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What you need to know about brain abscesses

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Abstract

A brain abscess is a focal accumulation of pus in the brain parenchyma arising from direct inoculation, contiguous spread from local anatomical structures or haematogenous seeding from a remote source of infection. It can result in significant morbidity and mortality, making early diagnosis and treatment vital. Only one fifth of patients present with the classic triad of headache, fever and focal neurological symptoms. More commonly patients show signs and symptoms of raised intracranial pressure alone, such as confusion or reduced conscious level, headache, nausea and vomiting, which can be a presentation of many intracranial pathologies. Distinguishing an abscess from other pathologies such as meningitis and tumours is crucial, as clinically these can present in similar ways, but their management and outcomes are very different. Diffusion-weighted magnetic resonance imaging brain scans can help localise the lesion and differentiate ring-enhancing lesions caused by a brain abscess from malignant tumours. Cerebral abscesses are considered a neurosurgical emergency; early stabilisation, diagnosis and management in a neurosurgical centre is important in reducing morbidity and mortality.

Key words: Bacterial; Brain abscess; Neurology; Neurosurgery; Postoperative infection

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Introduction

A brain abscess is a focal accumulation of pus within the brain parenchyma. Incidence has been estimated at 0.3–0.9 per 100 000 people, but is expected to be higher in immunocompromised patients and those who have undergone a neurosurgical procedure (Brouwer and van de Beek, 2017; Bokhari and Mesfin, 2019). Delays in the diagnosis and treatment of brain abscesses are associated with significant morbidity and mortality. As a result, early recognition and prompt initial management n is critical to ensure timely transfer of the patient to a neurosurgical unit for further management, which typically involves surgical aspiration and tailored antibiotic therapy.

Pathogenesis

Bacteria reach the brain either by direct inoculation (for example penetrating cranial trauma, neurosurgical procedures), contiguous spread from local anatomical structures (such as purulent sinusitis, mastoiditis) or haematogenous seeding from systemic sources (Chun et al, 1986). Examples of sources of infection which can lead to cerebral abscesses are listed in Table 1.

The most common bacterial species found in brain abscesses are those of the *Streptococcus anginosus* group and *Staphylococcus aureus* (Brouwer et al, 2014a); however, the precise pathogen involved will depend on the site of the primary infection, the age of the patient, their immune status, country of residence and travel history (Lakshmi et al, 1993). For example, in immunocompromised patients, *Mycobacterium tuberculosis, Toxoplasma gondii*, Nocardia spp. or fungal pathogens are sometimes isolated (Brook, 2017).

While direct or contiguous spread of infection often results in a single nidus of abscess formation, haematogenous seeding can result in multiple abscesses, often distributed in the vascular territory of the middle cerebral artery (Bakshi et al, 1999). Cerebral abscesses secondary to skin, pelvic and intra-abdominal infections frequently present with this pattern of distribution (Bakshi et al, 1999).

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Table 1. Sources of infection pre-disposing to cerebral abscesses and their associated micro-organisms		
Source	**Example**	**Associated micro-organisms**
Direct inoculation	Penetrating trauma or neurosurgery	*Staphyloccus aureus, S. epidermidis,* Streptococcus spp., Enterobacterales, Clostridium spp.
Contiguous spread of bacteria	Otitis media or mastoiditis	Streptococcus, Bacteroides and Prevotella spp.; Enterobacterales
	Paranasal sinusitis	Streptococcus, Bacteroides and Haemophilus spp.; Enterobacterales, *S. aureus*
Haematogenous spread of bacteria	Dental infection	Fusobacterium, Prevotella, Actinomyces, Bacteroides and Streptococcus spp.
	Bronchiectasis, lung abscess, empyema	Fusobacterium, Actinomycines, Bacteroides, Prevotella, Nocardia and Streptococcus spp.
	Bacterial endocarditis	*S. aureus* and Streptococcus spp. (esp. viridans group)
	Congenital heart disease	Streptococcus and Haemophilus spp.
	Diverticulitis, gastrointestinal malignancy or perforation	Streptococcus, Bacteroides and Prevotella spp.; Enterobacterales

