CNS infections 2

Brain Abscess/subdural empyema

Sources /tables and figures:

Harrisons Infectious diseases 2nd ed Ch 31

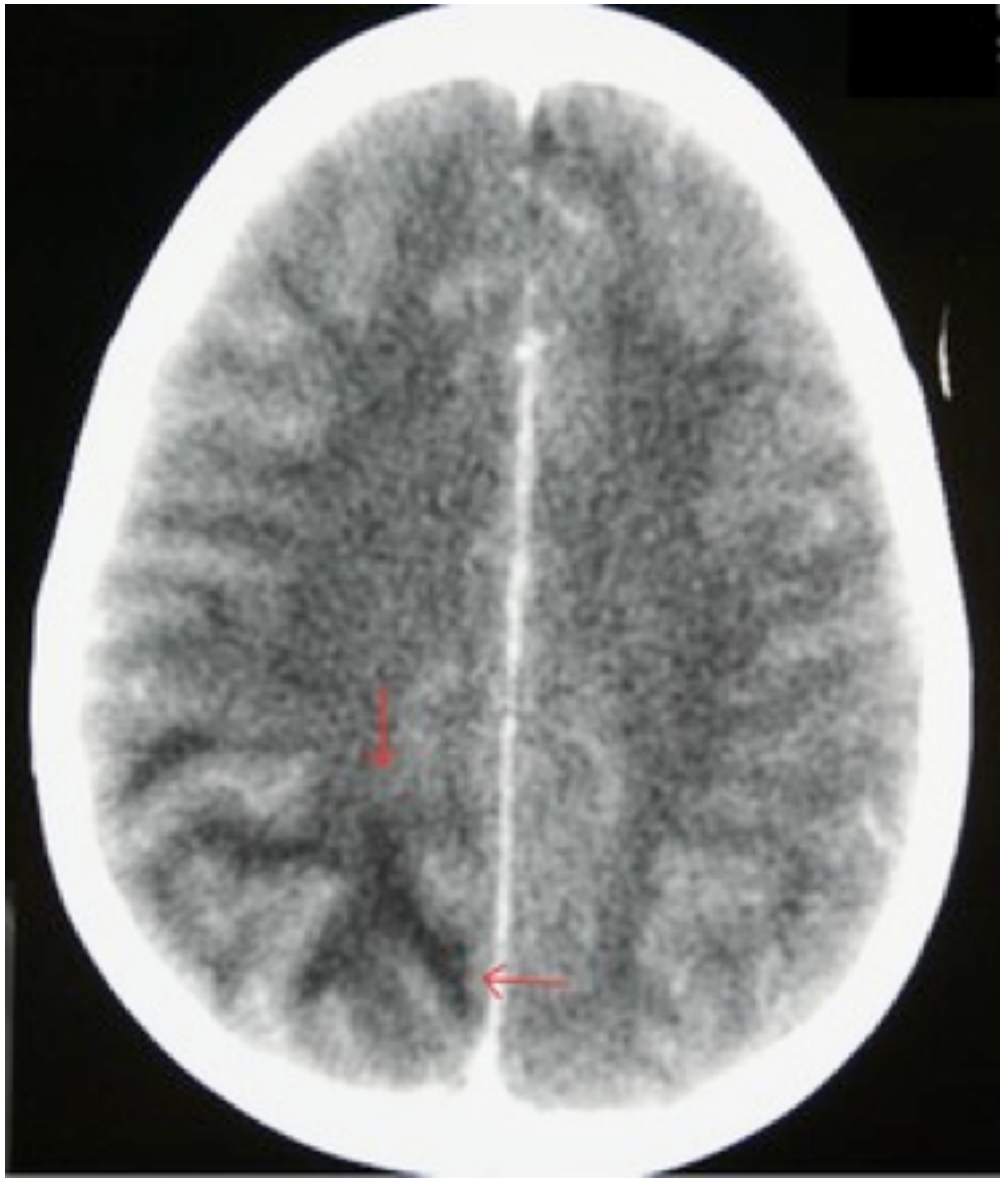
Oxford Handbook of Infectious diseases and microbiology 2nd ed Ch 19

Brain abscess

- A focal (not all over the brain), suppurative (pus forming) intracerebral infection.
- That begins as a local area of cerebritis which develops into a collection of pus surrounded by a well-vascularized capsule (abscess).
- If bacteria remain unfocalized the resulting syndrome is called cerebritis only.
- Entry of bacteria to the brain can either be a direct spread from:

→contiguous areas in the skull (close anatomic site : ear, sinus, teeth, or post-neurosurgery)

→ seeding from the blood from another point of infection, further anatomic sites (e.g. endocarditis, lung, abdomen, skin).



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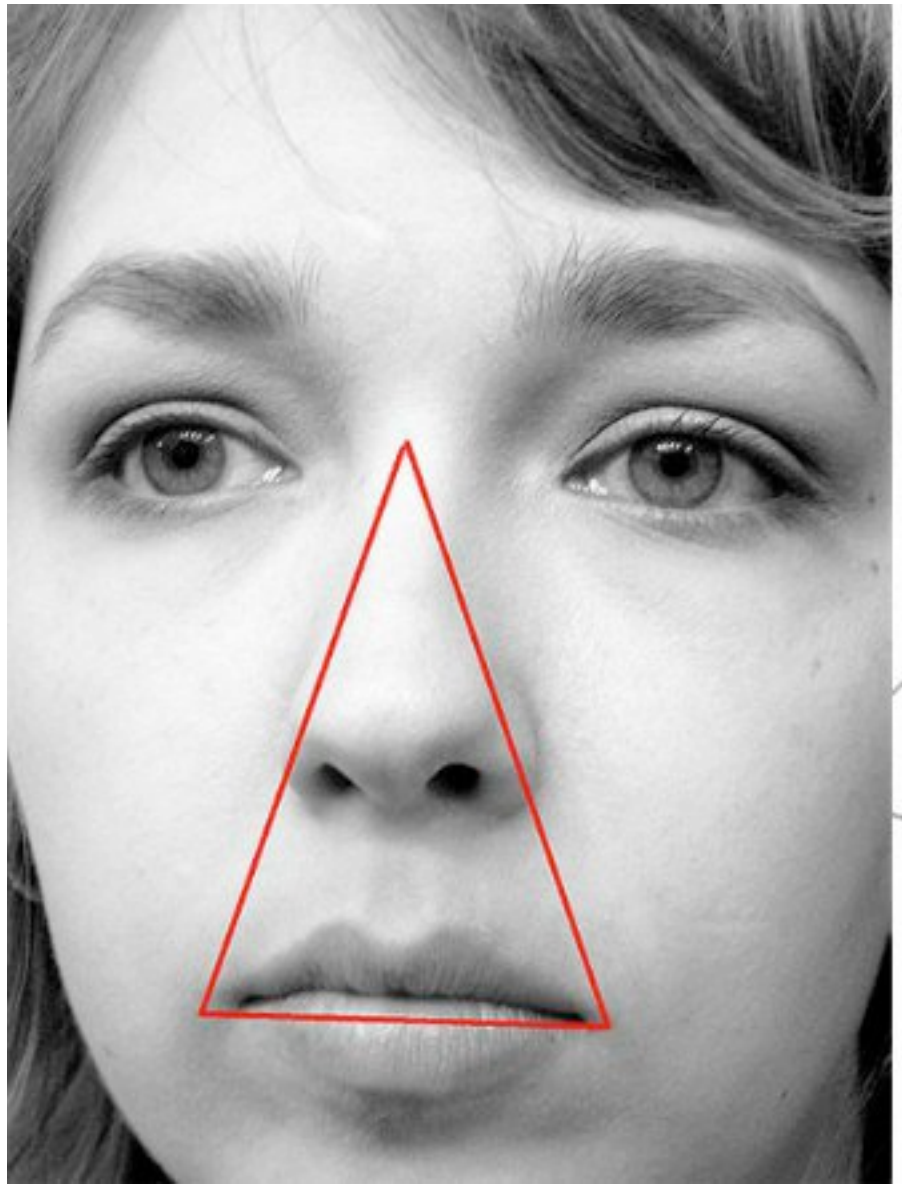

