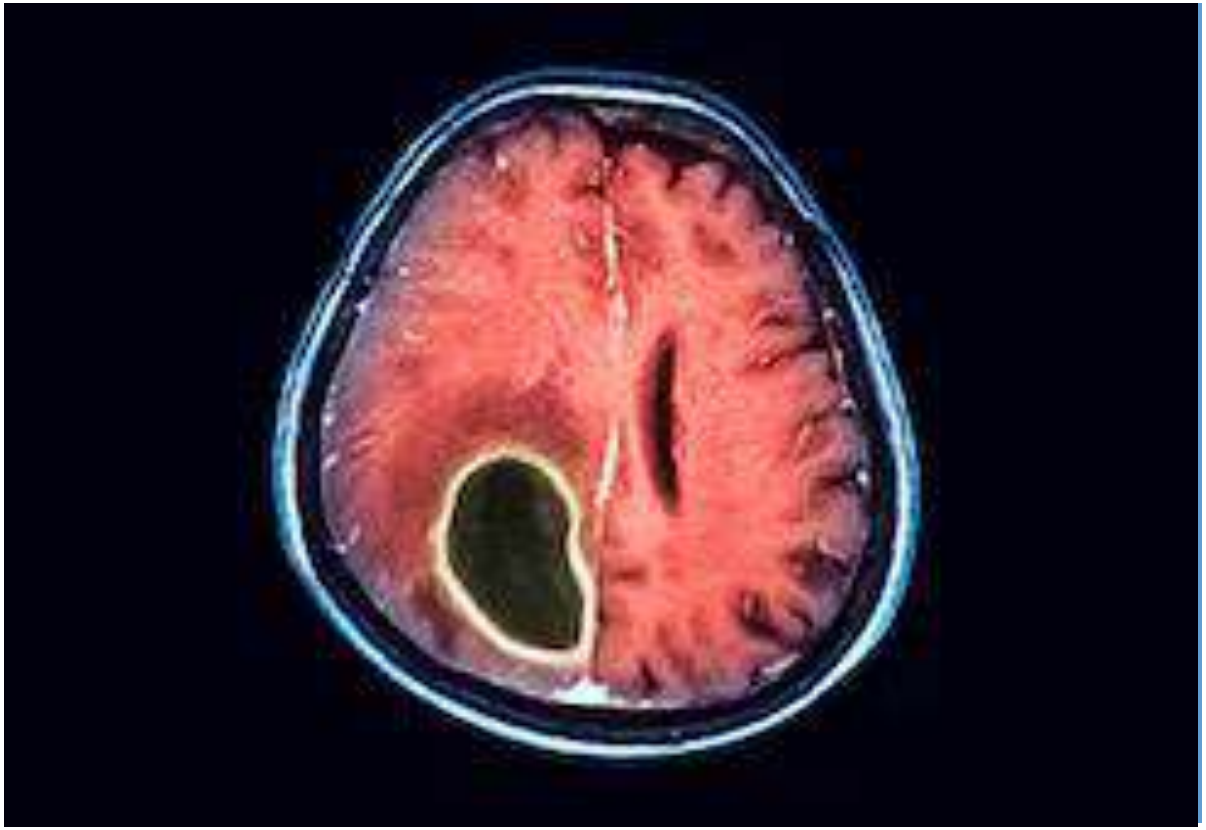
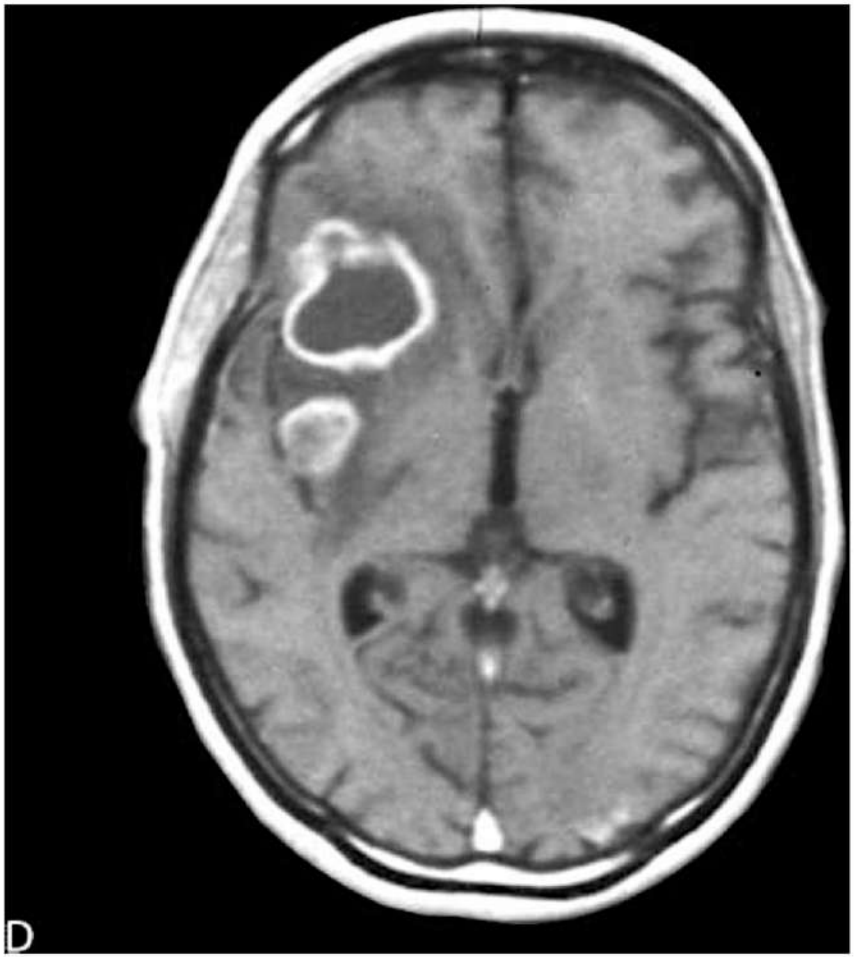


BRAIN ABSCESSES

Dr. Claire Karekezi
Consultant Neurosurgeon

DEFINITION

A focal intracranial infection that is initiated as an area of cerebritis and evolves into a collection of pus surrounded by a vascularized capsule.



Mathisen GE, Johnson JP: Brain abscess. Clin Infect Dis 1997; 25:763-781.

HISTORY

- Hippocrates – Purulent otorrhea and delerium
- The first successful operation for brain abscess - S.F. Morand (France) in 1752 on a temperoethmoidal abscess.
- "Pyogenic Disease of the Brain and Spinal Cord, Meningitis, Abscess of the Brain, Infective Sinus Thrombosis" (1893) - William Macewen – Father of modern day abscess management
- King (1924) – marsupialization
- Dandy (1926) – aspiration
- Sargent (1928) – enucleation
- Vincent (1936) – complete excision
- Heineman et al (1971) – successful medical management

BRAIN ABSCESS

- Was uniformly fatal before the late 1800's
- Mortality down to 30-60% from WWII-1970's
  - Introduction of abx (penicillin, chloramphenicol...)
  - newer surgical techniques
- Mortality down to 0-24% over the past three decades, with:
  - Advent of CT scanning (1974), MRI
  - Stereotactic brain biopsy/aspiration techniques
  - Further improvement in surgery
  - Newer abx (e.g. cephalosporins, metronidazole..)
  - Better treatment of predisposing conditions

CHANGES IN EPIDEMIOLOGY OF BRAIN ABSCESS

(in the last 2-3 decades)

- Incidence 8% of all intracranial lesions in developing countries and 1-2% western world
- Lower incidence of otogenic brain abscesses
  - improved treatment of chronic ear infections
- Marked drop in mortality overall
- With increase in No. of immunosuppressed patients:
  - increased incidence of brain abscess seen in that population (Transplant, AIDS,…)
  - More incidence of brain abscess caused by opportunistic pathogens (fungi, toxo…)

PATHOGENESIS

- Direct spread from contiguous foci (40-50%)
- Hematogenous (25-35%): remote foci
- Penetrating trauma/surgery (10%)
- Cryptogenic (15-20%)

DIRECT SPREAD
(from contiguous foci)

- Occurs by:
  - Direct extension through infected bone
  - Spread through emissary veins, diploic veins, local lymphatics
- The contiguous foci include:
  - Otitis media/mastoiditis
  - Sinusitis
  - Dental infection (<10%), typically with molar infections
  - Meningitis rarely complicated by brain abscess (more common in neonates with *Citrobacter diversus* meningitis, of whom 70% develop brain abscess)