From Brouwer et al (2014b)

Clinical approach

Presentation

The mean age at presentation is 34 years with a male:female ratio of 2.4:1 (Brouwer et al, 2014a). The classic triad of headache, fever and focal neurological deficit only occurs in 20% of cases (Brouwer et al, 2014a). No symptoms are specific for brain abscesses, but most will relate to symptoms of raised intracranial pressure such as headache, nausea or vomiting and reduced level of consciousness. Headaches tend to be most severe at night and early in the morning as a result of an increase in intracranial pressure in the supine position. Nausea and vomiting are also frequently reported upon waking (Brouwer et al, 2014a). Fever is an unreliable clinical sign, being absent in up to 68% of cases of cerebral abscesses (Widdrington et al, 2018). These non-specific symptoms can progress to focal neurological deficits (such as hemiparesis, speech deficit) or seizures. The latter occur in 25% of cases and may even be the first presenting symptom (Seydoux and Francioli, 1992).

At the point of presentation, clinical predictors of long-term disability and/or death include a reduced conscious level, seizures and presence of a focal neurological deficit (Widdrington et al, 2018). Alongside neurological symptoms, patients may present with symptoms relating to the original site of infection (eg sinusitis, otitis media). If previously treated with antibiotics, the clinical features of both the primary source of infection and evolving cerebral abscess can be more subtle, resulting in delayed presentation (Kraus and Tovi, 1992; Petersen et al, 1998). Patients with immune deficiency (eg HIV, steroid use, recent chemotherapy) are more likely to develop multiple cerebral abscesses and may therefore have a complex presentation with multiple focal neurological deficits (Patel and Clifford, 2014).

Examination

Patients with cerebral abscesses can present with a deteriorating level of consciousness, seizures or, more rarely, signs of systemic sepsis. As a result, it is advisable to use an airway-breathing-circulation-disability-exposure (ABCDE) approach to initial examination and resuscitation. Once stabilised, a full neurological examination can be performed, which may reveal focal signs related to the site of abscess formation (such as hemiparesis, dysphasia, visual field defects). As abscesses increase in size, or perilesional oedema worsens, patients can also develop signs of raised intracranial pressure including a reduction in Glasgow Coma Scale, papilloedema and pupillary abnormalities (Seydoux and Francioli, 1992).

Investigation

Following initial ABCDE assessment and resuscitation, neuroimaging should be requested early with the aim of identifying the size and location of the suspected abscess, as well as to help distinguish it from key differential diagnoses: primary or secondary brain neoplasms, radiation necrosis, demyelinating lesion, subacute infarct or resolving cerebral contusion or haematoma (Erdoğan and Cansever, 2008). While scan findings can favour a diagnosis of a cerebral abscess, the diagnosis is not confirmed until pus is aspirated from the lesion at the time of surgical drainage. Similarly, it is not possible to exclude an abscess on the basis of neuroimaging alone. Surgical aspiration would still be warranted if there is clinical suspicion of an abscess, despite inconclusive scan appearances.

Computed tomography head scan

Computed tomography head scans are not as sensitive as magnetic resonance imaging, but are often more accessible and quicker to perform. As a result, they are often the initial imaging modality of choice in the emergency department, particularly in patients with signs of systemic sepsis or elevated intracranial pressure. Administration of intravenous contrast is critical in order to improve visualisation of brain abscesses (Figure 1). The appearance of the lesion will vary depending on its stage of development, progressing from a small non-enhancing hypodense region in the early stages to a clearly defined ring-enhancing lesion with perilesional oedema once a definite abscess with a thick inflammatory capsule has formed (Britt and Enzmann, 1983).