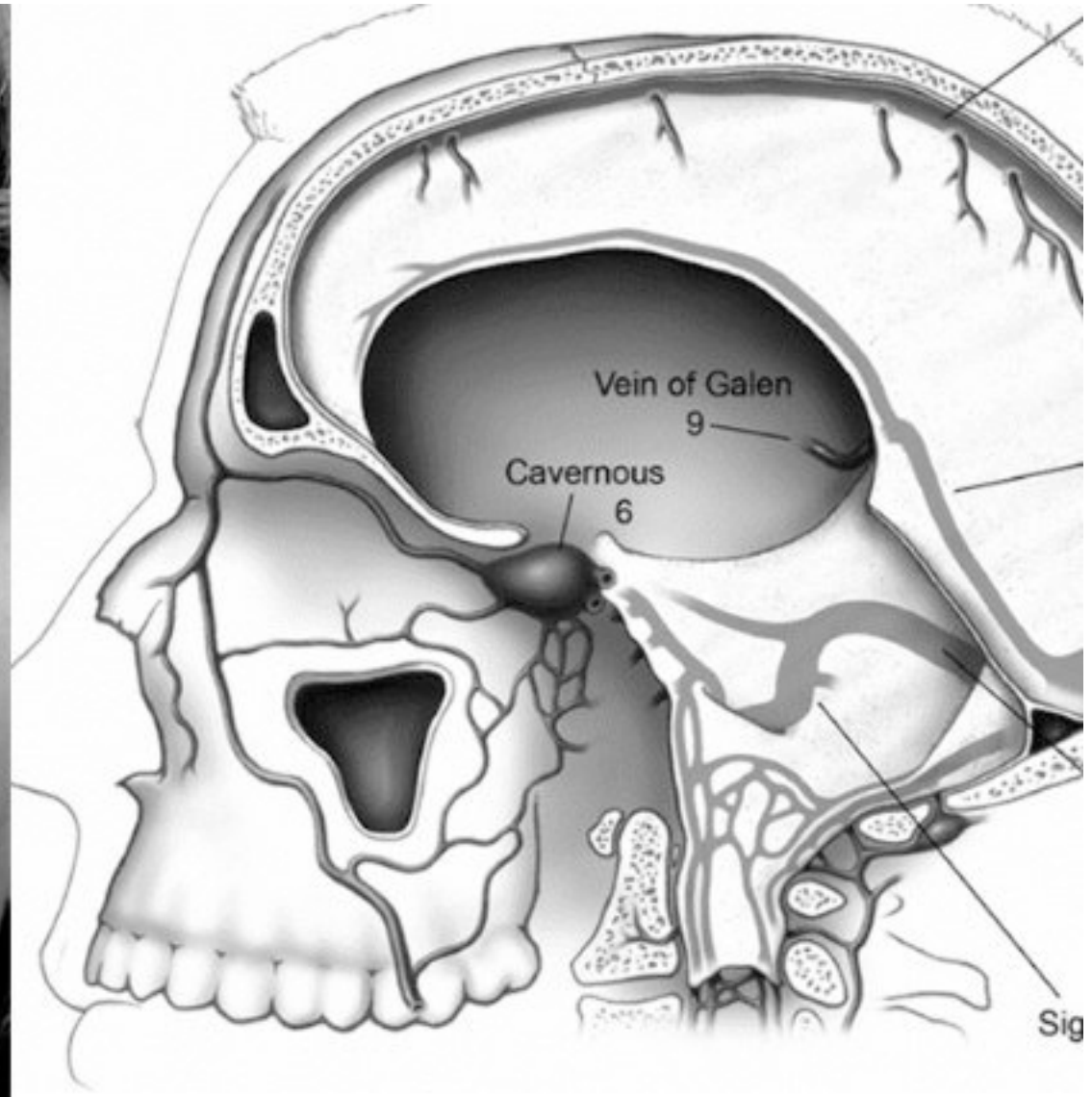

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Epidemiology

- Although brain abscesses are uncommon it is however a severe, disease (incidence of ~0.3–1.3:100,000 persons per year).
- Predisposing conditions are usually present that push patients defences and cause abscess formation in the brain.
- Contiguous site infections of the skull: **otitis media**, mastoiditis, paranasal sinusitis, **dental infections**, pyogenic infections in the chest or other body sites, penetrating head trauma or **neurosurgical procedures** are considered the major predisposing factors (more than hematologic spread)
- Brain abscess is seen more in males in the age group of 30-40 years.

- Case fatality rates range from 0% to 24% (usually large discrepancy in numbers like this indicate discrepancy in level of care).

Pathogens involved

- Most commonly **a single organism** is involved, less commonly (23%<) polymicrobial, with predilection to the FRONTAL lobe.

- However, source also indicates site (ear-temporal lobe – see pathogens involved with site on next slides).

- Left sided > right side
- Usually due to trauma perhaps being more on the left due to handedness

- Pathogens involved are mostly aerobes (stertococci) > anaerobes (bacteroides, peptostreptococcus)
- This is due to the fact that the brain is highly perfused tissue (lots of oxygen), anaerobes will require poor circulation to succeed in early infection
- → thus anaerobes are commonly seen in polymicrobial abscesses- anywhere- they wait for aerobes to create favorable conditions and then they start growing.
- A facultative anaerobe like strep and less so staph can overcome the oxygen requirements more requirment

Spectrum of organisms differs by anatomic source.

Source	Most Commonly Cultured Organisms
Paranasal sinus infection	Streptococcus spp
	Staphylococcus spp
	Enterobacteriaceae (especially Hemophilus spp, *Pseudomonas aerugonisa*)
Otogenic infection	*Proteus mirabilis*
	Streptococcus milleri group organisms
	Streptococcus pneumoniae
	Staphylococcus aureus
Dental infection	Streptococcus spp
	Bacteroides fragilis
Traumatic brain injury	*Staphylococcus aureus*
	Staphylococcus epidermidis
	Enterobacteriaceae (most commonly *P aerugonisa*, Enterobacter spp)
Neurosurgical procedure	*Staphylococcus aureus*
	Staphylococcus epidermidis
	Pseudomonas aeruginosa
	Propionibacterium acnes
	Streptococcus spp.
Hematogenous spread	*Staphylococcus aureus*
	Streptococcus viridans
	Klebsiella pneumoniae

