes</em>, <em>C. diversus</em></td>
</tr>
<tr>
<td>cyanotic heart disease</td>
<td>streptococci, <em>Haemophilus</em> spp</td>
</tr>
<tr>
<td>bacterial endocarditis</td>
<td><em>S. viridans</em>, <em>Staphylococcus</em> spp, enterococci, <em>Haemophilus</em> spp</td>
</tr>
<tr>
<td>pyogenic lung disease</td>
<td>streptococci, <em>N. asteroides</em>, <em>Actinomyces</em> spp, <em>Bacteroides</em> spp</td>
</tr>
<tr>
<td>T-cell deficiency</td>
<td><em>Toxoplasma gondii</em>, <em>Nocardia</em> spp, <em>L. monocytogenes</em></td>
</tr>
<tr>
<td>trauma</td>
<td><em>S. aureus</em>, <em>Enterobacteriaceae</em> spp</td>
</tr>
</tbody>
</table>
1. When should brain abscess be suspected?
Patients who present with features of raised intracranial pressure (headache, vomiting, visual disturbance) or seizure, altered consciousness or neurological deficit with any of these following predisposing factors
- Chronic ear infection (CSOM, mastoiditis)
- Chronic sinusitis
- Congenital cyanotic heart disease
- Immunocompromised state (HIV infection, chronic steroids, immunosuppressants)
- Compound fracture of the skull, bullet injury

2. When should you refer a patient to a higher center?
If the diagnosis of brain abscess is established on CT imaging, the patient will require definitive treatment (aspiration/excision and pus culture) along with antibiotics. If neurosurgical expertise is not available in the hospital, it is advisable to refer the patient. Empirical antibiotics are not recommended except if there is strong clinical suspicion of a brain abscess – cerebritis in the CT/MRI image, in the setting of chronic ear infection or paranasal sinusitis.

3. Immediate management before referral:

1. **Start an anti-epileptic drug** – Phenytoin, phenobarbitone or valproate are preferable since they have a broad spectrum of activity and intravenous preparations are available in case of an active seizure.

   Dose of Phenytoin
   Loading dose: 15-18 mg/kg single dose IV to be given as a slow drip at a rate of 50mg/minute (to avoid cardiac arrhythmias) followed by Tab. Phenytoin 5-7 mg/kg/day in three divided doses

2. **If the patient is drowsy** - A low level of consciousness usually is an indicator of raised intracranial pressure due to cerebral oedema. Treatment will need to be initiated as soon as possible. If the patient is being referred, anti-oedema measures like an intravenous dose of Inj. mannitol may be lifesaving.

   **Mannitol**
   Dose: 1-1.25 gm/kg/day IV in four divided doses. (20% mannitol contains 20 gm of mannitol in 100ml of solution)

   **Dexamethasone**
   Corticosteroids are not advisable in the presence of an infection, but a single dose before referral may be life-saving if the patient is drowsy because of raised intracranial pressure.
   Dose: Inj. Dexamethasone 4-6 mg IV in adults (single dose), 0.5 mg/kg IV in children (single dose)
Brain abscess - Diagnosis and management

Clinical features

1. Features of raised intracranial pressure – Headache, vomiting, altered consciousness and visual disturbances (blurred vision, diplopia) are the commonest symptoms. Alteration in consciousness is seen in up to two-third of patients.

2. Seizures – is seen in up to 50% of cases

3. Focal neurological deficits – like weakness of the limbs, cerebellar dysfunction (impaired balance, gait ataxia), and other deficits are seen depending on the site and size of the abscess.

   It should be noted that fever is not a common presenting symptom and if present, is usually low grade. Absence of fever should not exclude the suspicion of brain abscess. Brain abscess is more common in the younger age group and for some reason, more common in males.

Investigations and Diagnosis

If a patient with predisposing conditions like an ear infection or congenital cyanotic heart disease presents with features of raised intracranial pressure, the possibility of brain abscess must be considered and investigated.

