

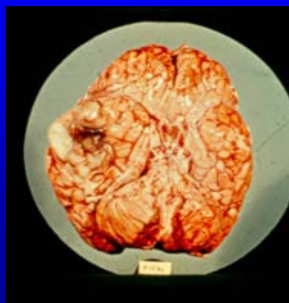
The Parameningeal Infections

Adolf W. Karchmer M.D.
Professor of Medicine
Harvard Medical School
Division of Infectious Diseases
Beth Israel Deaconess Medical
Center

Intracranial Parameningeal Infections

- Brain abscess
- Subdural empyema
- Epidural abscess
- Suppurative intracranial thrombophlebitis

Brain Abscess - Temporal Lobe



Brain Abscess

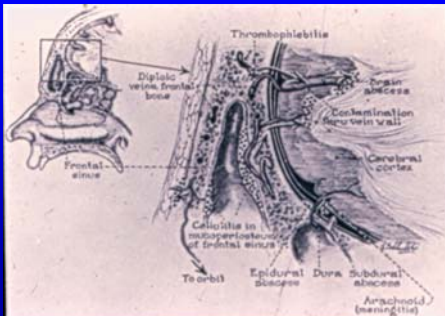
- **Epidemiology:**
 - 1,500 – 2,500 cases in US/year
 - 0.9/10⁵ person years
 - Male predominance
 - Age: Infants to elderly, depending on predispositions
 - 8% of intracranial masses developing countries vs. 1-2% in developed world
 - Case fatality rate 30-60% until late 1970, with CT scan 0-20%

Erdogan and Causever, Neurosurg Focus 2008; 24.

Brain Abscess – Pathogenesis and Predispositions

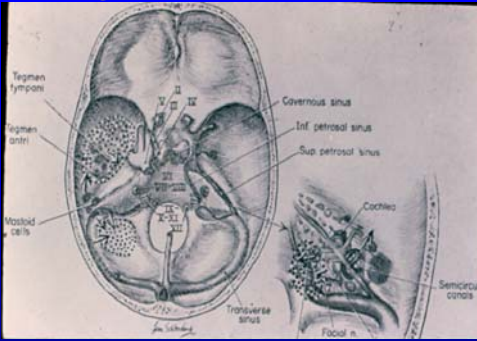
- Spread from contiguous focus of infection
 - Chronic suppurative otitis media – mastoiditis
 - Paranasal sinusitis – frontal, ethmoid, sphenoid
- Hematogenous spread from distant focus
 - Bacteremia (*S. anginosus*, *S. aureus*, Listeria)
 - Chronic pyogenic pulmonary disease
 - Cyanotic congenital heart disease
 - Pulmonary AV malformation
 - Endocarditis – rarely macroscopic
 - Odontogenic
- Trauma: Neurosurgery, penetrating
- Immunosuppressive states
- Cryptogenic 20-35%

Rhinogenic Brain Abscess - Pathogenesis



Pathogenesis of Subdural Empyema and Epidural Abscess is Similar

Pathogenesis of Brain Abscess

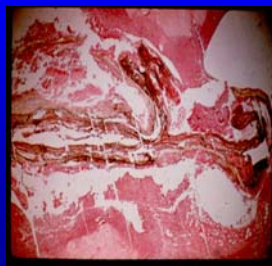
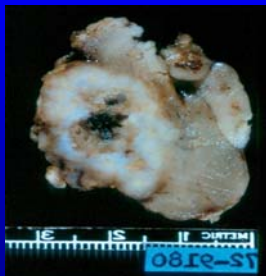


Impact of predisposing contiguous focus on lesion site

Brain Abscess – Pathogenesis and Predispositions

- Spread from contiguous focus of infection
 - Chronic suppurative otitis media – mastoiditis
 - Paranasal sinusitis – frontal, ethmoid, sphenoid
- Hematogenous spread from distant focus
 - Bacteremia (*S. anginosus*, *S. aureus*, *Listeria*)
 - Chronic pyogenic pulmonary disease
 - Cyanotic congenital heart disease
 - Pulmonary AV malformation
 - Endocarditis – rarely macroscopic
 - Odontogenic
- Trauma: Neurosurgery, penetrating
- Immunosuppressive states
- Cryptogenic 20-35%