HEMATOGENOUS SPREAD

(from remote foci)

- Sources:
  - Empyema, lung abscess, bronchiectasis, endocarditis, wound infections, pelvic infections, intra-abdominal source, etc…
  - may be facilitated by cyanotic HD, AVM.
- Results in brain abscess(es) at middle cerebral artery distribution
- Often multiple, deep

Microbiology of Brain Abscess

- Dependent upon:
  - Site of primary infection
  - Patient's underlying condition
  - Geographic location
- Usually streptococci and anaerobes
- Staph aureus, aerobic GNR common after trauma or surgery
- 30-60 % are polymicrobial

Predisposing Conditions & Microbiology of Brain Abscess

Predisposing Condition	Usual Microbial Isolates
Otitis media or mastoiditis	Streptococci (anaerobic or aerobic), *Bacteroides* and *Prevotella* spp., *Enterobacteriaceae*
Sinusitis (frontoethmoid or sphenoid)	Streptococci, *Bacteroides* spp., Enterobacteriaceae, *Staph. aureus*, *Haemophilus* spp.
Dental sepsis	*Fusobacterium*, *Prevotella* and *Bacteroides* spp., streptococci
Penetrating trauma or postneurosurgical	*S. aureus*, streptococci, Enterobacteriaceae, *Clostridium* spp.

MICROBIOLOGY OF BRAIN ABSCESS

AGENT	FREQUENCY (%)	
Streptococci (*S. intermedius*, including *S. anginosus*)	60–70	
Bacteroides and *Prevotella* spp.	20–40	
Enterobacteriaceae		23–33
Staphylococcus aureus	10–15	
Fungi*	10–15	
Streptococcus pneumoniae	<1	
Haemophilus influenzae	<1	
Protozoa, helminths† (vary geographically)	<1	

*Yeasts, fungi (*Aspergillus* Agents of mucor *Candida* Cryptococci Coccidiodoides *Cladosporium trichoides Pseudallescheria boydii)*

†Protozoa, helminths (*Entamoeba histolytica,* Schistosomes Paragonimus Cysticerci)

PREDISPOSING CONDITION & LOCATION OF BRAIN ABSCESS

Otitis/mastoiditis	Temporal lobe, Cerebellum
Frontal/ethmoid sinusitis	Frontal lobe
Sphenoidal sinusitis	Frontal lobe, Sella turcica
Dental infection	Frontal > temporal lobe.
Remote source	Middle cerebral artery distribution (often multiple)

PATHOPHYSIOLOGY

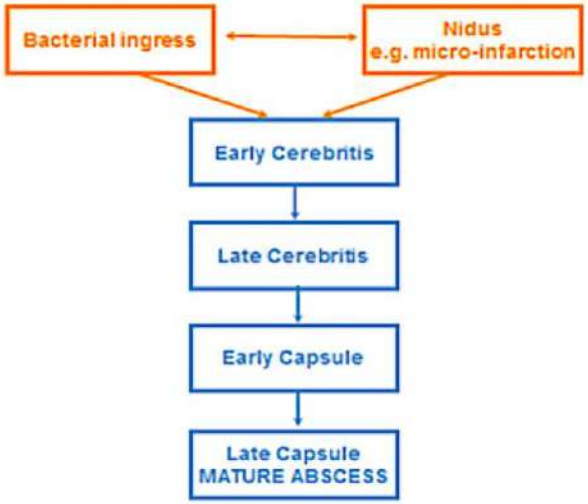
- Begins as localized cerebritis (1-2 wks)
- Evolves into a collection of pus surrounded by a well-vascularized capsule (3-4 wks)

- Lesion evolution (based on experimental animal models):
  - Days 1-3: "early cerebritis stage"
  - Days 4-9: "late cerebritis stage"
  - Days 10-14: "early capsule stage"
  - > day14: "late capsule stage"

Stages of abscess formation

1. **Early Cerebritis**

Days 1-3: Perivascular inflammation, characterised by neutrophil infiltration, occurs around the site of focal infection with a surrounding area of oedema.



2. **Late Cerebritis**

Days 4-9: A central area of necrosis develops as the surrounding oedema progresses. Peripheral accumulation of fibroblasts preludes the development of a capsule.

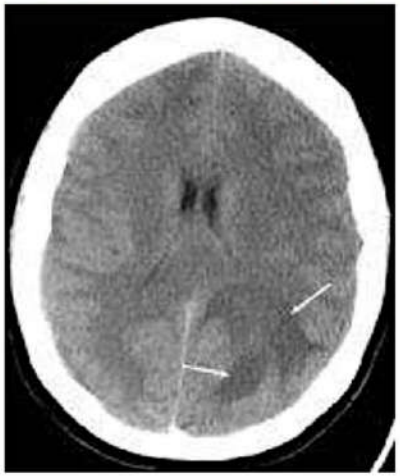
3. **Early Capsule**

Days 10-14: Establishment of a ring-enhancing capsule of well-vascularised tissue with further fibroblast migration and adjacent reactive astrocytosis.

4. **Late Capsule**

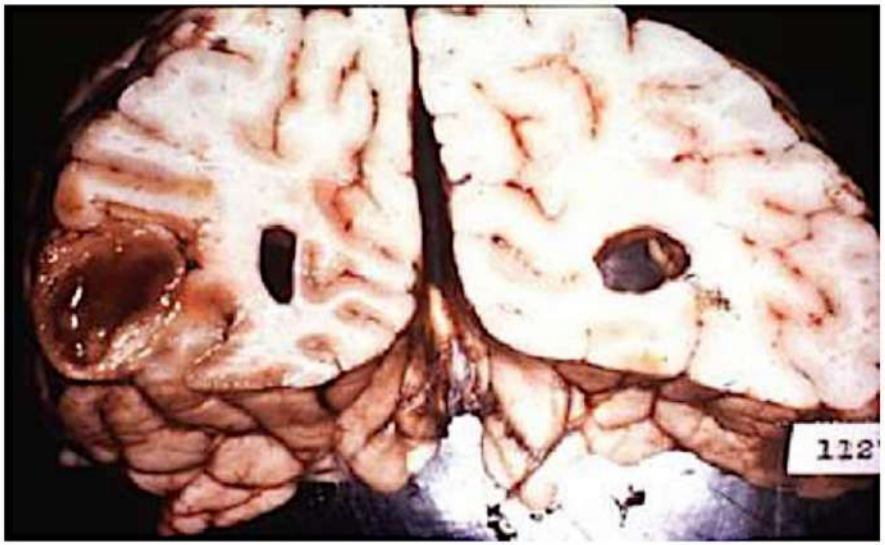
Day 14 and beyond: Collagen fibre and granulation tissue deposition leads to a thickening of the capsule effectively walling off the area of focal suppurative infection.

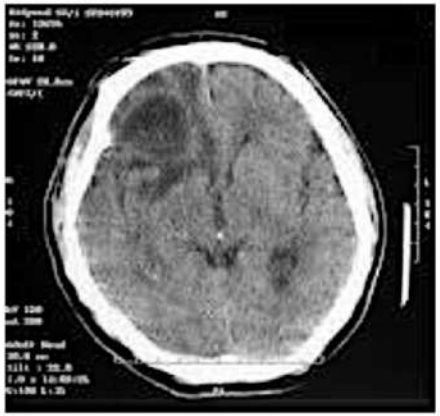
Early cerebritis



- Acute inflammatory infiltrate
- Marked edema
- Invisible on CT OR
- Poorly marginated cortical /subcortical hypodensity with mass effect with no enhancement

