

Approach & Management of Neuroinfections

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Case - 1

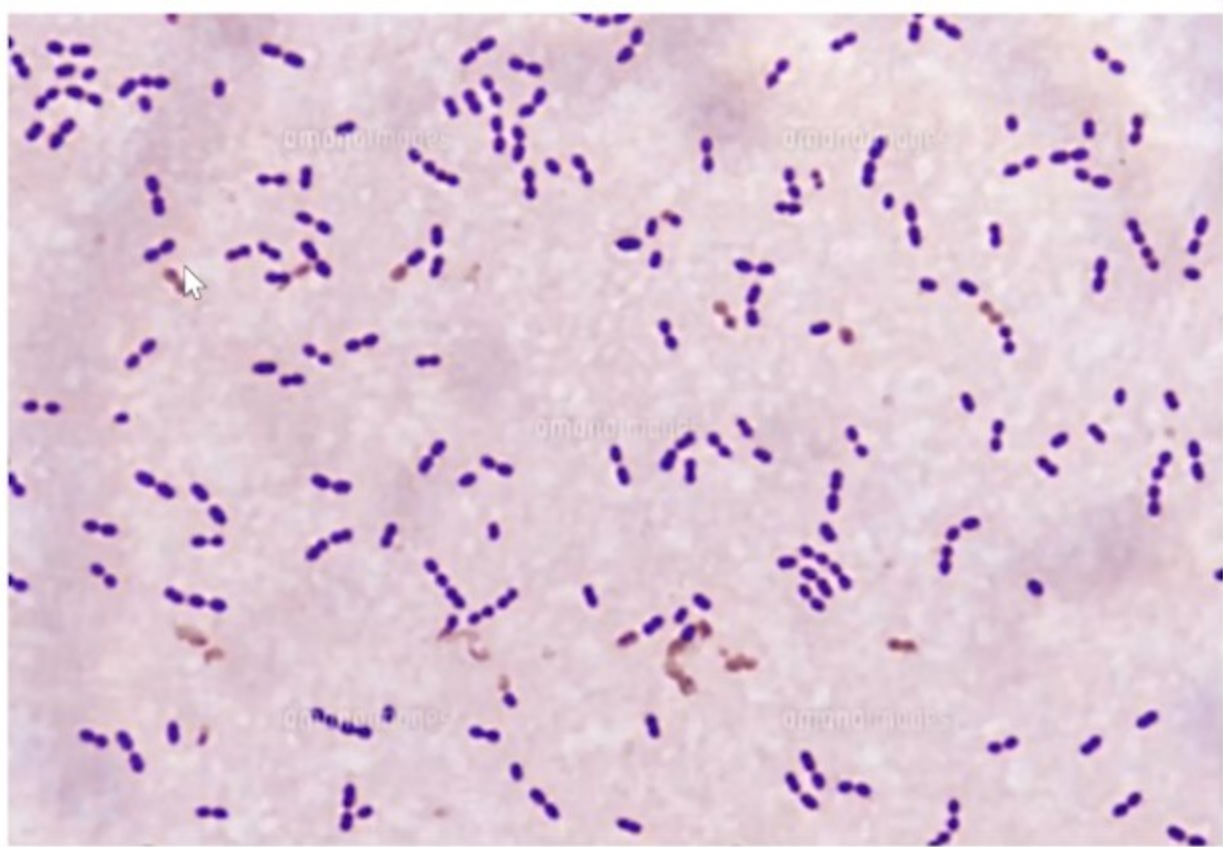
- 19/M,
- H/o fever, headache and vomiting x 1 day
- H/o left ear discharge x 5 days.

- O/e: No rash, febrile (101F), photophobia +, neck rigidity+

- Blood culture sampling
- Dexamethasone 0.15mg/kg
- Empirical treatment: Ceftriaxone 2 g, Vancomycin 0.15 mg/kg