Radiological imaging:

A computerized tomography (CT) with contrast administration is the quickest and cheapest investigation to confirm diagnosis and plan treatment. The abscess is usually seen as a ring-enhancing lesion with surrounding oedema. The enhancing rim is the capsule and this may be thin or absent in an early abscess.

MRI scans with gadolinium may be used when available. The advantage of MRI is that it can detect very small abscesses and the multiple planes of imaging aid in planning for surgery. In most cases however CT imaging is more than adequate.

Ultrasound imaging can be used to detect abscesses in children with an open anterior fontanelle.

If a brain abscess is diagnosed, further investigation to detect the source of the infection is important. The CT or MRI of the brain can detect sinusitis involving the paranasal sinuses, mastoiditis, fractures of the skull. Further imaging of the abdomen and thorax may be necessary to look for infections in these regions. A consultation with an ENT surgeon is recommended to rule out an ear infection even if the imaging is negative.

Laboratory investigations

Lumbar puncture for CSF analysis is contraindicated as it can lead to life-threatening transtentorial herniation and transforaminal herniation of the brain. The process of herniation of the brain is slow (over several days) and may not manifest immediately after a lumbar puncture. Moreover, CSF analysis does not contribute to diagnosis since a brain abscess is a localized infection in the brain parenchyma unlike a meningitis and CSF analysis may be normal or inconclusive.

Routine blood investigations like Total WBC counts and ESR are usually normal or mildly elevated and do not contribute to diagnosis. Haemoglobin, serum creatinine, virology screening and crossmatch for transfusion may be sent if surgical intervention is planned.

Pus for culture: Pus from the abscess, once obtained must be sent immediately for aerobic, anaerobic and acid-fast bacilli (AFB) and fungal culture and sensitivity for a definitive diagnosis. Cultures must be sent immediately because delayed incubation can lead to false negative results and difficulty in antibiotic selection.

Differential diagnosis in CT/MRI:

The differential diagnoses in a patient with a ring enhancing lesion on imaging are high grade brain tumour and metastasis. Cystic lesions like solitary cysticercal granuloma are also ring enhancing lesions. The enhancing rim in a brain abscess is usually thinner and more uniform than in a brain tumour. Cysticercal lesions are usually small (less than 2 cms) and may be multiple and they usually present with seizures.

Fever is not a common presenting symptom.

Lumbar puncture for CSF analysis is contraindicated. It can lead to life threatening brain herniation.
The treatment of brain abscess is administration of parenteral administration of antibiotics after confirmation of the diagnosis by microscopic examination of pus (obtained by aspiration or surgical excision) and culture(1,2,3,5,6,7).

**Aspiration of pus:**
This may be done using a twist-drill / burr-hole and cannula or with stereotactic guidance. Aspirated pus has to be sent immediately for culture and sensitivity after which antibiotics are started as soon as possible. The pus has to be sent for aerobic, anaerobic, fungal and AFB (acid-fast bacilli) culture. Serial weekly CT scans may be done to monitor the size of the abscess. Repeated aspirations may be necessary. In case of multiple abscesses, the largest abscess must be aspirated, followed by antibiotics.

**Antibiotics**
Antibiotics need to be given for 6-8 weeks and the choice of antibiotics is based on sensitivity of the organism. The antibiotics of choice are crystalline penicillin, chloramphenicol and metronidazole followed by antibiotics based on the sensitivity report. Third generation cephalosporins (ceftriaxone) may be used as an alternative to chloramphenicol. At least 2 weeks of parenteral antibiotics followed by 4 – 6 weeks of oral antibiotics is recommended. Empirical antibiotic therapy is not advisable because a definitive diagnosis of brain abscess either by aspiration of pus or excision and isolation of the micro-organism is essential to treatment. The antibiotic schedule followed in CMC Vellore is as follows.