Magnetic resonance imaging brain scan

A magnetic resonance imaging brain scan is the gold standard imaging modality since it allows detection of abscesses at earlier stages of development, improves pick-up of multiple abscesses and can also facilitate differentiation from other ring-enhancing pathologies such as malignant brain tumours (Leuthardt et al, 2002). It is therefore recommended in all patients with a suspected brain abscess and should be performed preoperatively unless associated with significant delay to surgery or the patient is considered clinically unstable as a result of systemic sepsis. On T2-weighted imaging an abscess appears as a high signal lesion with a thin rim of low intensity surrounded by an area of high signal representing reactive oedema (Figure 2). In contrast to brain neoplasms, abscesses can display a core of restricted diffusion on diffusion-weighted imaging (Greenberg, 2016).

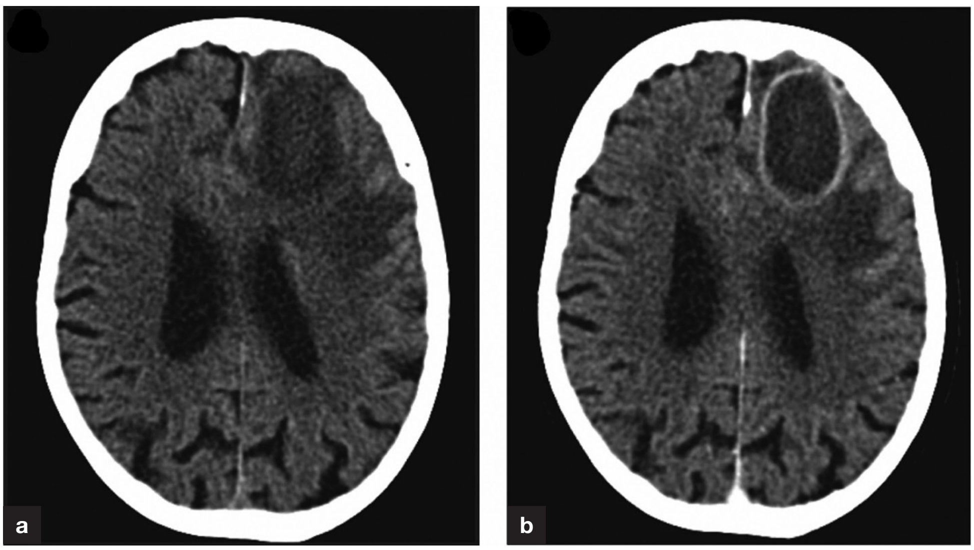

Figure 1. Computed tomography head of a 91-year-old woman with a cerebral abscess. a. Unenhanced axial computed tomography image shows a large hypodense lesion in the left frontal lobe with mass effect on the frontal horn of the left lateral ventricle. b. Following administration of intravenous contrast, the same lesion demonstrates ring enhancement with central hypoattenuation and surrounding vasogenic oedema.

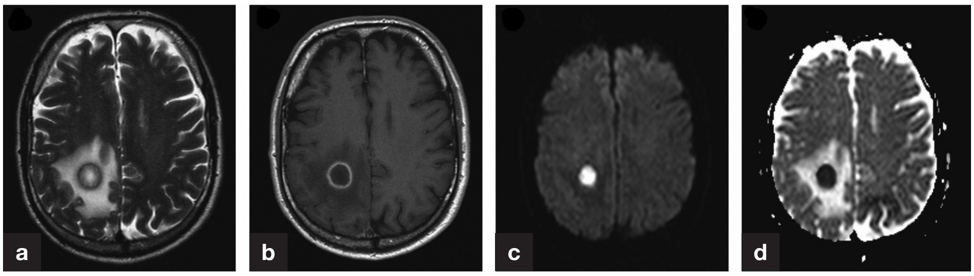

Figure 2. Magnetic resonance imaging head of a 45-year-old man with a cerebral abscess. a. An axial T2-weighted magnetic resonance image shows a solitary lesion in the right parietal lobe with a central region of increased intensity and low intensity peripheral rim, surrounded by vasogenic oedema. b. Contrast-enhanced T1-weighted magnetic resonance image of the same lesion shows ring-enhancement. The centre of the lesion is characterised by (c) high signal on diffusion-weighted imaging and (d) low signal on apparent diffusion-coefficient imaging.