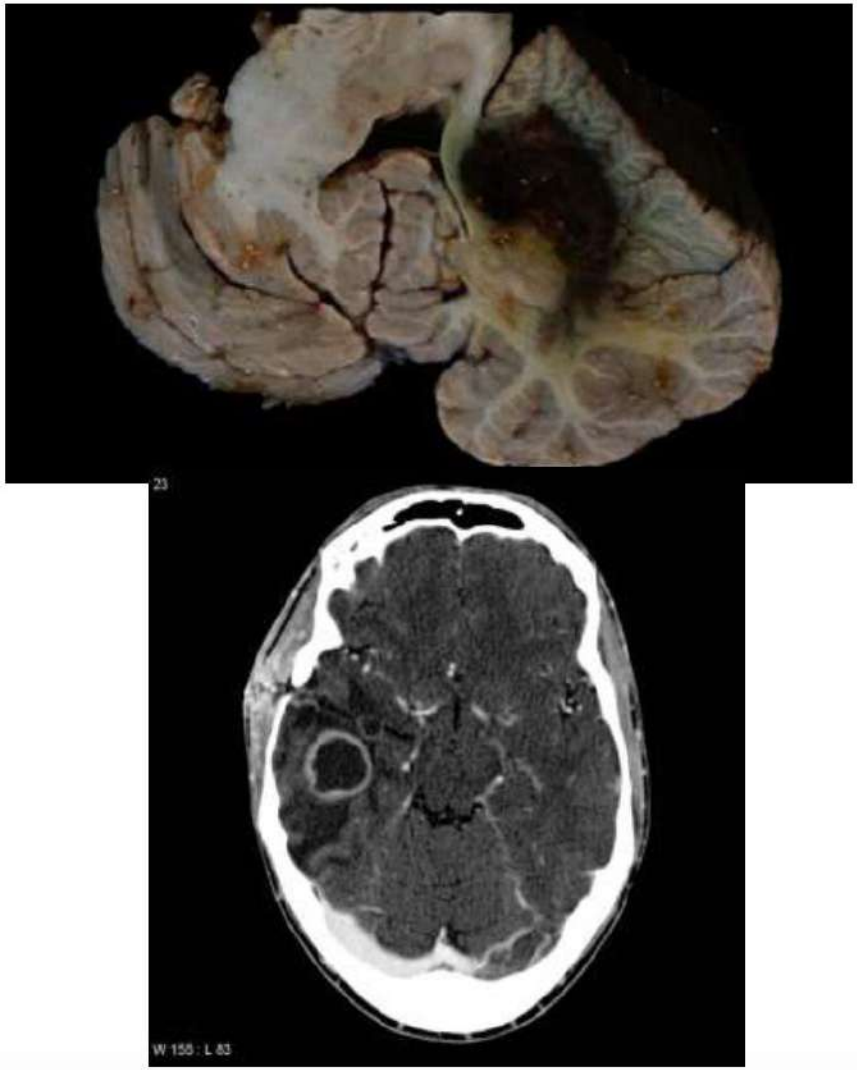
Late cerebritis





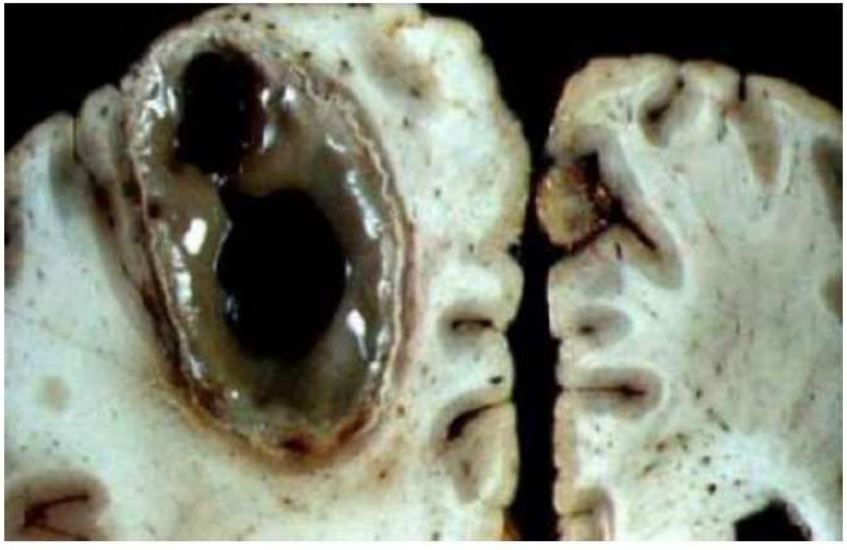
- Central necrosis
- Macrophages and fibroblasts
- Vascular proliferation
- Maximum edema
- Irregular rim enhancing lesion with hypodense center, better defined than early cerebritis

Early capsule formation

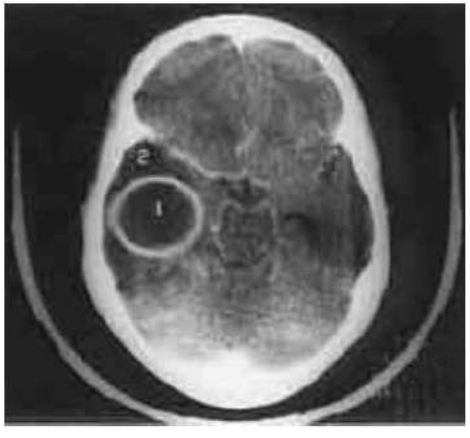


- Necrotic centre ↓
- Collagenous capsule
- Edema starts to regress
- Well-defined rim enhancing mass; an outer hypodense and inner hyperdense rim (double rim sign)

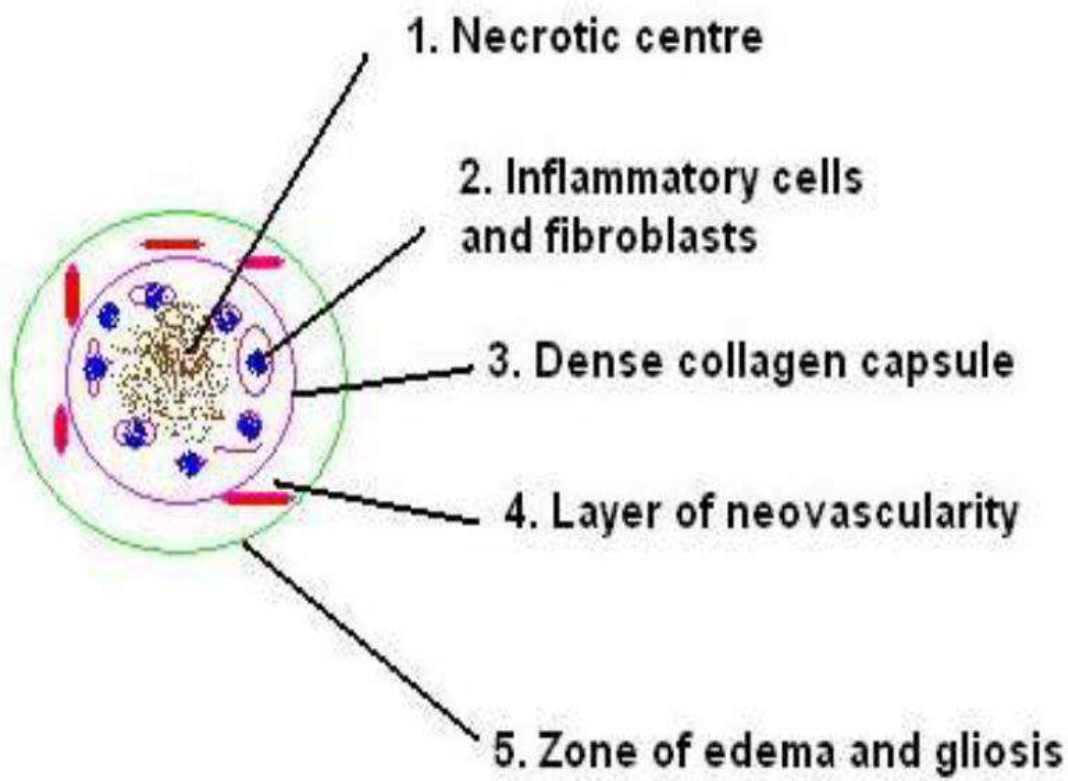
Late capsule formation



- Collagen capsule complete
- ↑ density and thickness
- Rim enhancing lesion with thickened capsule and diminished hypodense central cavity