Penetration Trauma Induced Brain Abscess



Brain Abscess: Pathogenesis and Pathology

- Infection at gray-white matter junction; a low flow area
- Days 1-3: Early cerebritis
 - Rapid infiltration neutrophils, mononuclear cells, local edema
 - Pro-inflammatory cytokines, chemokines released by microglia and astrocytes via toll-like receptor pathway
- Day 4-9: Late cerebritis
 - Macrophage and fibroblast infiltration, central necrosis
- Day 10-13: Early capsule formation
 - More prominent on control vs. ventricular side
- Day 14+: Late capsule formation
 - Circumferential capsule, collagenous granulation layers
- Excessive cytokine release injures tissue
- Corticosteroid Rx decrease cytokine release, capsule formation, increase bacteria

Kiellian, et al., J Neuro Inflamm 2004.
Konat, et al., J Neurochem 2006.

Microbiology of 262 Pyogenic Brain Abscesses

Organism	No. Isolation	Organism	No. Isolation
Gram pos cocci		Enterobacteriaceae	
Streptococci	33	Klebsiella	8
<i>S. aureus</i>	13	Enterobacter	4
Coag-neg staph	1	Serratia	2
Gemella	1	Salmonella	2
Enterococci	2	HACEK	7
Gram pos bacilli		<i>P. aeruginosa</i>	3
Nocardia	3	Other gram neg	5
Actinomyces	3	Anaerobes	
Diphtheroids	3	Peptostreptococci	9
<i>Bacillus</i> sp.	1	Bacteroides	15
Rhodococcus	1	Fusobacteria	15
Other gram positives	5	Prevotella	5
<i>Mycobacterium tuberculosis</i>	1	Culture sterile	83

Xiao, et al., Surg Neuro 2005; 63:442-450.
Kao, et al., J Microbiol Immunol Infect 2003; 36:129-136.
Memon, et al., J Medical Microbiol 2008; 57:1259-1268.

Microbiology of Brain Abscess

PREDISPOSITION	LIKELY PATHOGENS
Otitis media/mastoiditis	Streptococci, <i>B. fragilis</i> , Enterobacteriaceae
Paranasal sinusitis	Streptococci, <i>Bacteroides</i> sp., <i>S. aureus</i> , Enterobacteriaceae
Odontogenic	Streptococci, Fusobacterium, Bacteroides, <i>A. actinomycetemcomitans</i> , Prevotella
Meningitis	<i>L. monocytogenes</i> , <i>C. diversus</i>
Pyogenic lung disease	Streptococci, Nocardia, Actinomyces, Bacteroides, Prevotella
Trauma	<i>Staphylococcus aureus</i> , Streptococci, Enterobacteriaceae
Immunodeficiency	<i>T. gondii</i> , Nocardia, <i>L. monocytogenes</i> , Candida, molds, cryptococcus, Enterobacteriaceae

Brain Abscess Following Neurosurgery 1986-2004

- 31/1860 operations (0.17%), 31/167 total brain abscesses (18%)
- Onset 8-35 d postop (~ 20d)
- Sx – somewhat indolent HA, altered consciousness, focal signs, fever (55%), seizure
- Microbiology: Gram-neg bacilli, streptococci, staphylococci, 19% cult negative, 29% polymicrobial, occasional resistant GNR, MR staph
- Treatment: Antimicrobials – empiric (cefazidime/vanco), culture based, 8 weeks
- Surgery - aspiration or excision
- Mortality: 5/31 (16%)

Yang, et al., *Infection* 2006; 34:247.

Brain Abscess: Microbiologic Dx

- **Necessary:**
 - Aspirate specimen, CSF rarely helps
 - Blood culture occasionally diagnostic
- **Aspirated material:**
 - Delay antibiotic therapy if feasible
 - Anaerobes common = $\geq 40\%$
 - Polymicrobial infection common = 15-20%
 - Optimal technique = 95-100% positive
 - Negative cultures = ~ 30% prior antibiotics