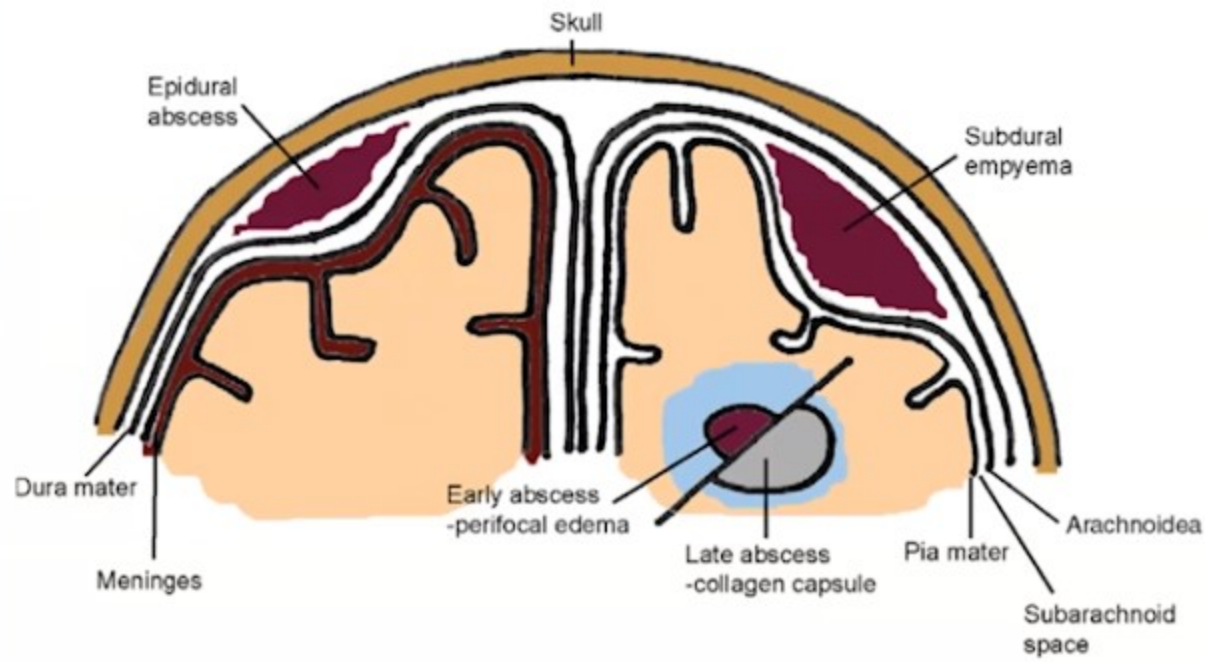
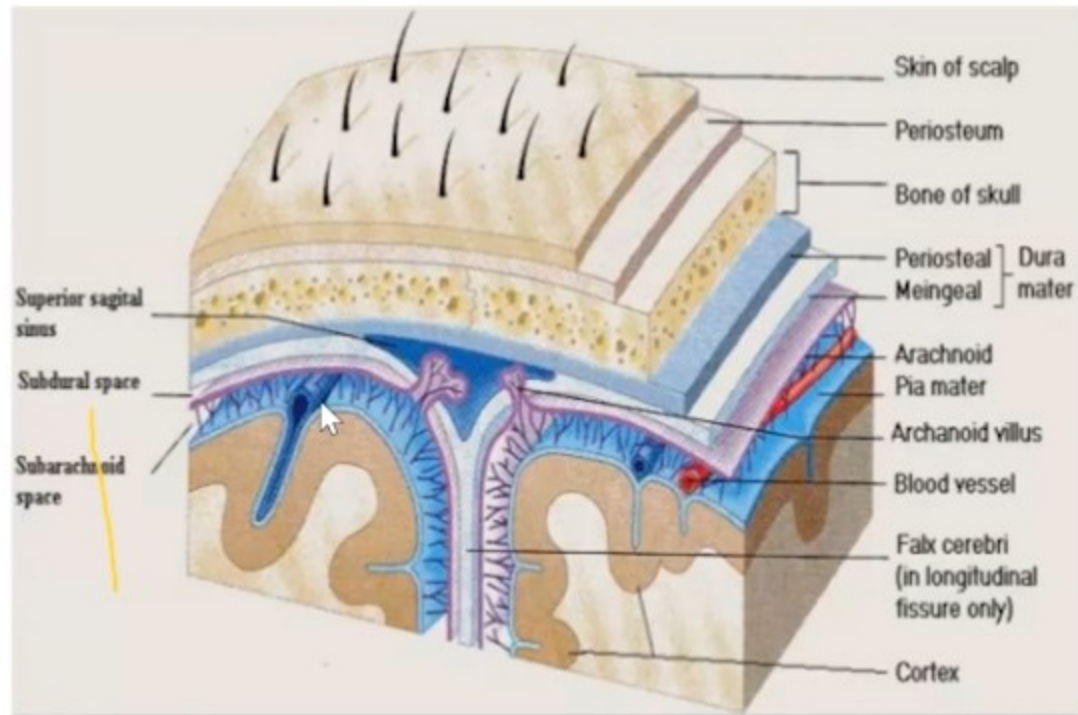
- CT brain and CSF LP if not contraindicated
- CSF shows 1500 TLCs, 90% PMNs, gram stain shows gram positive cocci in pairs, glucose 15 mg/dl (blood glucose 130 mg/dl), CSF protein 150 mg/dl