Table 19.10 Factors predisposing to cerebral abscess

Predisposing condition	Microorganisms
Otitis media/mastoiditis	Streptococci, *Enterobacteriaceae*, *Bacteroides* spp., *P. aeruginosa* Proteus esp, usually non fecal origin
Sinusitis	Streptococci, *Haemophilus* spp., *Bacteroides* spp., *Fusobacterium* spp.
Dental sepsis	Streptococci, *Haemophilus* spp., *Bacteroides* spp., *Fusobacterium*, *Prevotella*
Pulmonary/pleural sepsis	Streptococci, *Fusobacterium*, *Actinomyces*, *Bacteroides*, *Prevotella* spp., *Nocardia* spp.
Endocarditis	*S. aureus*, streptococci
Congenital heart disease	Streptococci, *Haemophilus* spp.
Urinary tract	*Enterobacteriaceae*, *P. aeruginosa*
Head trauma	*S. aureus*, *Enterobacter* spp., *Clostridium* spp.
Neurosurgery	*Staphylococcus* spp., *Streptococcus* spp., *P. aeruginosa*, *Enterobacter* spp.
Immunocompromised hosts	*T. gondii*, *L. monocytogenes*, *N. asteroides*, *Aspergillus*, *C. neoformans*, *C. immitis*, *Candida* spp., mucormycosis, zygomycosis
HIV infection	*T. gondii*, *Nocardia* spp., *Mycobacterium* spp., *L. monocytogenes*, *C. neoformans*

In immunocompetent

- The encountered pathogens are:

Streptococci.

- Viridans (40%) group Streptococci is the dominant pathogen in this group.

- Anaerobic - peptostreptococcus usually seen in immune-competent patients

- Group A, *S. pnuemoniae* are rarley seen (immune competent patient usually has encountered these organisms and have antibodies formed)

Although streptococci have virulence factors which enable direct spread but proximity is the most dominant factor as seen by pathogen make up and usual niche occupied (viridans group, which is most commonly seen in the skull and especially the pharynx-)

those that depend on evading immune system in the blood –*S. pneumoniae*- are rarley seen inside the brain, however these are common in meningitis (> hematogenous route).

Immune competent patient, other causes

- Enterobacteriaceae [*Proteus, E. coli, Klebsiella*. (25%)]
- Anaerobes [Bacteroides spp. Fusobacterium spp. (30%)],
- Staphylococci (10%).

In immunocompromised

(typically HIV infection, cancer, or immunosuppressive drugs):

-Nocardia

-Toxoplasma gondii,

-Aspergillus (mold mc)

-Candida

-Cryptococcus neoformans (yeast, aerobe).

Typically if you see molds, yeasts or some parasites in tissues that are not typically exposed to them (skin), you must ask your self, why did the immune system fail for so long to mount an effective immune response against a less aggressive, typically slower growing organisms?

→ Another factor is emerging drug resistance in these organisms, that is slowly making them rival bacterial infections.

Etiology

- 1- from a contiguous cranial site of infection, such as paranasal sinusitis, otitis media, mastoiditis, or dental infection (most common ~ 50%)
- 2- following head trauma or a neurosurgical procedure (with direct spread, account for 25- 50%)
- 3- as a result of hematogenous spread from a remote site of infection (25%).
- In up to 25% of cases, no obvious primary source of infection is apparent (cryptogenic brain abscess).

Hematogenous abscesses

- These are often multiple (due to seeding), thus multiple abscesses often (50%) are traced to a hematogenous origin, and have certain characteristics:
- -These abscesses have a pattern of sprouting in the distribution of the middle cerebral artery (posterior, frontal , parietal lobes).
- -They are often found at the junction of the white and grey matters
- -They are often poorly encapsulated.
- The pathogens present in these abscecces depend on the source of infection (cardiac,skin..etc)
- Typically caused by pneumonia and endocarditis