Brain Abscess: Microbiologic Dx

- 24 consecutive cases – abscess aspiration
 - 21 positive standard culture
 - ✦ 6 blood flask only
 - ✦ 15 solid media \pm blood culture flask
 - Mixed anaerobes (24 hr Rx)
 - Streptococci, *H. aphrophilus* (24 hr Rx)
 - Fusobacterium (48 hr Rx)
 - *S. mitis* (4 days Rx)
 - *S. aureus* (20 days Rx)
 - ✦ 3 PCR 16S rRNA/16S DNA
 - Actinomyces (10 d Rx)
 - *S. constellatus* (21 d Rx)
 - *Fusobacterium nucleatum* (35 d Rx)
 - Empiric therapy (cefotaxime/metronidazole) 3 inadequate
 - Re-aspirate (4-20 d):
 - ✦ 3 culture positive day 8, 15, 18, Rx
 - ✦ 2 Culture negative day 6, 20, Rx
 - Molecular techniques not routine but useful

deLastours, et al., *Operative Neurosurg* 2008; 63:362.

Brain Abscess: Clinical Presentation

Symptoms/Signs	Number (%) N=177
Headache	112 (64)
Nausea/vomiting	80 (45)
Seizure	35 (20)
Fever	107 (60)
Mental status changes	71 (40)
Focal neurologic signs	106 (60)
Hemiparesis/palsy (N=128)	19 (15)

*Brain abscess triad only in 15-30%

Erdogan, et al., Neurosurg Focus 2008; 24.
 Menon, et al., J Med Microbiol 2008; 57:1259.
 Kao, et al., J Microbiol Immunol Infect 2003; 36:129

Management of Patient with Brain Abscess

- Image – contrast CT or MRI
- Blood culture
- Invasive therapy – urgently
 - Lesions > 2.5 cm diam, excise or aspirate (stereotactically or free hand) – material pathology, microbiology
 - Lesions cerebritis or < 2.5 cm aspirate
- Empiric antimicrobial therapy – broad spectrum
 - Based on predisposing conditions
 - Based on remote source infection
- Corticosteroids only if severe edema and mass effect
- Seizure prophylaxis

Erdogan and Causever, Neurosurg Focus 2008; 24:E2.
 Moorthy and Rayshekhar, Neurosurg Focus 2008; 24:E3.
 Hakan, Neurosurg Focus 2008; 24:E4.

Brain Abscess: Treatment

- Usually combined antibiotics and surgical Rx
- Medical therapy alone – ideally if known pathogen
 - Single/multiple smaller abscess < 2 cm
 - Critical co-morbidity (stereotactic aspiration local anesthesia)
 - Abscess inaccessible location
 - Cerebritis stage
 - Concomitant meningitis
 - Not if diagnosis is doubtful
- Antibiotics: Third gen cephs, meropenem, metronidazole, vancomycin, TMP/SMZ, fluoroquinolones, high dose, parenteral, ≥ 8 weeks, f/u oral Rx
- Monitor frequent imaging (recurrences 5-20%)
- Complications: Herniation, Rupture

Hakan, Neurosurg Focus 2008; 24:E4.
 Erdogan and Causever, Neurosurg Focus 2008; 24:E2.
 Hall and Truwit, Neurosurg 2008; 62(Suppl 2):519.

Brain Abscess - Potential Complications



Brain Abscess: Surgical Treatment

- **Optimal therapy usually requires surgery**
 - Aspiration or complete excision
 - No trials – individualize
- **Aspiration with CT/MRI stereotactic guidance preferred (not with coagulopathy) – safe**
 - Can aspirate abscesses ~ 1.5 cm diam
 - Endoscopic techniques
- **Excision preferred**
 - Posterior fossa; superficial with thick wall
 - Possible foreign material – penetrating injury
 - Presumed fungal infection
 - Diagnostic difficulty
 - Increased intracranial pressure – mass effect
 - Intraventricular rupture
 - Multi-loculated if fail aspiration

Hakan, Neurosurg Focus 2008; 24:4.
 Erdogan and Causever, Neurosurg Focus 2008; 24:E2.
 Hall and Truwit, Neurosurg 2008; 62 (Suppl 2):519.

Outcome Prognosis for Brain Abscess 1986-2004

- 142 patients – 105 favorable* vs. 37 unfavorable (24 died)

Variable	OR	P
Glasgow coma scale >12	6.20 (1.35-28.3)	0.019
Male	9.81 (2.29-42.0)	0.002
Free of sepsis	761.49 (19.9-291.44)	<0.001
Gram positive cocci	42.3 (2.23-803.7)	0.013

Type of surgical treatment not predictive

*Glasgow outcome score full recovery or disability but independent

Tseng and Tseng, Surg Neurology 2006; 65:557-562.