Layers of abscess

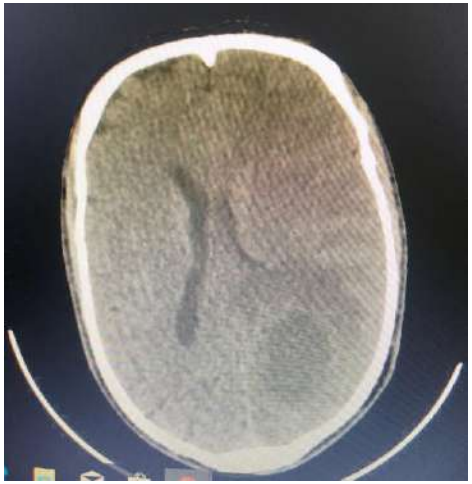


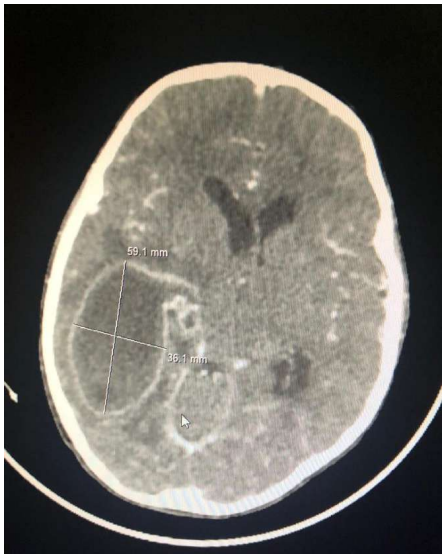
DIAGNOSIS

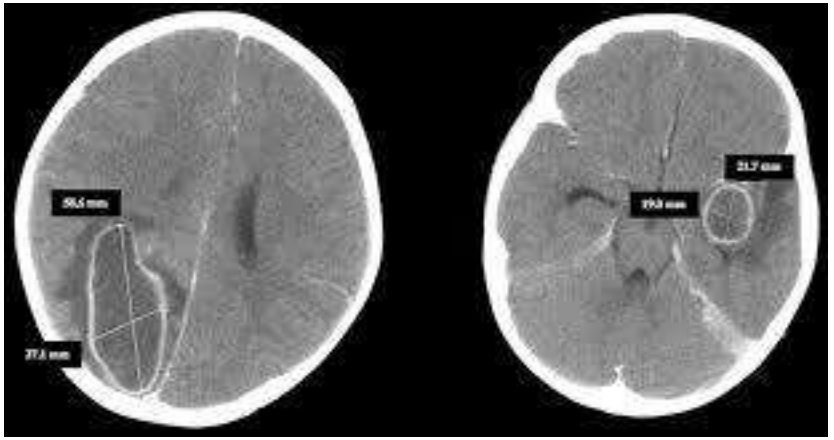
- High index of suspicion
- Contrast CT or MRI
- Drainage/biopsy, if ring enhancing lesion(s) are seen

IMAGING STUDIES

- **MRI**
  - more sensitive for early cerebritis, satellite lesions, necrosis, ring, edema, especially posterior fossa & brain stem
- **CT scan** with contrast
- **Skull x-ray :** insensitive,
  - if air seen, consider possibility of brain abscess

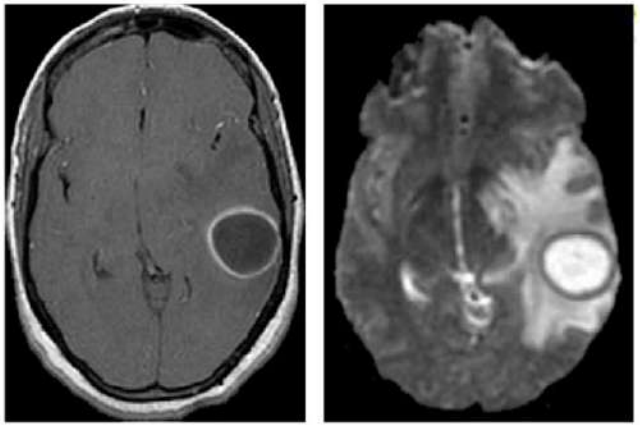






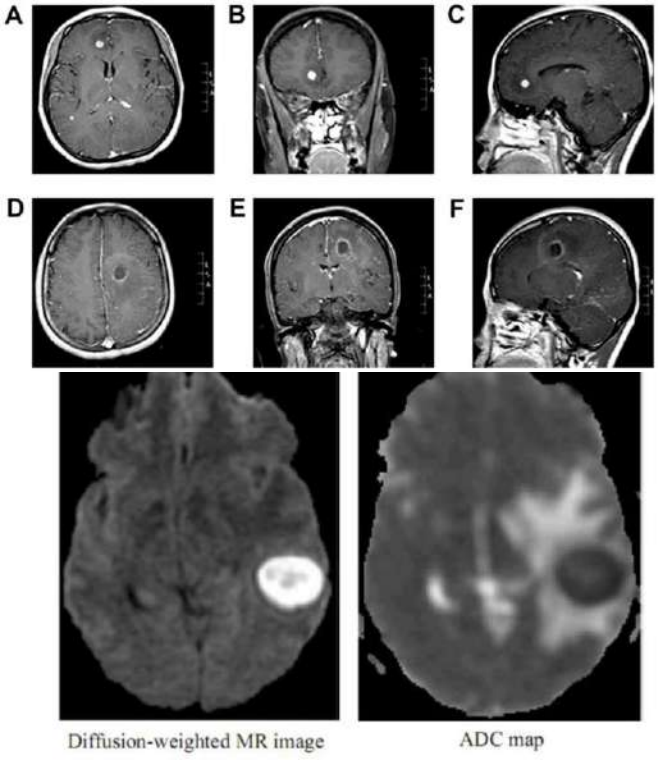
MRI Brain

- **T1**
  - Central low intensity (hyperintense to CSF)
  - Peripheral low intensity (vasogenic oedema)
  - Ring enhancement
  - Ventriculitis may be present, in which case hydrocephalus will commonly also be seen
- **T2 / FLAIR**
  - Central high intensity (hypointense to CSF, does not attenuate on FLAIR)
  - Peripheral high intensity (vasogenic oedema)
  - The abscess capsule may be visible as a intermediate to slightly low signal thin rim
- **DWI / ADC**
  - High DWI signal is usually present centrally
  - Low signal on ADC



T_1-weighted axial MR image T_2-weighted axial MR image

Surgical Neurology 66 (2006) 246–251

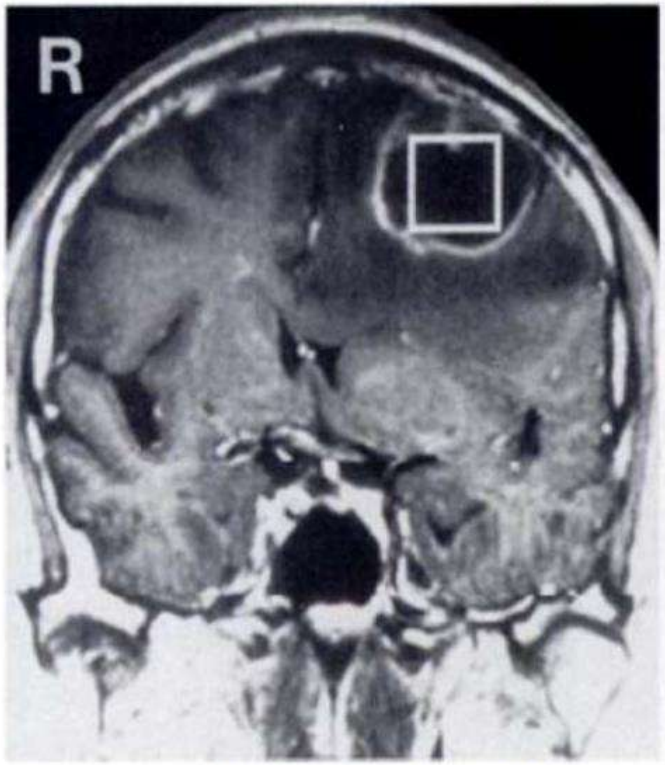


Diffusion-weighted MR image ADC map

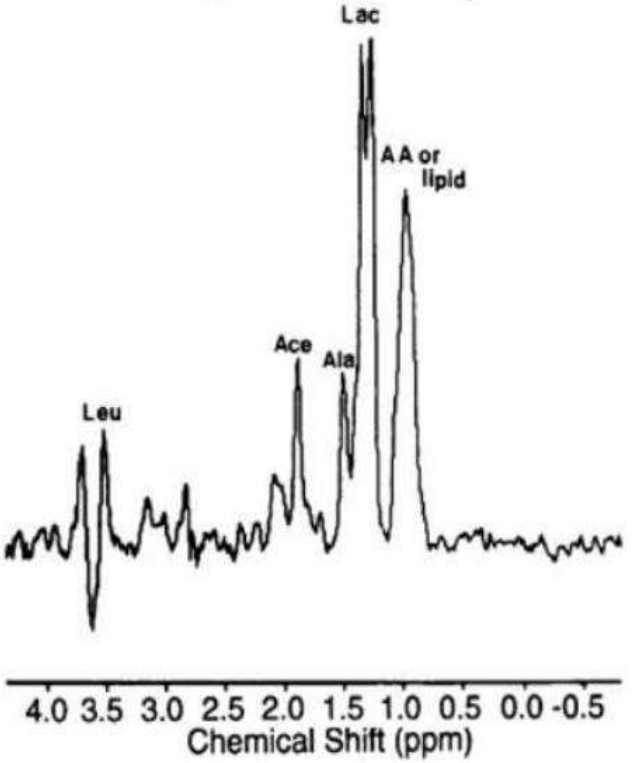
Surgical Neurology 66 (2006) 246–251

Brain Abscess and Brain Tumor: Discrimination with in Vivo H-1 MR Spectroscopy[1]