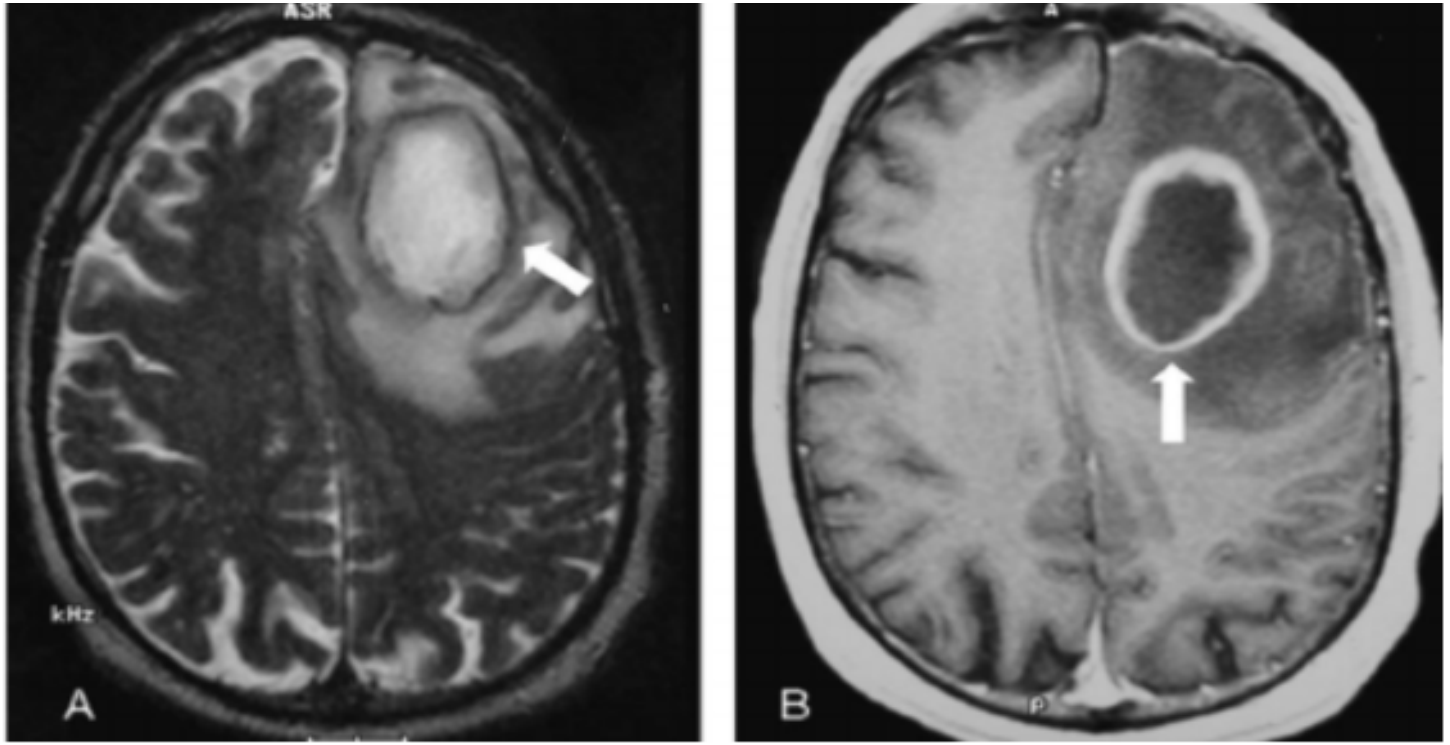
Clinical features

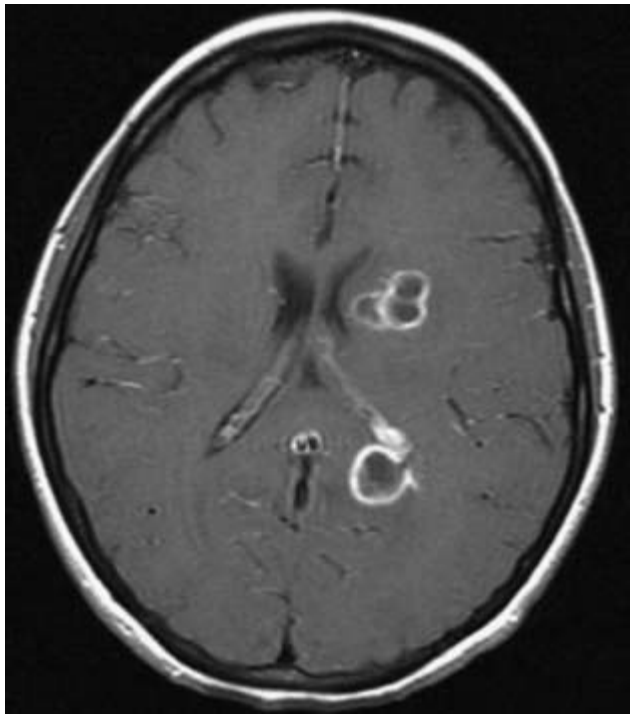
- Surprisingly, the initial clinical presentation-early cerebritis- is NON SPECIFIC! This results in delayed diagnosis. (the signs and symptoms **at first** don't point to brain lesion)
- The classic clinical triad of headache, fever, and a focal neurologic deficit is present in **less than 50% of patients**.
- Of these symptoms, headache is the most common (70%) and may be localized **to the side** of the abscess. Fever in about 50%, whereas focal neurological deficits (50%), seizures (25%), and neck stiffness (15%) are seen.

- Nausea, vomiting, cranial nerve palsies, and papilledema indicate raised ICP.
- Changes in mental status similar to meningitis is associated with higher mortality (lethargy, coma).
- Symptoms progress from nonspecific symptoms to more specific or variable symptoms progresses in a variable manner, which can range in time from hours to days to even weeks!, however, most patients present in 11-12 days from onset of symptoms.

Diagnosis

- • Imaging
- An urgent CT scan with contrast should be done to confirm the Dx.
- Early cerebritis (before focal abscess formation) appears as an area of low density, which does not enhance with contrast.
- As the lesion progresses and enlarges a capsule is formed that enhances with contrast CT
- MRI is more sensitive (it is not done in first line management as symptoms are non specific and no indication for MRI is present) ,MRI can visualize the brain stem better.
- • in the presence of focal symptoms or signs LUMBAR PUNCTURE IS CONTRAINDICATED →risk of brainstem herniation.
- **If bacterial meningitis is suspected, blood cultures should be taken and an LP *deferred* until a *mass lesion is excluded* by CT/MRI scan (or look at the fundus for papilledema)**





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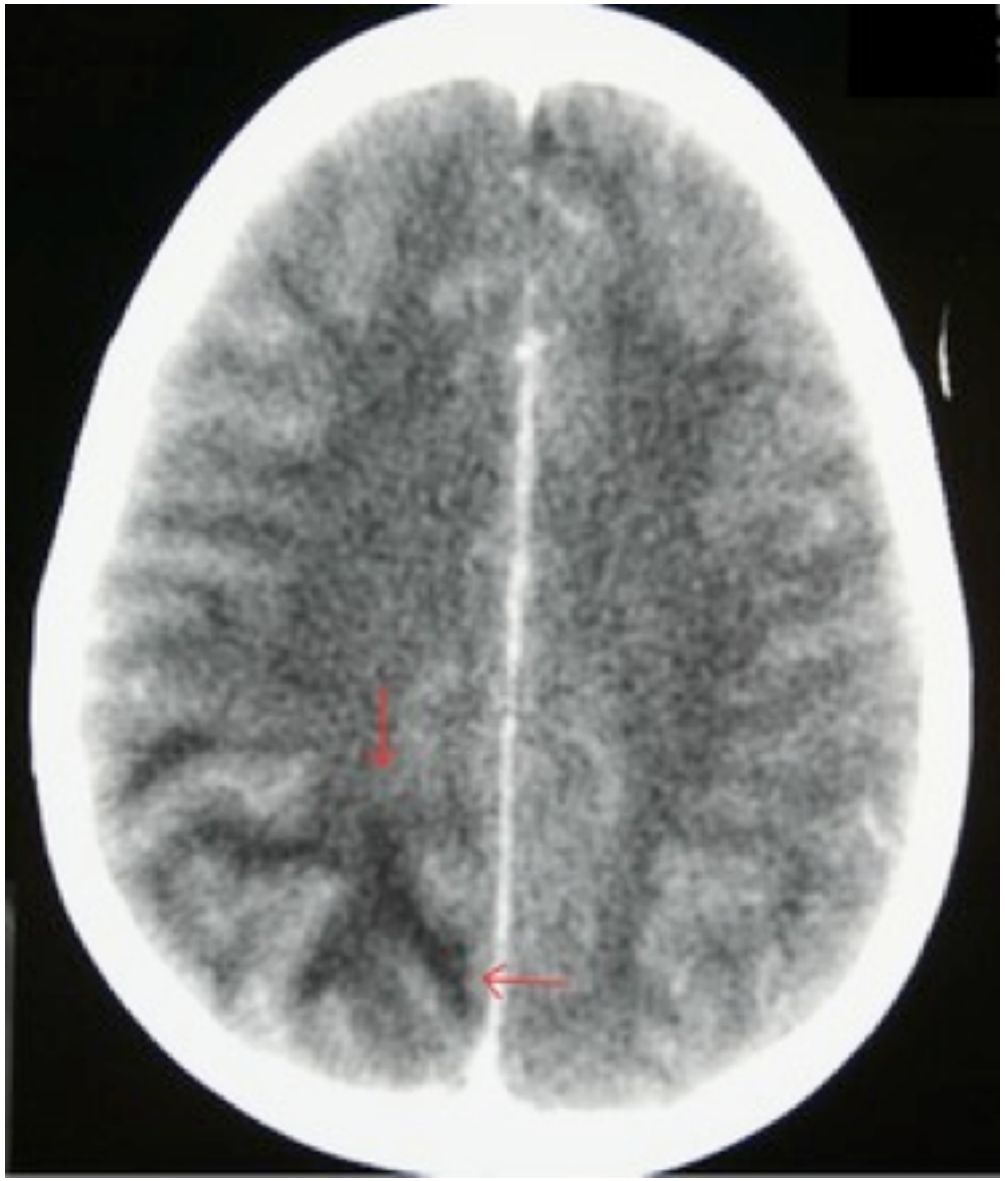
https://clinicalgate.com/wp-content/uploads/2015/03/B9781416053163000447_f043-001-9781416053163.jpg

Figure

Caption

FIGURE 8. Left frontal lobe abscess. A, Notice the hypointense rim of the abscess wall in this a postcontrast T1WI showing the thinner medial wall of this abscess (arrow).



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Dx. Cont.

- Culture—
- Once the lesions are identified, CT guided surgical aspiration is performed.
- Aspiration samples are cultured for bacterial growth as well as looking for TB and fungal cultures.
- 16S rRNA PCR may be helpful in culture-negative cases.
- (16s ribosomal RNA of the 30s subunit, used for phylogenetic analysis due to low evolution rate and can be used to distinguish between species with high specificity)
- Blood cultures should be performed as well (septic work up/should/would have been done)
- • in cases of cerebral toxoplasmosis and neurocysticercosis (Neurocysticercosis serology is used).