- CSF shows 1500 TLCs, 90% PMNs, gram stain shows gram positive cocci in pairs, glucose 15 mg/dl (blood glucose 130 mg/dl), CSF protein 150 mg/dl



- Probable etiology: **Strep pneumoniae**

Meningitis



**INFECTIOUS INFLAMMATORY DISEASES
OF CENTRAL
NERVOUS SYSTEM**

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graph TD; A[INFECTIOUS INFLAMMATORY DISEASES OF CENTRAL NERVOUS SYSTEM] --> B[Meningitis]; A --> C[Encephalitis]; A --> D[Myelitis]; A --> E[Poliomyelitis]; A --> F["Subacute sclerosing leukoencephalitis (demyelinating leuko- and panencephalitis)"];
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Meningitis

Encephalitis

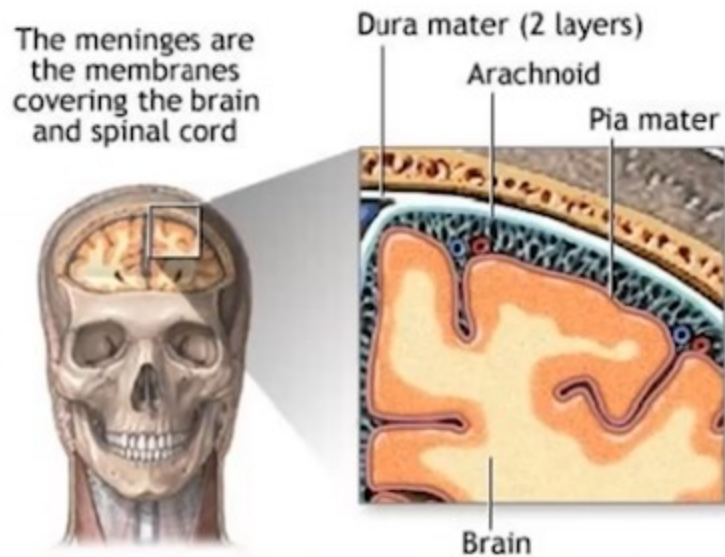
Myelitis

Poliomyelitis

**Subacute
sclerosing
leukoencephalitis
(demyelinating
leuko- and
panencephalitis)**

Introduction

- **Meningitis:** inflammation of the meninges = membranes surrounding the brain and spinal cord
- **Encephalitis:** inflammation of the brain parenchyma, present as diffuse and/or focal neuropsychological dysfunction. It is usually caused by one of many viruses; however, other pathogens are involved, such as: Bacteria, fungi, protozoa, and worms.
- **Meningoencephalitis :** inflammation of the meninges and brain parenchyma