**Until culture and sensitivity reports are obtained:**
- **Inj.** Crystalline Penicillin 50,000 units/Kg/dose every 2 hours IV (in children)
- 20 lakh units IV every 2 hours (adults above 60 Kg)
- **PLUS**
- **Inj.** Chloramphenicol 100 mg/Kg/ day IV in four divided doses (in children)
  1 gm IV every four hours (adults over 60 Kg)
  (in children – reduce the dose by half after 3 days)
- **PLUS**
  - Inj. Metronidazole 7.5 mg / Kg/ dose IV (every 8 hours)
  - Inj. Ceftriaxone (100mg/kg/day in children and 4 gm/day in adults in two divided doses) may be used instead of chloramphenicol in case of availability issues or adverse drug reactions.

**After culture and sensitivity report:** Antibiotics may be altered according to the sensitivity pattern obtained. After two weeks of intravenous antibiotics, oral antibiotics with good CSF penetration are recommended for 4 – 6 weeks depending on the causative organism. If no organism has been isolated, co-trimoxazole (double strength) may be given at the appropriate dose along with Rifampicin. If staphylococcal infection is suspected, an anti-staphylococcal penicillin like cloxacillin may be used. Vancomycin is reserved for penicillin resistant Gram positive organisms and in case of penicillin hypersensitivity.

**Anti-oedema measures:**
Anti-oedema measures may be necessary in case of low level of consciousness due to raised intracranial pressure or if the scan shows significant cerebral oedema with mass effect. Mannitol is effective in lowering intracranial pressure.

**Intravenous mannitol**
Dose: 1-1.25 gm/kg/day in four divided doses for two days, taper dose to half on the third day. There is no benefit in continuing Mannitol beyond three days. Corticosteroids for reducing oedema and intracranial pressure are not advisable in the presence of an infective process. A single dose of dexamethasone may be given as a life-saving measure before referring the patient. (See box 3)

**Anticonvulsant medication**
All patients with brain abscesses should be started on anticonvulsant drugs except for those with an abscess in the posterior fossa structures (cerebellum and brain-stem). An abscess in the cerebral parenchyma, especially within or close to the cortical grey matter is likely to cause seizure and an anticonvulsant drug with a broad spectrum of activity is recommended (Phenytoin, sodium Valproate or phenobarbitone). Phenytoin and sodium Valproate have the advantage of being available as intravenous preparations.
Brain abscess- Diagnosis and management
Anticonvulsant drugs will have to be continued long term even after medical therapy and/or surgery. This is especially important in patients who have presented with seizures; these individuals will require anticonvulsant drugs for at least 3 years after treatment.

Surgical excision:
Surgical excision of the abscess (craniotomy and excision) is recommend in either of these cases
1. the abscess is large with significant mass effect or multiloculated
2. The abscess is superficial and not in an eloquent area of the brain
3. Cerebellar abscess (they tend to cause rapid deterioration in clinical status especially if the abscess recurs after aspiration)
Surgical excision is not recommended if the abscess is deep-seated or is in an eloquent area of the brain or if the patient is clinically unfit for surgery. Aspiration of pus may be done in such cases with or without stereotactic guidance.

Role of stereotactic aspiration
Aspiration of pus and biopsy of the abscess wall may be done using stereotactic guidance in instances where the abscess is deep-seated or if the patient is unfit for surgery or if the abscess is in a region of the brain where surgery is not advisable because of the risk of severe neurological deficits (Eg. Thalamus, basal ganglia, brainstem abscesses). In stereotactic aspiration, the aspiration is done using a probe that is inserted using CT image guidance (usually under local anaesthesia). It is precise and effective in managing small, deep-seated abscesses with a very low risk to life and very little morbidity compared to surgery.(8,9).

Treatment of the source of infection
Treatment of brain abscess is incomplete if the source of the infection has not been identified and treated. A meticulous attempt has to be made to ascertain the source of the infection and treat the infection. Middle ear and paranasal sinus infections and common predisposing conditions and can be detected using clinical examination and imaging (X-rays and CT). Ultrasound/ CT of the abdomen to look for intra-abdominal collections and echocardiogram to detect cardiac anomalies and valvular vegetations are recommended. A chest x-ray can detect bronchiectasis or large abscesses in the lungs. A source of infection however, may not be detected in some despite extensive investigation.