- Most accurate step is to perform a gram stain on CT guided aspirate (will show organism as it is pus collection!)
- Aerobic, anaerobic bacterial cultures and mycobacterial and fungal cultures should be done on the sample (each has a specific medium and growth conditions).
- Up to 10% of patients will also have positive blood cultures (80-90% in Listeria).
- Additional laboratory studies may provide clues to the diagnosis of brain abscess in patients with a CNS mass lesion:
- - 50% show peripheral leukocytosis
- - 60% an elevated ESR
- - 80% an elevated C-reactive protein.

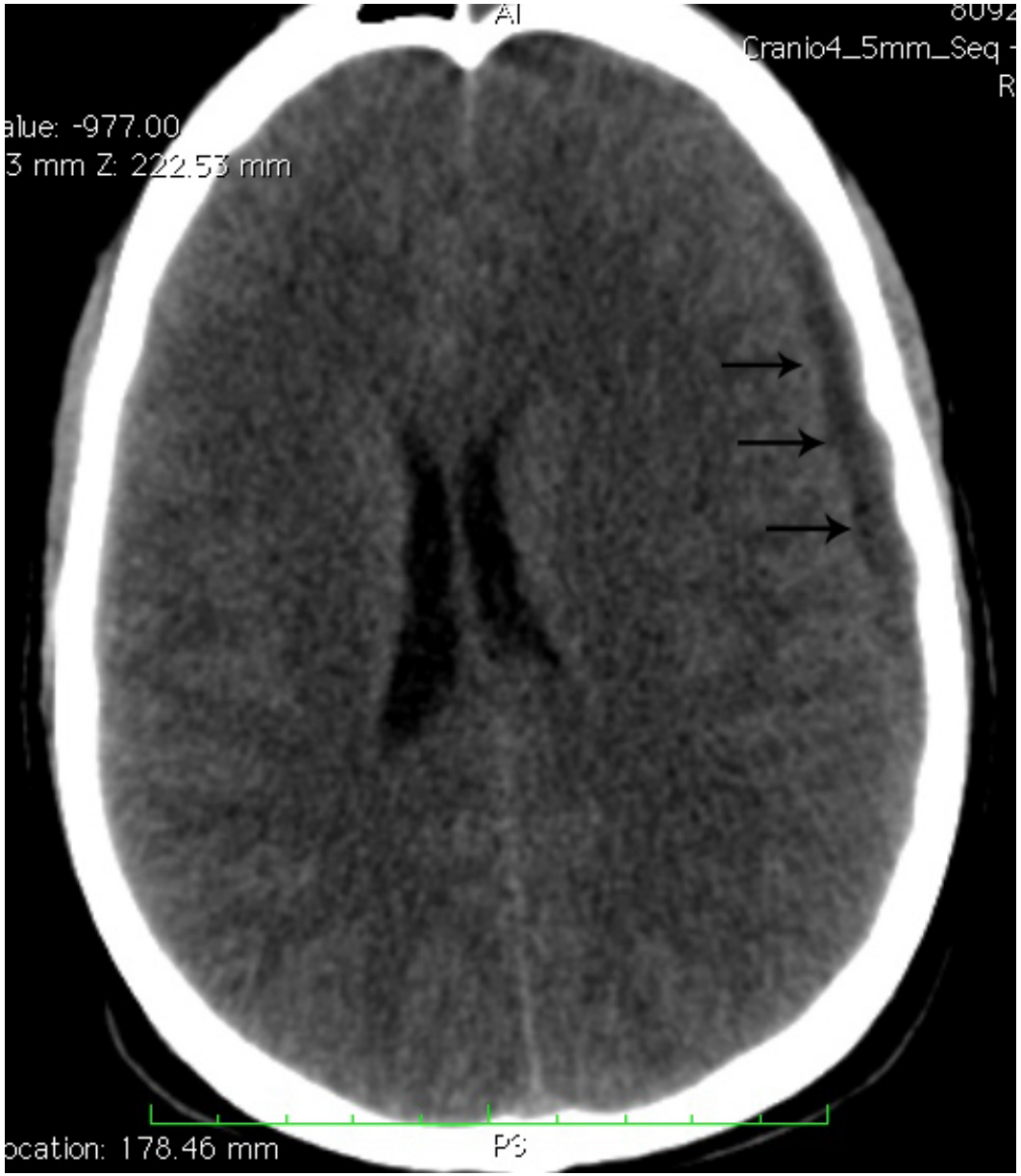
Treatment

- Depends on the type of abscess:
- -For brain abscess arising from local skull infection (dental, sinus, ear)
- → empirical therapy with **ceftriaxone 2g bd(2/day) IV** and **metronidazole 500mg tds (3/day) IV** is appropriate.
- -For brain abscesses arising from haematogenous spread (such as endocarditis),
- → vancomycin 15–20mg/kg/dose every 8–12h (up to 2g/dose) can be added to the regimen above.
- -For brain abscesses occurring post-neurosurgery
- → vancomycin 15–20mg/kg/dose every 8–12h (up to 2g/dose) + ceftazidime 2g tds IV or meropenem 2g tds IV is appropriate.

- Once culture results are available (specific pathogen is identified):
- →sensitivity test is done on the pathogen and appropriate antimicrobial therapy is given for 2–4 weeks IV, followed by 2–4 weeks PO.
- Patients with multiple lesions or multiloculated lesions or those who are immunocompromised may require longer courses.
- • Adjunctive corticosteroids should be given to patients with significant edema and mass effect.

Subdural empyema

- Defined as a collection of pus in the space between the dura and the arachnoid membranes



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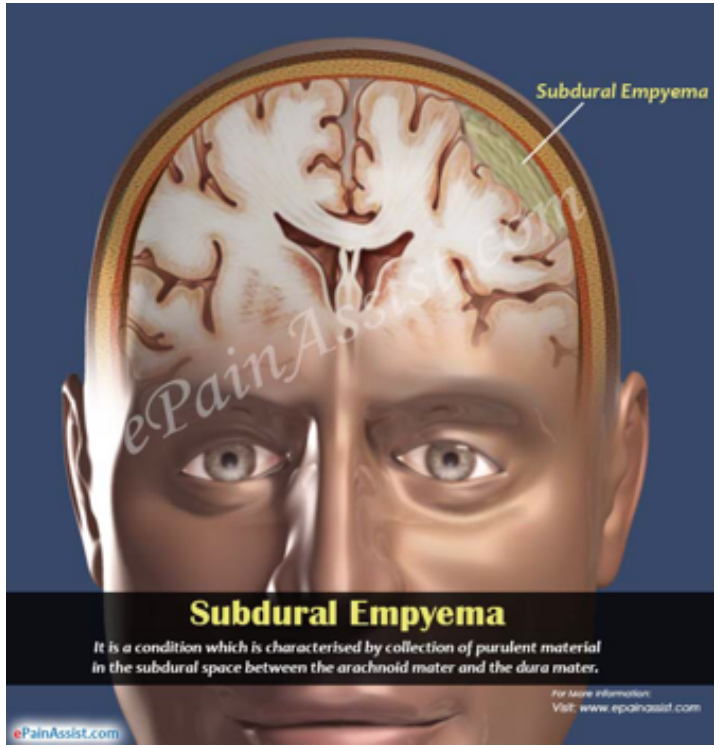


https://www.epainassist.com/brain/subdural-empyema

Epidemiology

- More rare than abscess =15–20% of localized/focal intracranial infections.
- Risk factors:
- Similar to brain abscess, local route from sinusitis, otitis media, mastoiditis, skull trauma, neurosurgery,
- Additional local risk factions: infection of preexisting subdural haematoma, nasal surgery, ethmoidectomy, or polypectomy (from nasopharynx).
- A complication of meningitis in infants (MRI from previous lecture).