Sung Hyun Kim, MD • Kee-Hyun Chang, MD • In Chan Song, PhD • Moon Hee Han, MD
Hee Chan Kim, PhD • Heung Sik Kang, MD • Man Chung Han, MD



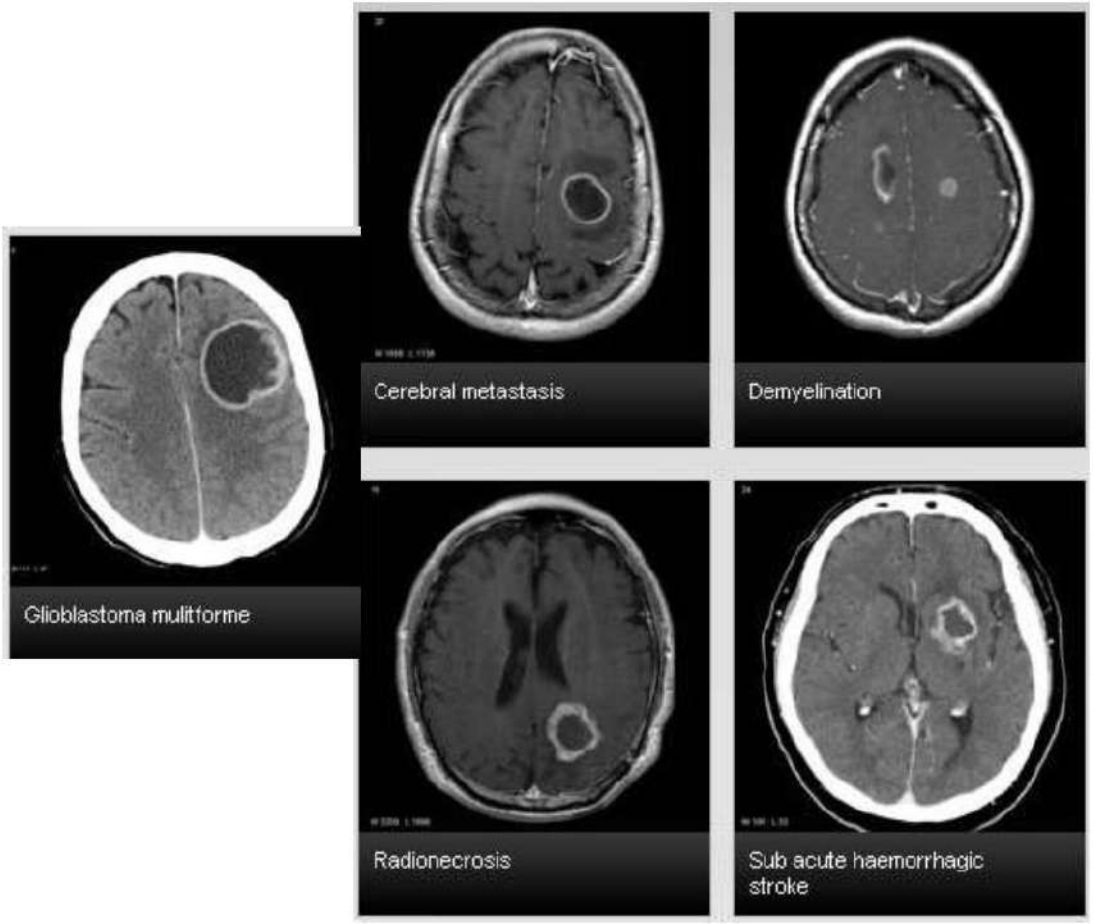
Pyogenic brain abscess



Radiology 1997; 204:239–245

DIFFERENTIAL DIAGNOSIS

- Malignancy
  - Abscess has hypo-dense center, with surrounding smooth, thin-walled capsule, & areas of peripheral enhancement
  - Tumor has diffuse enhancement & irregula borders.
  - SPECT (PET scan) may differentiate. CRP too?
- CVA
- Hemorrhage
- Aneurysm
- Subdural empyema/Epidur abscess



LABORATORY TESTS

- **Aspirate:** Gram/AFB/fungal stains & cultures, cytopathology (+/-PCR for TB)
- **WBC** Normal in 40% (only moderate leukocytosis in ~ 50% & only 10% have WBC >20,000)
- **CRP** almost invariably elevated: !!!! Baseline CRP → treatment response
- **ESR** Usually moderately elevated
- **BC** Often negative BUT *Should still be done*
- **LP** ***Contraindicated in patients with known/suspected brain abscess***
  Risk of herniation 15-30%
  *If done, m*ay have normal CSF findings, but:
  Usually elevated CSF protein & cell count (lymphs)
  Unremarkable glucose & CSF cultures rarely positive

CLINICAL MANIFESTATIONS

- Non-specific symptoms
- Mainly due to the presence of a space-occupying lesion → increased ICP
  - H/A, N/V, lethargy, focal neuro signs , seizures
- Signs/symptoms influenced by
  - Location
  - Size
  - Virulence of organism
  - Presence of underlying condition

Initial Findings in Patients with Brain Abscess Based on Intracranial Location

INTRACRANIAL LOCATION	FINDING
Parietal lobe	Headache
	Visual field deficits (ranging from inferior quadrantanopia to homonymous hemianopia)
	Endocrine disturbances
Frontal lobe	Headache
	Drowsiness
	Inattention
	Personality change
	Mental status deterioration
	Hemiparesis
	Motor speech disorder
Temporal lobe	Ipsilateral headache
	Aphasia or dysphasia (if in the dominant hemisphere)
	Visual field deficit (ranging from upper quadrant homonymous quadrantanopia to complete homonymous hemianopia)
Cerebellum	Headache
	Nystagmus
	Ataxia
	Vomiting
	Dysmetria
	Meningismus
	Papilledema
Brainstem	Cranial nerve involvement
	Deficits of ascending and descending pathways

- Frontal > Temporal > Parietal > Cerebellum > Occipital

TREATMENT

- Combined medical & surgical
  - Aspiration or excision
  - empirical abx
- Empirical antibiotics are selected based on:
  - Likely pathogen (consider primary source, underlying condition, & geography)
  - Antibiotic characteristics: usual MICs, CNS penetration, activity in abscess cavity
- Modify abx based on stains
- Duration: usually 6-8 wks
  - after surgical excision, a shorter course may suffice

SURGICAL THERAPY

- The optimal approach to patients with bacterial brain abscess
- Aspiration after bur-hole placement or complete excision after craniotomy (no prospective trial comparing these two)
- May be performed under stereotactic neuroimaging guidance
- Stereotactic aspiration is a useful approach even for abscesses located in eloquent or inaccessible regions; repeat aspiration should be considered if the initial aspiration proves ineffective or partially effective.
- Intraoperative ultrasound - for the aspiration of small abscesses and can delineate abscess pockets,
- Recurrence rates after stereotactic aspiration range from 0-24 %.