Triad of Meningitis

Fever

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graph TD; A[Fever] --> B[Headache]; B --> C[Meningism];
```

The diagram illustrates the triad of meningitis. It consists of three rounded rectangular boxes arranged in a descending staircase pattern from top-left to bottom-right. The first box is grey and contains the word 'Fever'. A grey L-shaped arrow points from the bottom of this box to the top of the second box. The second box is brown and contains the word 'Headache'. A yellow L-shaped arrow points from the bottom of this box to the top of the third box. The third box is a darker shade of brown and contains the word 'Meningism'.

Headache

Meningism

Types

Acute

< 1 week

Subacute

7-14 days

Chronic

> 4 weeks

EPIDEMIOLOGY

- 80% of pyogenic meningitis cases occur in children
- Fatal in 50% of cases if untreated
- 8-15% patients die after early diagnosis and treatment.
- 10-20% have residual brain damage sequelae.

Risk Factors

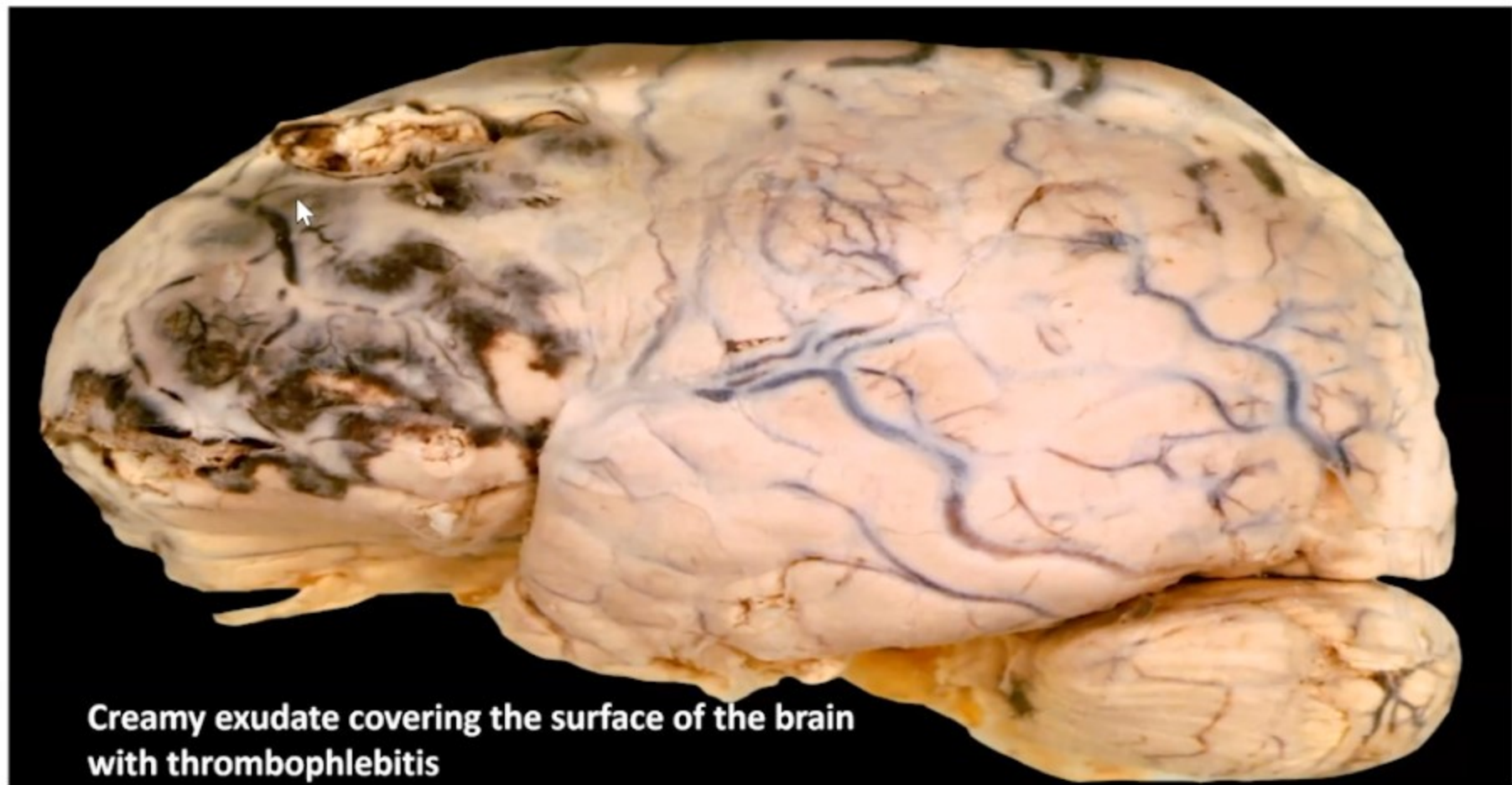
- Infants
- Immunocompromised state
- Overcrowding

Etiology

- Streptococcus pneumoniae (50%)
 - Neisseria meningitidis (25%)