Etiology

- Organisms usually seen are also similar :
- Streptococci, staphylococci, aerobic Gram –ve bacilli, and anaerobes.
- Polymicrobial infections are common. (abscess single organism more- as it is more distance, less distance in empyema=more bacteria found)
- Trauma/procedure related empyema is usually caused by staphylococci or aerobic Gram-negative bacilli.

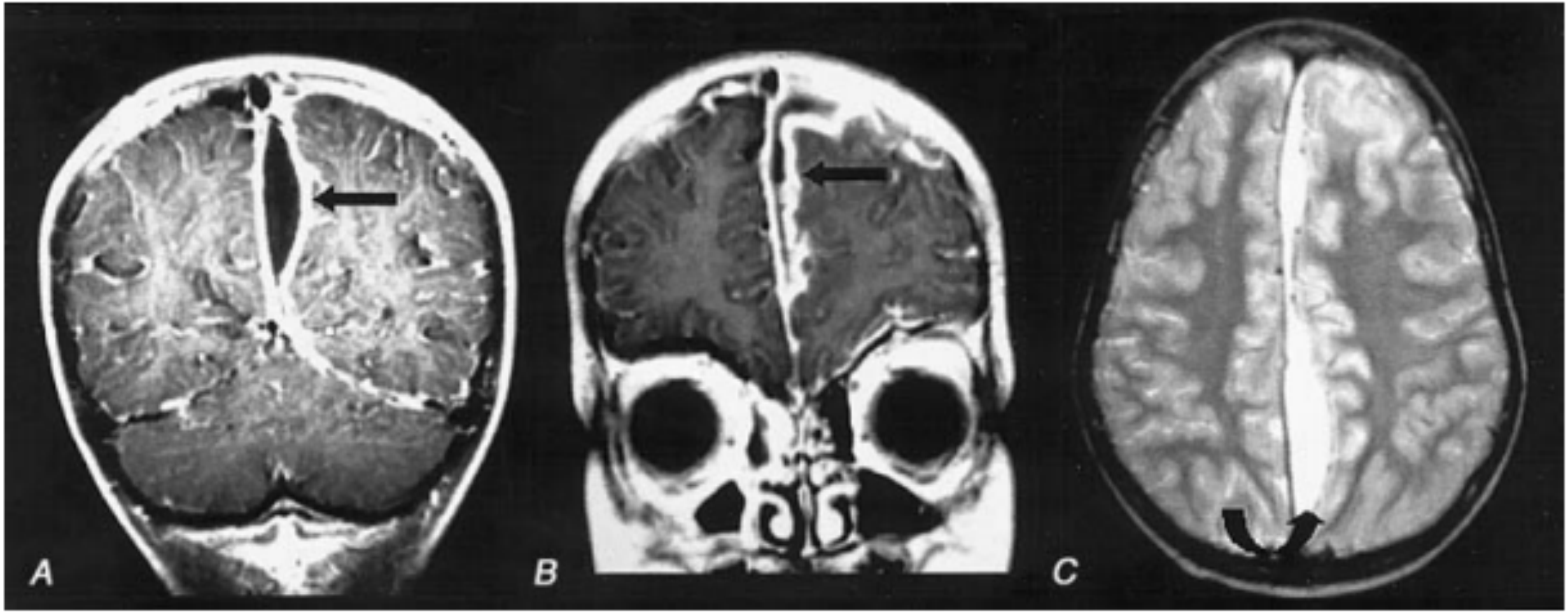
Clinical features

- **Acute** onset fever (bacteria/infection)
- Headache -mass effect, thus may be localized
- and vomiting (raised intracranial pressure)
- Note these symptoms (without fever also are seen in subdural hematoma)
- Additionally: altered mental state (disorientation, drowsiness, coma), and focal neurological signs (hemiparesis, cranial nerve palsies, dysphasia, homonymous hemianopia, cerebellar signs) these indicate damage to underlying brain tissue.

- 80% of patients have meningeal symptoms/signs.
- Seizures can occur in almost 50% of cases.
- There may be rapid neurological deterioration with signs of raised ICP and cerebral herniation (emergency).
- Complications are:
- septic venous thrombosis (proximity to veins + sluggish blood movement around the empyema site)
- And can progress to nonfocal (cerebritis) or focal cerebral abscess.
- In infants with subdural empyema, persistent fever, decline in neurological status, and seizures are seen.
- Spinal epidural abscess presents with radicular pain and signs of spinal cord compression

Diagnosis

- Consider the diagnosis in any patient with meningism and focal neurological signs.
- **AGAIN LP is contraindicated**.
- CT or MRI brain scan shows a crescentic or elliptical area of hypodensity with contrast enhancement.
- MRI is more sensitive than CT.


A
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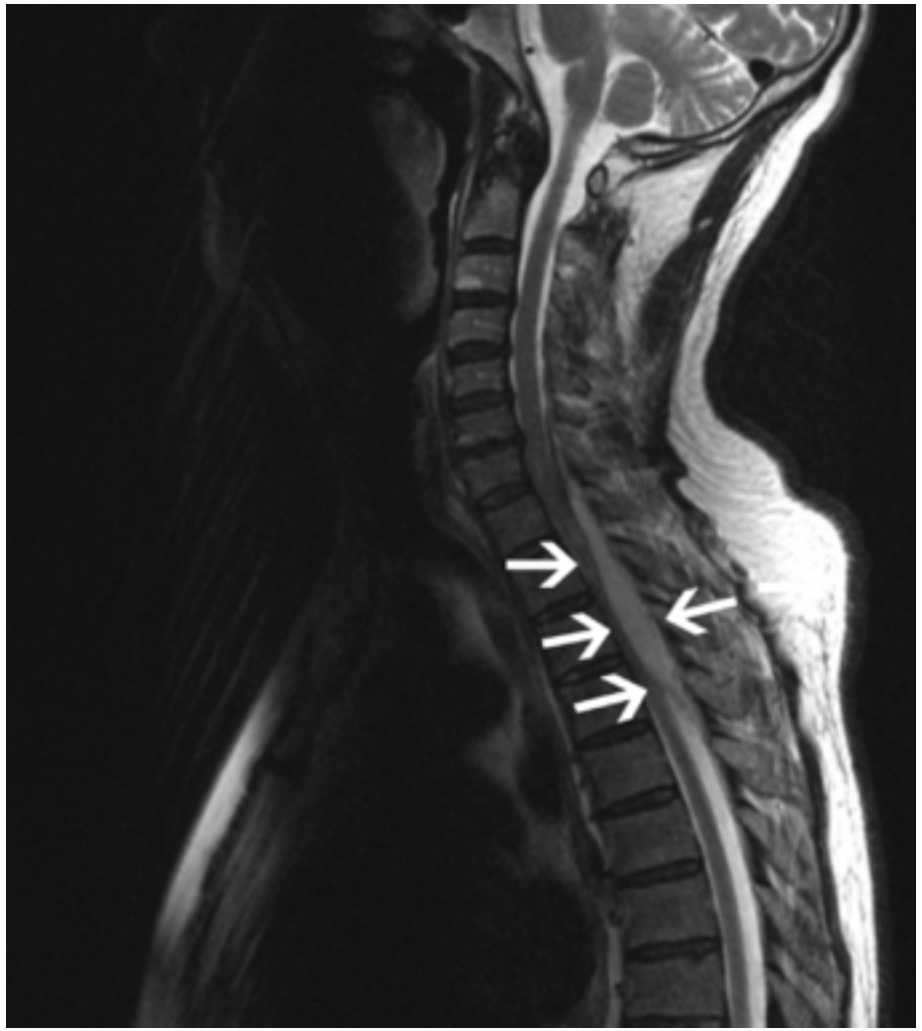
Management