Lumbar puncture

There is a limited role for lumbar puncture in the diagnosis of a brain abscess. Many patients present with signs of raised intracranial pressure, which contraindicates the procedure because of an associated risk of tonsillar herniation (Heilpern and Lorber, 1996). In addition, unless the abscess has ruptured into the ventricular system, results from any CSF sample obtained may be inconclusive (Ferré et al, 1999). The optimal method for identifying the causative organism(s) and antibiotic sensitivities is therefore to aspirate samples of pus from the abscess for microbiological culture during surgical drainage (Greenberg, 2016).

Source identification

In the absence of a history of penetrating brain injury or recent neurosurgery, all patients presenting with a cerebral abscess should be investigated for a primary source of infection. A detailed history should be taken, inquiring about any previous symptoms suggestive of infection in the teeth, sinuses, ear or bowel. An HIV antigen and antibody screening test should be offered to all patients early as, if positive, a broader range of candidate micro-organisms ought to be considered. Blood cultures should be obtained before starting antibiotic therapy. Despite yielding negative results in up to 86% of cases, occasional identification of an organism in blood cultures can help to locate a likely primary source and determine antibiotic sensitivities (Patel and Clifford, 2014).

Investigations to locate a primary source of infection will find an underlying cause in approximately three quarters of cases (Widdrington et al, 2018). The choice of tests may be partly guided by the specific micro-organism isolated from pus or blood cultures. Suspicion of contiguous spread from local anatomical structures such as the paranasal sinuses or mastoid air cells is supported by their opacification on computed tomography head imaging. In patients with suspected haematogenous spread, computed tomography of the chest, abdomen and pelvis can help to identify pulmonary and intra-abdominal sources of infection while an orthopantomogram is helpful in investigating for dental abscesses.

A transthoracic echocardiogram is recommended to establish whether there is any evidence of cardiac valve vegetations or congenital heart defects (such as a patent foramen ovale), which could facilitate haematogenous spread of septic emboli from systemic sources to the CNS. If this test shows no abnormality but there remains significant clinical suspicion of a cardiac source, a transoesophageal echocardiogram is also advised. If the isolated micro-organism is compatible with a potential bowel source that has not otherwise been identified, a colonoscopy should be considered. These investigations will typically be performed after neurosurgical intervention has taken place on the abscess itself and the patient has been stabilised, with the exception of infection within the paranasal sinuses. This is seen on the initial investigations and often surgically drained by the ear nose and throat surgeons at the same time as the abscess is drained.

Management

1. Resuscitate and stabilise the patient using an ABCDE approach
2. Obtain blood samples for blood cultures, full blood count, urea and electrolytes, liver function tests, coagulation screen, C-reactive protein, glucose and lactate levels
3. Commence empirical antibiotics. Only if surgical drainage is imminent in the next few hours, and the patient is clinically stable, may it be appropriate to delay antibiotics until after the surgical procedure. All brain abscesses should be managed in conjunction with local infection specialists
4. Corticosteroids can be used in the presence of increased intracranial pressure and therapy should be of short duration. They should not be routinely used as they can retard encapsulation, increase necrosis and reduce antibiotic penetration (Brook, 2017)
5. Consider starting anticonvulsant medication (eg levetiracetam) (Afshari et al, 2017)
6. Arrange an urgent magnetic resonance imaging scan of the brain with contrast and diffusion-weighted imaging. If there is a delay to scan, request a computed tomography scan of the head with contrast as an alternative
7. Refer the patient urgently to the local neurosurgery unit for consideration of surgical aspiration and antibiotic therapy. Ensure the patient is kept nil-by-mouth while awaiting transfer.