Congenital cyanotic heart disease
Congenital cyanotic heart disease (right to left shunt) is an important predisposing condition for development of brain abscess(1,2,3,11). It accounts for 12.8–69.4% of all cases of brain abscesses with identified risk factors in several series and the incidence of brain abscess in patients with cyanotic heart disease is between 5-18.7%. Tetralogy of Fallot is the commonest anomaly associated with brain abscess and most of the patients are children. In patients with cyanotic heart disease, there is a right-to left shunt of venous blood in the heart, bypassing the pulmonary circulation. Thus, bacteria in the bloodstream are not filtered through the pulmonary circulation, where they would normally be removed by phagocytosis. Patients with cyanotic heart disease could have low-perfusion areas in the brain due to chronic severe hypoxemia and metabolic acidosis as well as increased viscosity of blood due to secondary polycythemia. These low-perfusion areas commonly occur in the junction of gray and white matter, and they are prone to seeding by microorganisms that may be present in the bloodstream.

Individuals, especially children with cyanotic heard disease and a brain abscess may present only with headache and there should be a low threshold for performing a CT scan of the brain in this situation. Brain abscesses in these patients tend to be multiple. Since the cardio-pulmonary status in most patients is sub-optimal, general anaesthesia and surgical excision is usually contraindicated. These patients also have abnormal coagulation profile and are at high risk for open surgical procedure to excise the abscess. Repeated aspiration after correction of coagulation profile followed by antibiotics is the recommended treatment.

Fungal brain abscess:
Fungal infections may present as an abscess or granuloma in the brain although the rhinocerebral syndrome and meningitis are more common. Fungal infections are uncommon must be suspected if the patient is immunocompromised, though the infection may also seen in the immunocompetent. The
Brain abscess - Diagnosis and management

The commonest fungi that present a fungal mass in the brain are Phaeohyphomycosis spp., Zygomycetes spp., Candida spp., and rarely with Aspergillus spp. Most of the fungi are inhaled and initiate a primary lung infection which is usually self-limited. The infection may then spread by hematogenous dissemination with subsequent involvement of the central nervous system (CNS). Local extension from paranasal sinuses, ear and orbit and rarely trauma are some of the other ways in which a fungal infection reaches the CNS. 4

Outcomes and long term sequelae

The majority of patients with brain abscesses in the present era are cured with medical and surgical treatment. The cure rate reported in literature is about 90% for single and multiple abscesses. Early diagnosis by CT scan and the availability of antibiotics have reduced mortality rates significantly. Some conditions associated with higher mortality and morbidity are

1. Nocardial and listerial brain abscesses
2. Intra-ventricular rupture of brain abscess and
3. Low Glasgow Coma Scale score on presentation to hospital.

Cognitive dysfunction, delayed onset seizures and focal neurological deficits are some of the long term sequelae.

Discussion of case scenarios

Case 1

Brain abscess must be suspected in any patient with a background of cyanotic heart disease presenting with complaints of headache and vomiting. Imaging (CT or MRI) with contrast is the investigation of choice to arrive at a diagnosis. This patient was treated with aspiration of pus in multiple settings. Pus culture did not grow any organism since the child had been treated elsewhere with multiple antibiotics empirically. Definitive treatment in the form of aspiration or excision with pus smear and culture is a necessity in the treatment of brain abscess so that appropriate antibiotics can be administered. Empirical treatment with antibiotics without pus culture is usually ineffective and leads to diagnostic dilemmas.

Case 2

This lady had been on oral prednisolone for three years and in this setting, brain abscess should be suspected if there are symptoms of raised intracranial pressure or seizure. An empirical diagnosis of tuberculosis was made elsewhere and she was managed with ATT (anti-tuberculcous therapy) without pus smear or culture and her symptoms worsened. The pus culture after CT guided stereotactic aspiration grew Nocardia and she improved with co-trimoxazole therapy. Nocardia and fungal species are uncommon causative organisms and emphasizes the need for sending all possible cultures in brain abscess (aerobic, anaerobic, fungal and AFB).

References