INDICATIONS FOR SURGERY

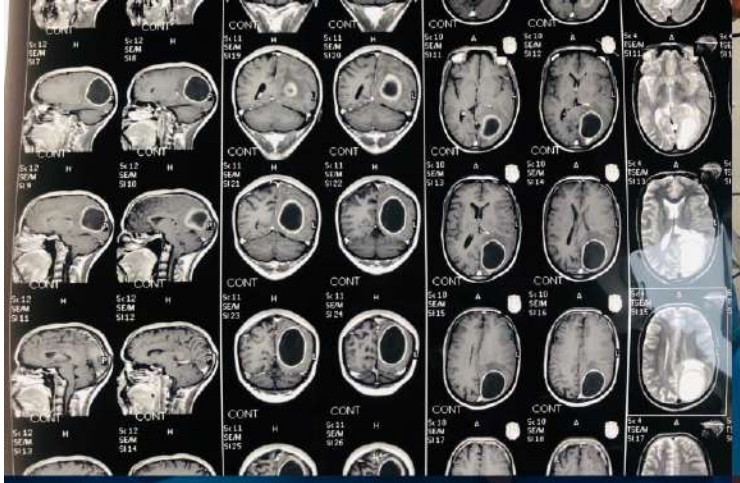
1. Significant mass effect exerted by lesion (on CT or MRI)
2. Difficulty in diagnosis (especially in adults)
3. Proximity to ventricle: indicates likelihood of intraventricular rupture which is associated with poor outcome
4. Evidence of significantly increased intracranial pressure
5. Poor neurologic condition (patients responds only to pain, or does not even response to pain)
6. Traumatic abscess associated with foreign material
7. Fungal abscess
8. Multiloculated abscess
9. Follow-up CT/MRI scans cannot be obtained every 1-2 weeks

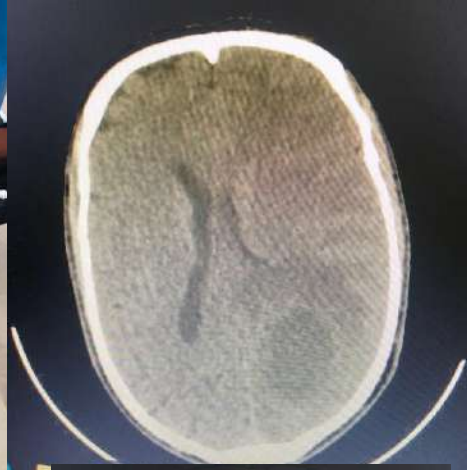
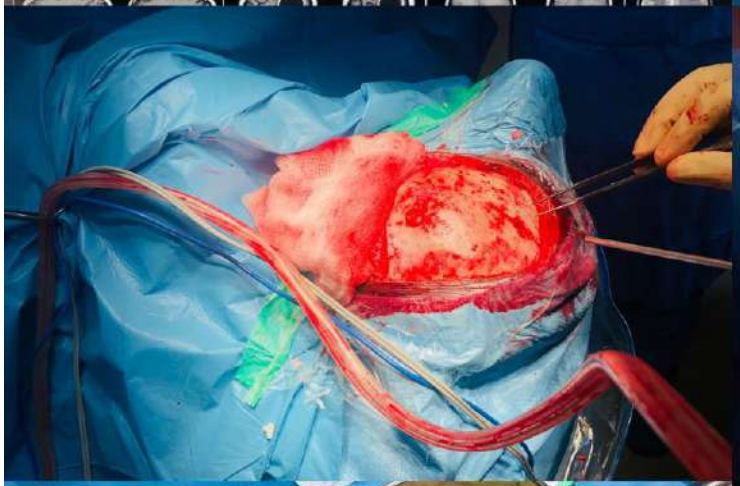
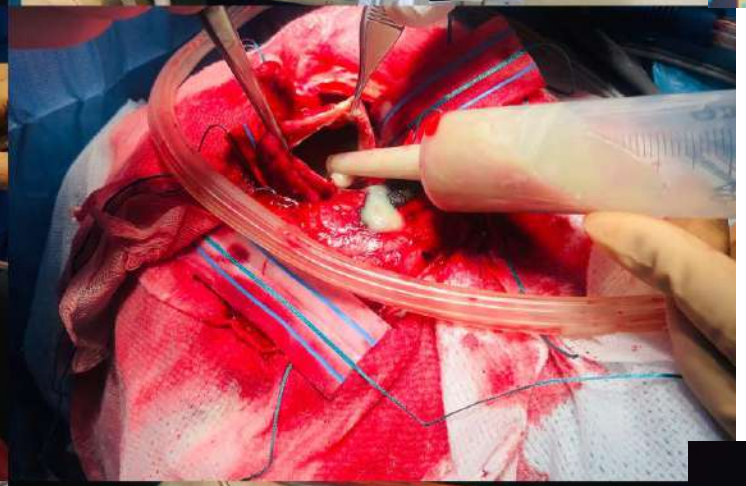
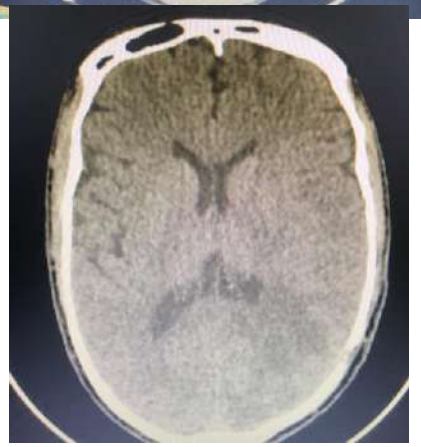
What are the indications for complete excision by craniotomy ?

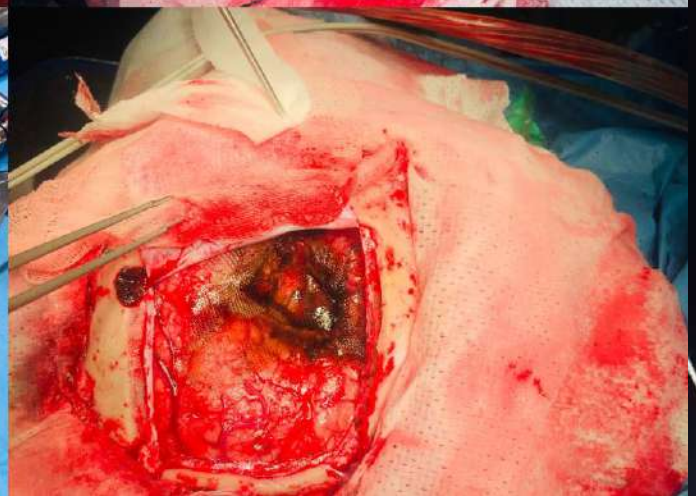
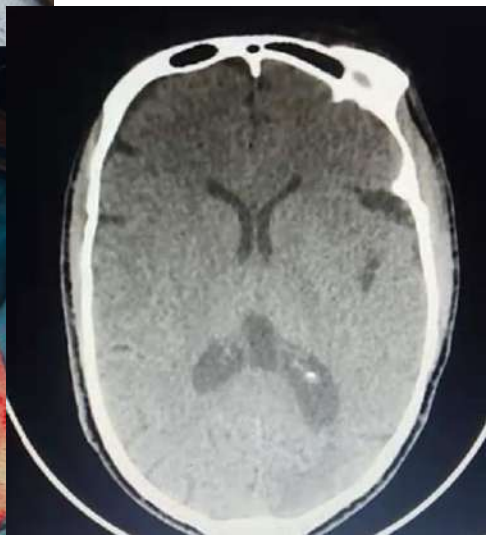
- Multiloculated abscesses in whom aspiration techniques have failed
- Abscesses containing gas
- Abscesses that fail to resolve
- Posttraumatic abscesses that contain foreign bodies or retained bone fragments to prevent recurrence
- Abscesses that result from fistulous communications (e.g., secondary to trauma or congenital dermal sinuses)
- Abscess localized to one lobe of the brain and contiguous with a primary focus.
- Cerebellar abscess in children
- Difficulty in diagnosis
- Suspected fungal abscess

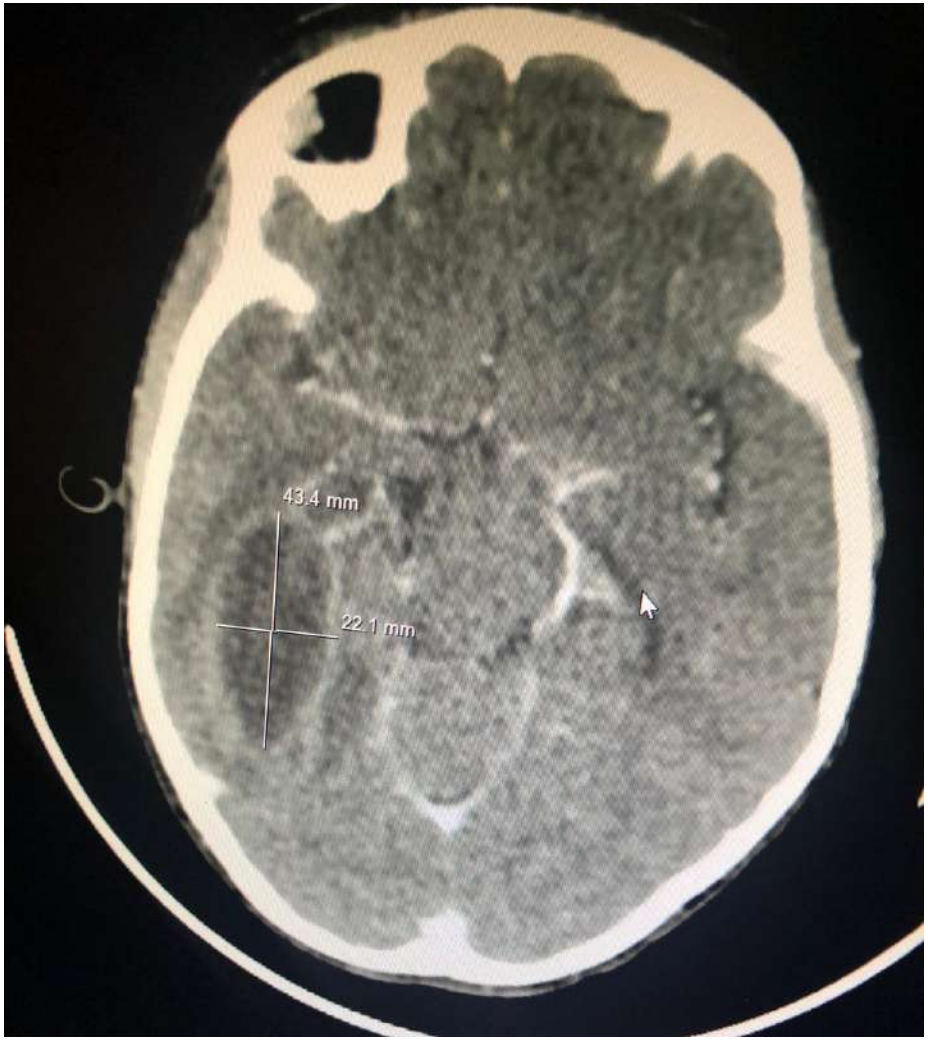
What are the contraindications for craniotomy and evacuation?