 - Group B streptococcus (15%)
 - Listeria monocytogenes (10%)
 - Hemophilus influenzae type B (<10%)
- N. meningitidis is the causative organism of recurring epidemics of meningitis every 8–12 years*

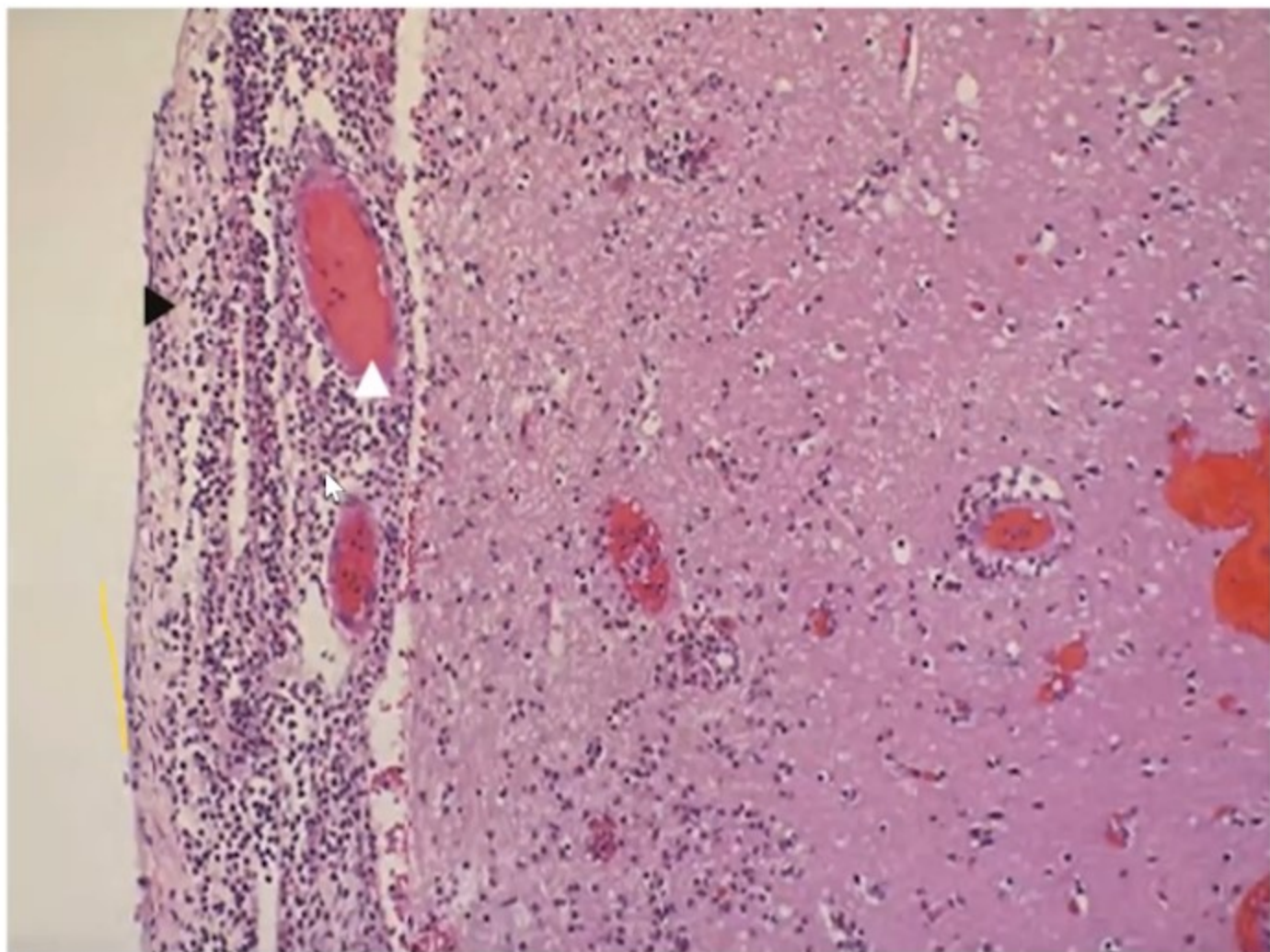
Age Group	Organism
Neonates	Group B Streptococcus, Escherichia coli, Listeria monocytogenes
Infants and Children	Group B Streptococcus, Escherichia coli, Listeria monocytogenes
Adolescents and Young Adults	Neisseria meningitidis, Streptococcus pneumoniae, H influenzae
Older Adults (>50 years)	Streptococcus pneumoniae, Neisseria meningitidis, Listeria monocytogenes

Gross Pathology



**Creamy exudate covering the surface of the brain
with thrombophlebitis**

HistoPathology



Acute meningitis, microscopic

A neutrophilic exudate (▶) involves the meninges on the left, with prominent dilated vessels (▲). Edema and focal inflammation (extending into superficial brain parenchyma through the Virchow-Robin space) are present in the neocortex to the right. This acute meningitis is typical of a bacterial infection. This edema can lead to brain swelling with herniation and death. Resolution of infection may be