Outcome Prognosis: Imaging vs Glasgow Coma Score

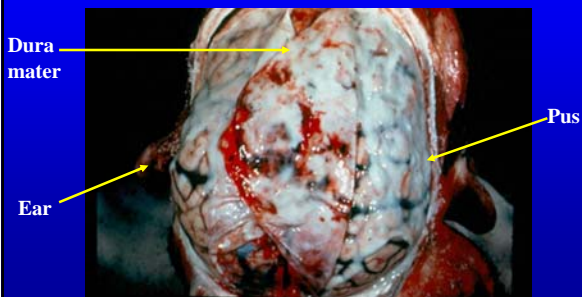
- **Imaging Index:**
 - **Number:** Solitary = 1
Multiple = 2-6
 - **Location:** Superficial = 1
Deep = 2
Combined = 3
 - **Diameter:** < 2 cm = 1
2-4 cm = 2
> 4 cm = 3
 - **Edema:** Minimal = 1
Moderate = 2
Large = 3
 - **Midline Shift:** Mild (< 5 mm) = 1
Moderate (5-10 mm) = 2
Severe (> 10 mm) = 3

Outcome Prognosis: Imaging vs Glasgow Coma Score

- 96 patients (55 CT; 41 CT and MRI), 18 unfavorable outcome (8 died), 78 favorable
 - ISI >8: unfavorable (sensitivity 92.7%, specificity 69.1%)
 - GCS <12: unfavorable (sensitivity 43.9%, specificity 87.3%)
- | | Score | Unfavorable (%) | Score | Unfavorable (%) |
|-------|-------|-----------------|-------|---------------------|
| ✧ ISI | ≤8 | 3/41 (7) | ≥ 9 | 38/55 (69) p<0.0001 |
| ✧ GCS | ≥13 | 23/71 (32) | ≤ 12 | 18/25 (72) p 0.0013 |
- ISI better predictor

Demir, et al., Clin Radiol 2007; 62:564-572.

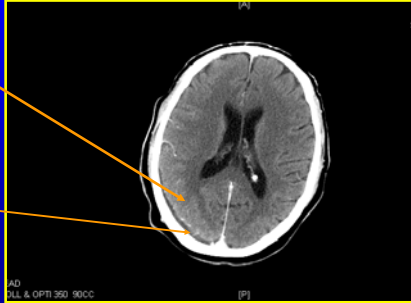
Bilateral Subdural Emphyema



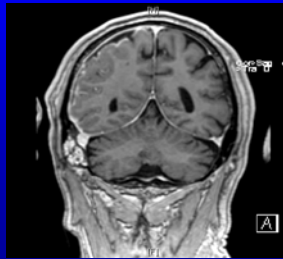
Subdural Empyema

Edema /cerebritis

Collection



Mastoiditis with Subdural Empyema



Subdural Empyema

- Pus in space between dura and arachnoid
- Predisposition similar to brain abscess
 - Otogenic – Chronic suppurative otitis/mastoiditis 15-20%
 - Rhinogenic - Chronic sinusitis: frontal/ethmoid 60%
 - Trauma 8%
 - Surgery 4%
 - Infection of subdural hematoma
 - Meningitis – infection subdural effusion (infants)
- Males > females, second-third decade

Hall and Truwit, Neurosurg 2008; 62:519.
Venkatesh, et al., J Neurosurg 2006; 105 (Suppl 5):370.
Nathoo, et al., Neurosurg 1999; 44:529.

Subdural Empyema: Location

Site	Percent
Cerebral convexity	52
Parafalx	21
Convexity + parafalx	28
Tentorial	3
Extradural + subdural	15
Bilateral	15
Rarely infratentorial (otogenic)	

Nathoo, et al., Neurosurg 1999; 44:529.