- Abscess in the cerebritis stage
- Deep-seated abscess in eloquent area
- Multiple abscesses

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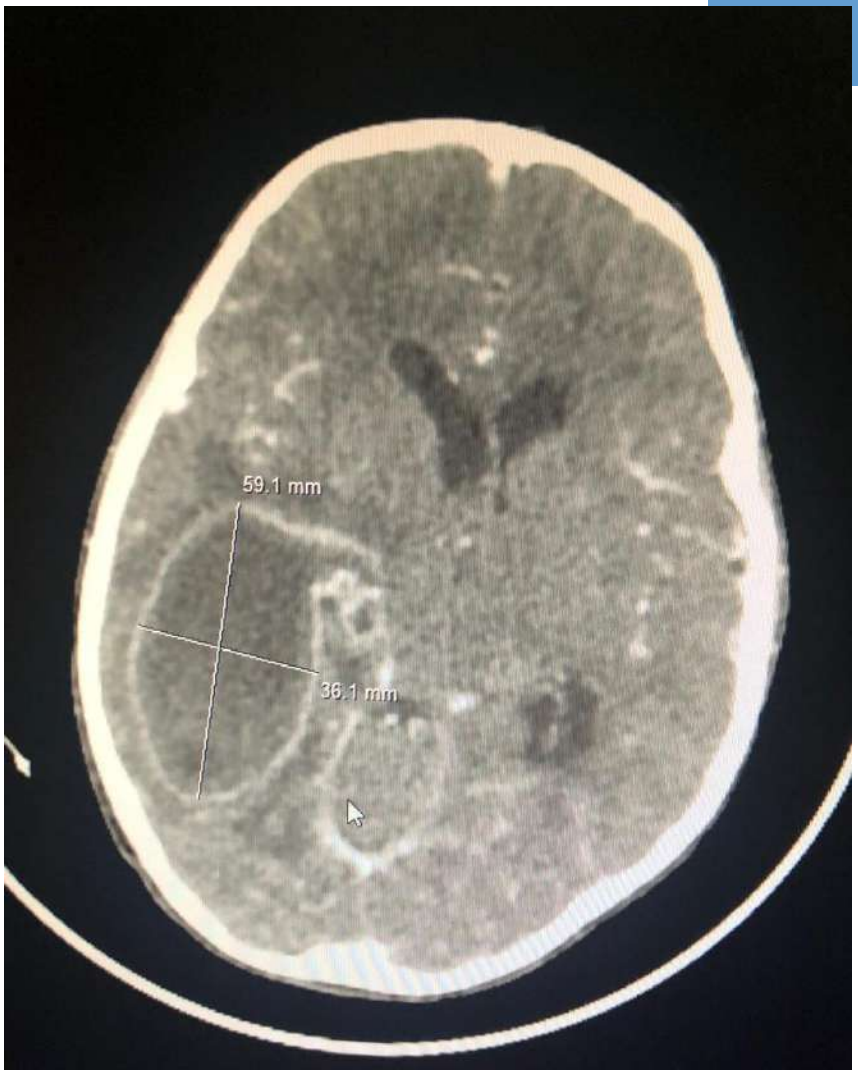
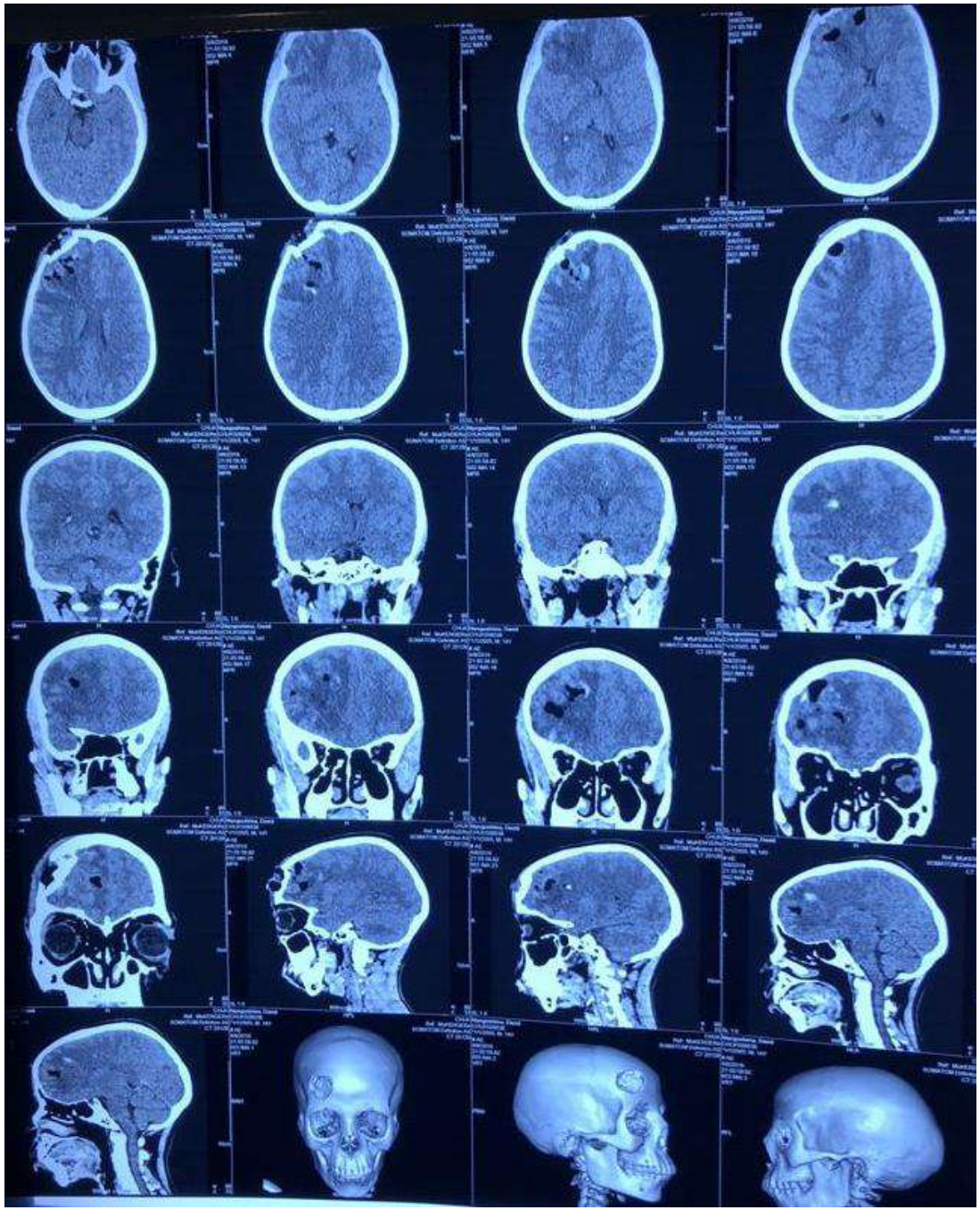
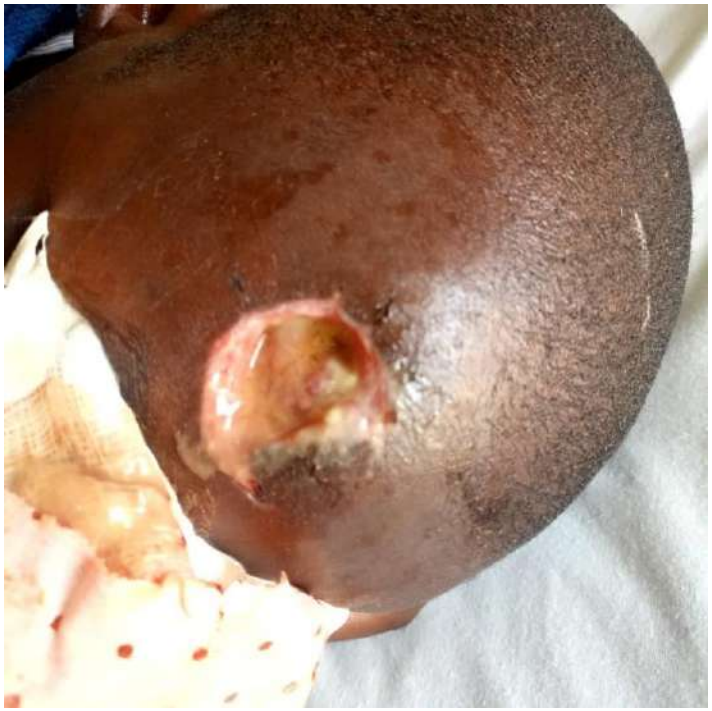
22.1 mm