followed by adhesive arachnoiditis with obliteration of the subarachnoid space leading to obstructive hydrocephalus. Diagnosis is aided by performing lumbar puncture to obtain CSF that typically shows increased leukocytes, mainly neutrophils, decreased glucose, and increased protein. Gram stain, serologies, and culture help identify specific microorganisms.

CASE -2

- 6mon/ female
- H/O: incessant cry since 2 days
 - Decreased intake, refusal of feeds
 - Irritable, moaning continuously
- O/E: no eye to eye contact, not moving to sound or light stimuli,
 - Bulging anterior fontanelle

INFANTS



Fever, possibly with cold hands & feet



Refusing feeds or vomiting



High pitched moaning cry or whimpering



Dislike of being handled or fretful



Neck retraction with arching of back



Blank & staring expression



Child is difficult to wake, lethargic



Pale, blotchy complexion

CHILDREN/ADULTS



Stiff neck



Headache



Fever



Vomiting



Light Sensitivity



Drowsiness or
confusion



Joint pain



Fitting



Meningococcal rash

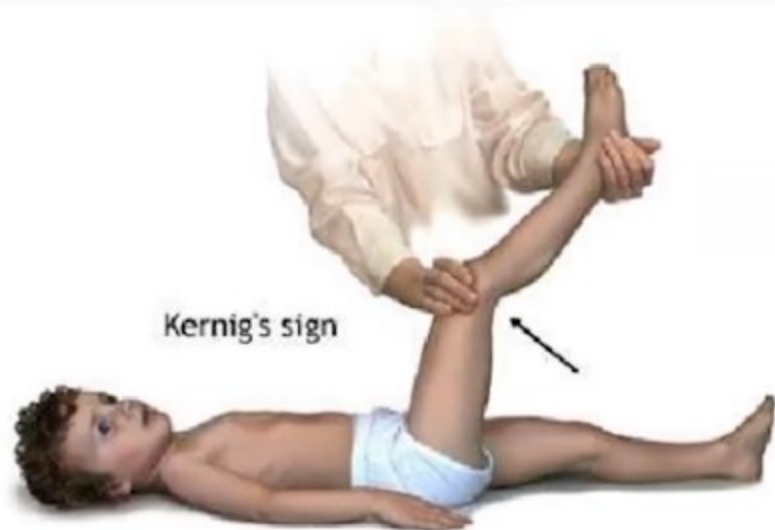


RASH- EARLY STAGES



RASH- FINAL STAGES





Kernig's sign