- Subdural empyema is an emergency → immediate surgical management.
- As in abscess, must send samples for urgent microscopy and culture.
- Commence empiric IV antibiotics immediately after aspiration.
- This would be based on the likely infecting organisms (ceftriaxone and metronidazole).
- Vancomycin should be added for suspected staphylococcal infection (especially with history of neurosurgical procedures).
- One identification and sensitivity are ready = specific treatment to culture results.
- As in all cases of neurological infections: Prognosis is better if patient is conscious at presentation (>90% for patients who are awake/alert)

Epidural abscess

- collection of pus between the dura mater and the overlying skull or vertebral column. May be complicated by subdural empyema.



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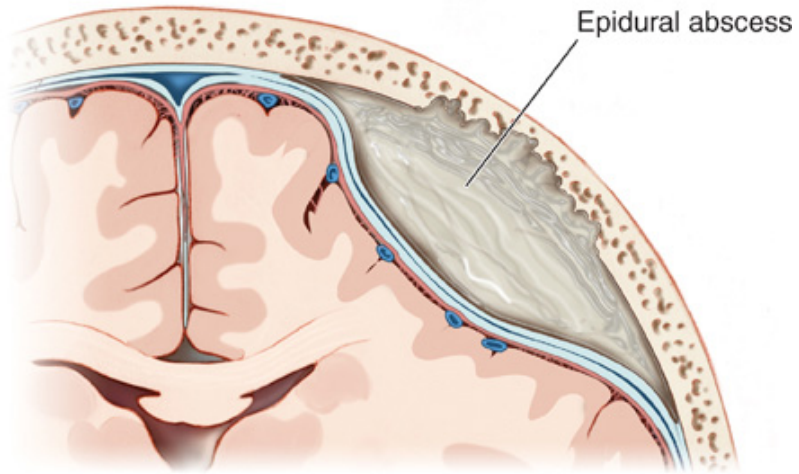


Source: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine, 18th Edition*: www.accessmedicine.com

http://accessmedicine.mhmedical.com/data/books/harr/harr_c381f007.jpg

Epidemiology

- The epidemiology of cranial epidural abscess is similar to that of subdural empyema.
- However, spinal epidural abscess usually occurs due to haematogenous spread or due to progression of vertebral osteomyelitis (bone infection).
- Risk factors:
- -bacteraemia
- -DM
- -skin infection (has to penetrate one layer-bone-)
- spinal procedures (surgery/epidural medication/trauma/LP).

Etiology

- Similar microbiology spectrum that is seen in subdural empyema
- **S. aureus is the commonest cause of spinal epidural abscess.**
- Others include aerobic and anaerobic streptococci, aerobic Gram-negative bacilli (e.g. E. coli and P. aeruginosa); 5–10% are polymicrobial.
- Unusual causes include Nocardia, MTB, and fungi (endemic or immunocpmpromised).

Clinical features

- The presentation maybe nonsepecific, with local infection masking the symptoms (by the primary focus of infection, e.g. sinusitis, otitis media).
- Headache is common, and focal neurological signs and seizures eventually develop, followed by signs of raised ICP.
- Spinal epidural abscess can be acute or chronic depending on source:

→hours/days with haematogenous spread

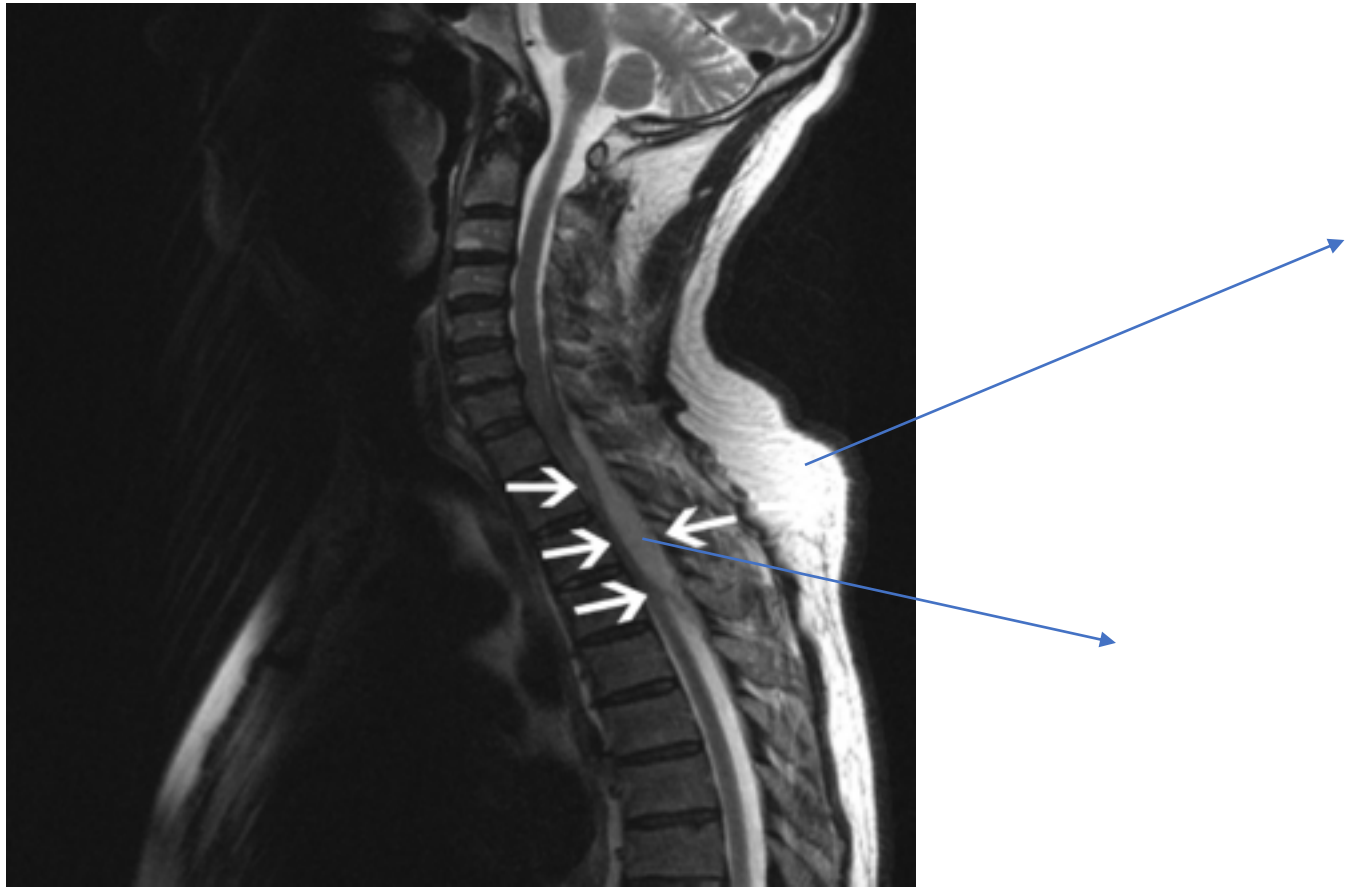
→week/months with vertebral osteomyelitis.