59.1 mm
36.1 mm





MEDICAL TREATMENT ONLY

- Only in pts with prohibitive surgical risk:
  - poor surgical candidate,
  - multiple abscesses,
  - in a dominant location,
  - Abscess size ≤2.5 cm
  - concomitant meningitis, ependymitis,
  - early abscess (cerebritis?)
  - with improvement on abx,

[Better-vascularized cortical lesions more likely to respond to abx alone]

[Subcortical/white-matter lesions are poorly vascularized]

TREATMENT DURATION

- Bacterial brain abscess –6-8 weeks IV → 2-3 months oral antimicrobial therapy
- Post-surgical excision -Courses of 3 to 4 weeks of antimicrobial therapy
- Medical therapy alone -up to 12 weeks with parenteral agents
- A combination of surgical aspiration or removal of all abscesses larger than 2.5 cm in diameter →6 weeks or more of antimicrobial therapy, and weekly neuroimaging to document abscess resolution
- Repeat neuroimaging studies -biweekly for up to 3 months after completion of therapy

Predisposing Conditions and Probable Etiologic Agents in Brain Abscess

PREDISPOSING CONDITION	POSSIBLE MICROBIAL CAUSES
Otitis media or mastoiditis	Streptococci (aerobic or anaerobic), *Bacteroides* spp., *Prevotella* spp., Enterobacteriaceae
Sinusitis (frontoethmoidal or sphenoidal)	Streptococci, *Bacteroides* spp., Enterobacteriaceae, *Haemophilus* spp., *Staphylococcus aureus*
Dental infection	Mixed *Fusobacterium*, *Prevotella*, *Actinomyces*, and *Bacteroides* spp.; streptococci
Penetrating trauma or secondary to neurosurgical procedure	*Staphylococcus aureus*, Enterobacteriaceae, *Clostridium* spp.
Lung abscess, empyema, or bronchiectasis	*Fusobacterium*, *Actinomyces*, *Bacteroides*, and *Prevotella* spp.; streptococci; *Nocardia* spp.
Bacterial endocarditis	*Staphylococcus aureus*, streptococci
Congenital heart disease	Streptococci, *Haemophilus* spp.
Immunocompromised state	
Neutropenia	Aerobic gram-negative bacilli, *Aspergillus* spp., Mucorales, *Candida* spp., *Scedosporium* spp.
Transplantation	Enterobacteriaceae, *Listeria monocytogenes*, *Nocardia* spp., *Aspergillus* spp., *Candida* spp., Mucorales, *Scedosporium* spp., *Toxoplasma gondii*
HIV infection	*Listeria monocytogenes*, *Nocardia* spp., *Mycobacterium* spp., *Cryptococcus neoformans*, *Toxoplasma gondi*

Predisposing Conditions and Empirical Antimicrobial Therapy in Patients with Presumed Bacterial Brain Abscess

PREDISPOSING CONDITION	ANTIMICROBIAL THERAPY
Otitis media or mastoiditis	Metronidazole + a third-generation cephalosporin*
Sinusitis (frontoethmoidal or sphenoidal)	Metronidazole + a third-generation cephalosporin* + vancomycin†
Dental infection	Penicillin + metronidazole
Penetrating trauma or secondary to a neurosurgical procedure	Vancomycin + a third- or fourth-generation cephalosporin‡
Lung abscess, empyema, or bronchiectasis	Penicillin + metronidazole + a sulfonamide§
Bacterial endocarditis	Vancomycin + gentamicin
Congenital heart disease	Third-generation cephalosporin*
Unknown	Vancomycin + metronidazole + a third- or fourth-generation cephalosporin‡

Antimicrobial Therapy for Brain Abscess Based on Isolated Pathogen

ORGANISM	STANDARD THERAPY
BACTERIA*	
Actinomyces spp.	Penicillin
Bacteroides fragilis	Metronidazole
Enterobacteriaceae[†]	Third- or fourth-generation cephalosporin
Fusobacterium spp.	Penicillin G
Haemophilus spp.	Third-generation cephalosporin[‡]
Listeria monocytogenes	Ampicillin[§] or penicillin G[§]
Mycobacterium tuberculosis	Isoniazid + rifampin + pyrazinamide + ethambutol
Nocardia spp.[‖]	Trimethoprim-sulfamethoxazole
Prevotella spp.	Metronidazole
Pseudomonas aeruginosa	Ceftazidime,[§] cefepime,[§] or meropenem[§]
Staphylococcus aureus (methicillin sensitive)	Nafcillin or oxacillin
Staphylococcus aureus (methicillin resistant)	Vancomycin
Streptococcus anginosus (*milleri*) group, other streptococci	Penicillin G

MULTIPLE BRAIN ABSCESSES

- Incidence –10-50%
- Emergent stereotactic aspiration for all lesions > 2.5 cm diameter and those causing mass effect, located deep in brain stem or close to ventricular wall
- If all the lesions are < 2.5 cm and not producing mass effect, the largest one should be aspirated for diagnostic cultures.
- Antibiotics withheld till culture results
- Antibiotics for 3 months (Immunosuppressed –1 yr)
- Repeat surgical aspiration if
  - radiographic enlargement after 2 weeks of therapy
  - Failure to diminish in size after 4 weeks of antibiotics
  - Clinical deterioration

CYANOTIC HD WITH BRAIN ABSCESS

- 5-18% population with CHD. 10 times more prone. M.C –TOF
- Intracardiac right to left shunt by-pass allows direct entry of blood containing bacteria to the cerebral circulation without pulmonary filtration.
- Anaerobic streptococci (Sterile cultures are reported in 16-68%)
- Cardiopulmonary risk, coagulation defects and variable degree of immunodeficient states
- A deeply located parieto-occipital abscess larger than 2 cm diameter which causes mass effect, should be aspirated immediately even in late cerebritits stage using stereotactic or CT guided methods to decrease intra-cranial pressure and avoid intraventricular rupture of brain abscess.
- Intravenous Beta-lactam antibiotics are started immediately.

POOR PROGNOSTIC MARKERS

- Delayed or missed diagnosis
- Inappropriate antibiotics.
- Multiple, deep, or multi-loculated abscesses
- Ventricular rupture (80%–100% mortality)
- Fungal , resistant pathogens.
- Neurological compromise at presentation
- Short duration w severe AMS,
- Rapidly progressive neuro. Impairment
- Immunosuppressed host
- Poor localization, especially in the posterior fossa (before CT)

SEQUELAE

- 30-50% of survivors are found to have neurological sequelae.
- The incidence of residual neural deficits -hemiparesis, cognitive and learning deficits in children, is less with aspiration than excision.
- About 72% of patients can have epileptic seizures upto five years of diagnosis. This incidence is less with aspiration than excision.
- 5 to 10% abscesses recur due to inadequate or inappropriate antibiotics, failure of removal of foreign body, dural fistula or failure of eradication of primary source.
- Hydrocephalus may also develop