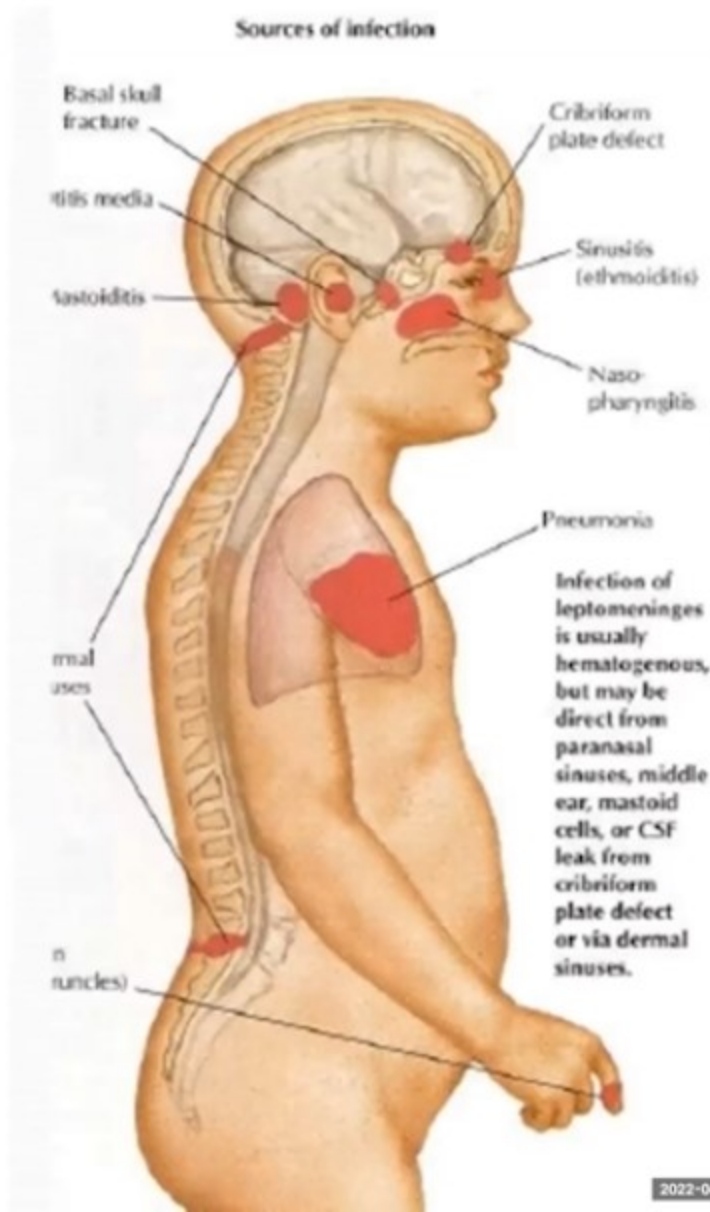
Brudzinski's neck sign

Case -3

- 12/M,
 - Fever x 1 day
 - Headache and vomiting +
 - H/o left ear discharge from 5 days.
 - O/E: no rash, febrile (101F), photophobia +, neck rigidity+
-
- Blood culture sample taken
 - Dexamethasone 0.15mg/kg; Ceftriaxone 2 g, Vancomycin 0.15 mg/kg
 - CT brain – Mild Cerebral edema
-
- CSF: TC: 1500 cells/cumm; 90% PMNs, gram stain shows gram positive cocci in pairs, G: 15 mg/dl (blood glucose 130 mg/dl), P: 150 mg/dl
 - Probable etiology: Strep pneumoniae Meningitis
-
- Past history of Similar condition 2 years back -----??????????

Recurrent Bacterial Meningitis

- Seen in 5% of ABM
- Predisposing condition: head injury and CSF leak
- Impaired cell mediated immunity (Adriani et al, 2007)
- Detection of B2 transferrin in nasal discharge – sensitive and specific for detection

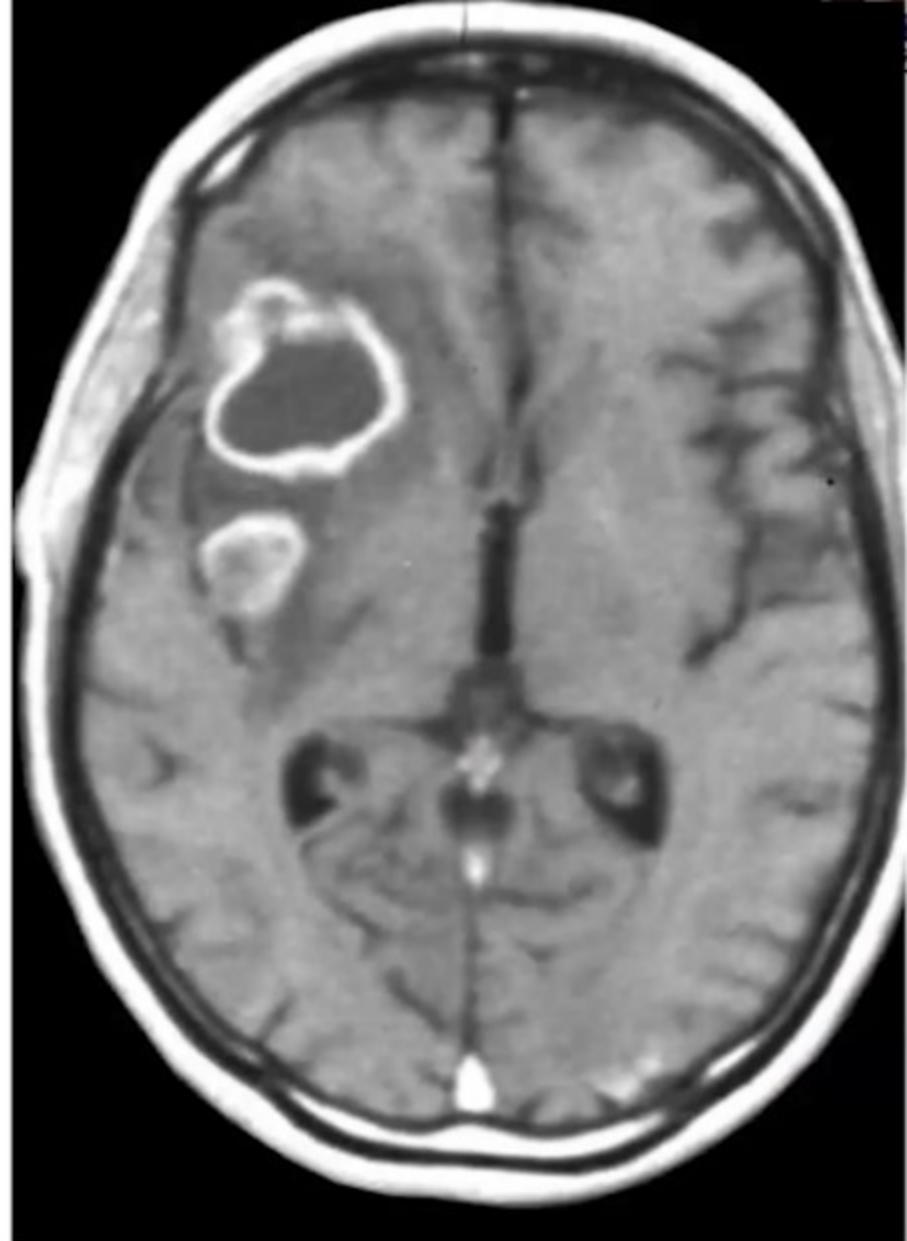


Case 4


- 16/M,
- Fever x 1 day ,Headache and vomiting +
- H/o Seizures followed by altered sensorium x 1 day
- H/o sinusitis x 3 months
- O/E: febrile (101F), photophobia +, neck rigidity+, left hemiparesis

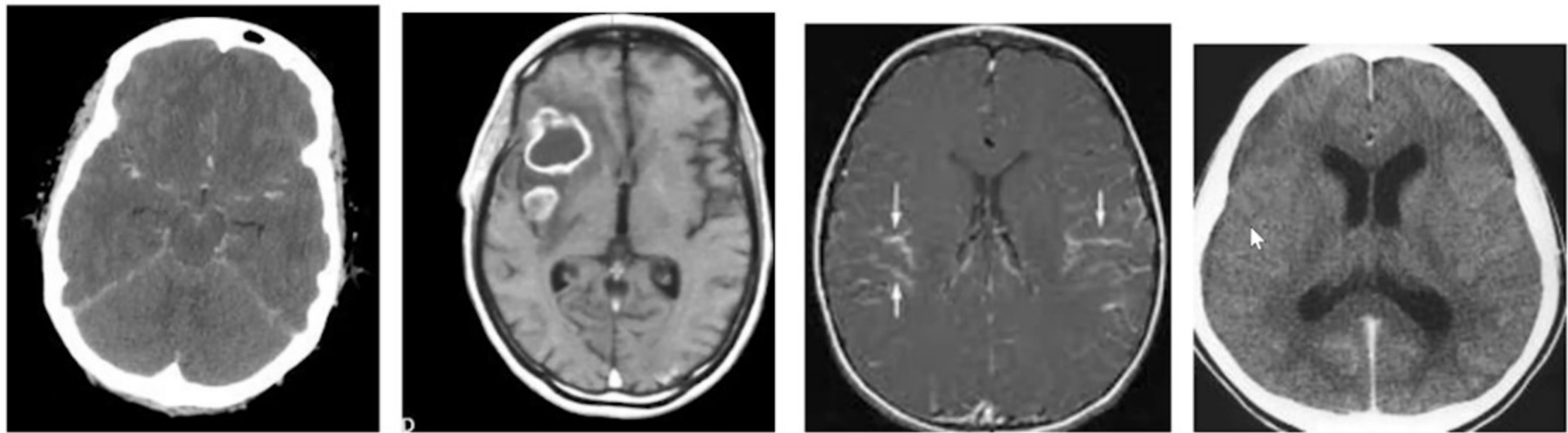