Pain is the commonest symptom (70–90%), followed by fever (60–70%).

Stages are related to progression of the abscess and its effect on the spinal nerve roots, thee four clinical stages: (1) back pain and tenderness→ (2) nerve root pain → (3) spinal cord symptoms (motor or sensory, sphincter dysfunction in lower spine) → (4) paralysis.

Diagnosis

- Gadolinium-enhanced MRI is the gold standard tool for Dx.



Management

- As with all abscesses the basic Rx is drainage and Abx.
- → Cranial epidural abscess—surgical drainage and antibiotics (for 3–6 weeks).
- → Spinal epidural abscess—surgical decompression (laminectomy) and antibiotics.
- Empirical therapy should cover staphylococci (e.g. vancomyin) this is due to the close proximity to skin, staphlycocci are common.
- Also aerobic Gram-negative bacilli (e.g. ceftriaxone, ceftazidime, or meropenem).
- The outcome of spinal epidural abscess depends on the level of neurological deficit before decompression.

CSF shunt infections

- Infection is a common complication of neurosurgical procedures that are used to treat hydrocephalus
- These can occur in up to 75% of cases!
- Most type of devices can be infected, these are foreign bodies, pathogens are a common complication for any FB introduced into the body, more so in the CNS, where immunity my be less quick to respond.
- Seen in ventricular shunts, Ommayma drains..etc
- Some classify the shunt infections as internal (CSF abnormalities) or external (soft tissue abnormalities).

Etiology

- As you might expect, SKIN flora is typical culprit
- • *S. epidermidis* is the MCC.
- • *S. aureus*, including MRSA.
- • *Streptococci, enterococci*.
- • *P. acnes* (Propionbacterium acnes, involved in …acne, the skin condotion)
- • Gram-negative organisms, including P. aeruginosa.
- • Mycobacteria.
- • Fungi.

Pathogenesis

- The pathogenesis can be predicted from the microbiology of these infections:

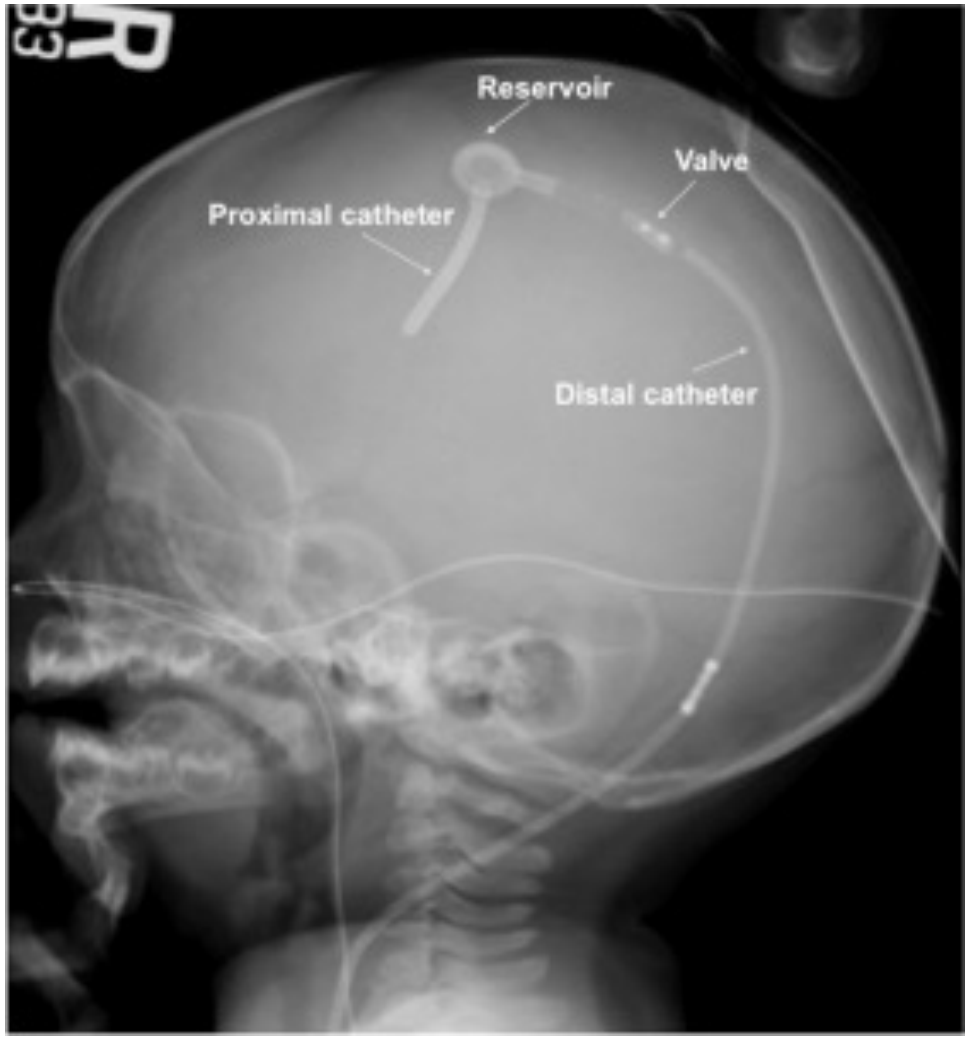
- Typically
- → contamination (at time of implantation of the device)
- → externalization (erosion of shunt through the skin)
- → retrograde (perforation of VP shunt through the bowel)
- → haematogenous (rare).

Clinical features

- Depend on site of infection, age of the patient, and whether the shunt failed and signs of increase ICP is evident
- Symptoms:
- -fever, headache signs of infection
- nausea, vomiting (ICP signs) neck stiffness (meningeal signs) and impaired conscious level (late sign)

Laboratory diagnosis

- direct aspiration of the shunt and CSF examination
- CSF samples should be taken for urgent microscopy, culture, protein, and glucose
- . Blood tests and cultures in conjunction with CSF analysis (ESR, leukocytes,CRP..etc)
- BCs—90% positive with Venticuo Atrial shunt infections.
- • CT/MRI
- • CXR if VA or ventriculopleural shunt.
- • Abdominal ultrasound/CT scan if abdominal symptoms/signs and VP or lumbar peritoneal shunt. • Consider echocardiogram if VA shunt.



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Management

- Removal and replacement of shunt once infection has cleared and CSF is sterile again (with Abx treatment)
- Abx
- Empiric antibiotic therapy should include : vancomycin IV and intrathecally, IV meropenem with abdominal symptoms or G-ve seen in CSF
- Specific therapy once culture and sensitivity is back