Primary sources of infection are common in the majority of patients, so it is important to identify and treat the initial focus of infection alongside the cerebral abscess to limit any further seeding of bacteria. For immunocompetent patients, until the source of infection and causative pathogen are found, empiric antimicrobial therapy consisting of a third-generation cephalosporin combined with metronidazole is usually recommended (Brouwer et al, 2014b). This should be guided by local microbiology guidelines. Duration of treatment is determined by the causative organism, size of abscess, surgical procedure(s) and response to treatment (Alvis Miranda et al, 2013), and close liaison with microbiologists is essential in guiding this. Arlotti et al (2010) have suggested that intravenous antibiotics should be administered for 4–6 weeks for a surgically-treated abscess and 6–8 weeks for a brain abscess which was solely treated medically. If the patient is immunocompromised or a less typical organism is suspected based on clinical or radiological features, early discussion with infection experts is recommended.

For patients who have had surgical drainage of a cerebral abscess, a postoperative contrast-enhanced computed tomography head (or magnetic resonance imaging head with gadolinium) should be obtained within 24 hours to establish a baseline for radiological surveillance. The authors advise repeating this imaging again after 1 week to ensure initial improvement since starting antimicrobial therapy. The timing and frequency of further interval contrast-enhanced computed tomography head scans should be guided by discussion with the neurosurgery, radiology and microbiology teams. Serial neuroimaging is valuable in monitoring for re-accumulation of the abscess. Subsequent follow-up imaging is usually determined on a case-by-case basis, taking into account clinical response and recommended duration of antimicrobial therapy. Anticonvulsant medication can be safely weaned to stop after 1 year in patients receiving prophylactic therapy or after 2 years of seizure freedom in patients who have had a seizure as a result of their cerebral abscess (Afshari et al, 2017).

Complications

All-cause mortality rates for patients with cerebral abscesses varies from 5% to 32% (Patel and Clifford, 2014). Approximately half of patients treated for a cerebral abscess have persistent neurological deficits, including focal or generalised epilepsy, hemiparesis, dysphasia, visual field defects and cognitive dysfunction (Patel and Clifford, 2014; Greenberg, 2016).

Conclusions

Brain abscesses can arise by direct inoculation, contiguous spread from local anatomical structures or haematogenous seeding from a primary infection elsewhere in the body. They can present with symptoms related to elevated intracranial pressure, as well as focal

Key points

- Brain abscesses can result from direct inoculation, contiguous spread or haematogenous seeding of bacteria, most commonly Streptococcus or Staphylococcus organisms.
- Presenting symptoms can include headache, fever, focal neurological deficits, seizures, as well as symptoms of raised intracranial pressure, such as headache and confusion.
- A contrast-enhanced magnetic resonance imaging brain scan is the most sensitive imaging method to visualise brain abscesses, and diffusion-weighted imaging sequences can facilitate differentiation from other ring-enhancing lesions such as neoplasms.
- Brain abscesses are a surgical emergency and patients should be urgently referred to a neurosurgical centre after systemic stabilisation and neuroimaging.
- Cases of brain abscess should be discussed or managed in conjunction with local infection specialists.
- Complications of brain abscesses include secondary bacterial meningitis, recurrent seizures, permanent neurological deficits and death.

neurological deficits. The most sensitive way to diagnose a brain abscess is by magnetic resonance imaging with contrast enhancement, but computed tomography may be preferable in emergent situations. Initial management involves stabilisation of the patient using an ABCDE approach, arranging urgent neuroimaging and referring to a neurosurgery centre for ongoing care. The faster the diagnosis and subsequent treatment, the lower the risk of complications including permanent neurological deficits, epilepsy and death.

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Conflicts of interest

The authors declare no conflicts of interest.

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Curriculum checklist

This article addresses the following requirements from the neurosurgery (2015) curriculum: initial stage:

- Basic sciences: microbiology
- Basic sciences: imaging
- Core neuroscience knowledge: pathophysiology of intracranial disorders.

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