Subdural Empyema: Microbiology

Organisms	Number (% Patients)
	N= 638
Streptococci	191 (29)
<i>Staphylococcus aureus</i>	34 (5)
Coagulase negative staph	32 (5)
Other gram positive	7 (1)
<i>S. pneumoniae</i>	4 (0.6)
<i>Haemophilus influenzae</i>	26 (4)
Enterobacteriaceae	62 (10)
Non-fermentative GNR	17 (3)
Anaerobic GNB	45 (7)
Miscellaneous	3 (0.5)
Sterile	128 (20)
Polymicrobial	108 (17)

Nathoo, et al., Neurosurg 1999; 44:529.
Qurashi, et al., Ped Otolaryn 2006; 70:1581.

Adame, et al., Ped 2005; 116:461.
Venkatesh, et al., J Neurosurg 2006; 105:370.

Subdural Empyema: Clinical Features

Symptoms/Signs	Number (%)
	N=699
Fever	536 (77)
Headache	221 (32)
Nausea/vomiting	60 (9)
Seizure	280 (33)
Meningismus	514 (74)
Altered mental status	489 (70)
Potts puff tumor	234 (33)
Focal signs	410 (59)

Sx before adm 7.3 days (1-38)

Can progress rapidly – emergent care

Nathoo, et al., Neurosurg 1999; 44:529.

Subdural Empyema: Diagnosis-Treatment

- Think of Dx: Predisposition plus HA, fever, CNS Sx
- MRI most sensitive, CT with contrast, rapid-available
- No lumbar puncture –herniation risk
- Treatment – medical emergency
 - Antibiotics: Third generation cep / metronidazole or meropenem +/- vancomycin
 - Anticonvulsant therapy
 - Treat intracranial hypertension

Subdural Empyema – Treatment

- Surgery: drainage, decompression
 - More extensive/complex than imaging indicated*
- | | 1983-87 | 1998-97 |
|--------------|-----------|------------|
| | Burr Hole | Craniotomy |
| | N=90 | N=322 |
| Good outcome | 71% | 86% |
| Mortality | 23% | 8% |
- Treat predisposing process
 - Antibiotics: Refine with culture data, duration ~ 4-6 weeks, treat osteomyelitis if present
 - Outcomes: Good 82%, neurologic defects 6%, Death 12%, defects improve over time

*Nathoo, et al., Neurosurg 2001; 49:872.
Nathoo, et al., Neurosurg 1999; 44:529.

Intracranial Epidural Abscess

- Collection of pus in potential space between dura mater and skull
- Predispositions and microbiology similar to subdural empyema – paranasal sinus, middle ear-mastoid, trauma, surgery
- Sx: More indolent, fever, HA, local pain, nausea/vomiting
 - Gradenigo's syndrome – facial pain, lateral rectus weakness

Hall and Truwit, Neurosurg 2008; 62:519.

Intracranial Epidural Abscess

- Dx: MRI more sensitive, CT with contrast
- Rx:
 - Antibiotics 3-6 weeks (osteomyelitis longer)
 - Surgical drainage: craniotomy, craniectomy preferred over burr hole
- Complications:
 - Extension intracranially
 - Osteomyelitis of bone flap (lose 50%)

Hall and Truwit, Neurosurg 2008; 62:519.

Suppurative Intracranial Thrombophlebitis

- Involves veins or venous sinuses
- Complication of intracranial and paracranial/facial infection
 - Septic cavernous sinus thrombophlebitis
 - Otitis media/mastoiditis – lateral, inferior/superior petrosal sinuses
 - Subdural empyema, meningitis, epidural abscess – superior sagittal sinus, cortical veins

*Enbright, et al., Arch Int Med 2001; 161:2671.

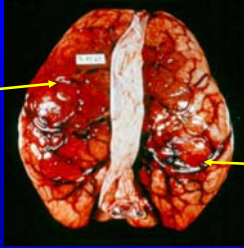
Suppurative Intracranial Thrombophlebitis

- Microbiology related to local infection
- Dx: MRI angiography/venography
- Rx:
 - Precipitating infection
 - Antibiotics \geq 4 weeks
 - Anticoagulation (heparin)
 - ❖ Cavernous sinus – begin early*
 - ❖ Lateral, sagittal sinus - ? Benefit, risk cortical vein hemorrhage

*Enbright, et al., Arch Int Med 2001; 161:2671.

Suppurative Intracranial Thrombophlebitis
Superior sagittal sinus phlebitis

Hemorrhagic
infarction



Occluded
Cortical
veins