- **Brain Abscess**

- Brain abscess is a focal area of purulent exudate surrounded by a well-developed capsule in the brain parenchyma (Calfee and Wispelwey)



Investigations

- Imaging of the Brain (CT / MRI)

- Lumbar puncture – CSF analysis
- Blood culture



Imaging in Pyogenic Meningitis

Cerebrospinal fluid drawn
from between two vertebrae



- **Macroscopic appearance-**
- Hazy/cloudy/turbid-pleocytocis/
- **CSF glucose-**
- <45 mg/dl-bacterial.

- **CSF protein-**
- >55 mg/dl-bacterial/fungal/tubercular



Empirical therapy for bacterial meningitis

Predisposing Factor		Antimicrobial therapy
Age	Neonate	Ampicillin plus cefotaxime; or ampicillin plus an aminoglycoside
	Infant (1-23 months)	Vancomycin plus a third or fourth generation cephalosporin ^a
	Children & adults (2-50 years)	Vancomycin plus a third or fourth generation cephalosporin ^{a,b}
	Adults (>50 years)	Vancomycin plus ampicillin plus a third or fourth generation cephalosporin ^a
Immuno-compromised state		Vancomycin plus ampicillin plus either cefepime or meropenem
Basilar skull fracture		Vancomycin plus a third or fourth generation cephalosporin ^a
Head trauma		Vancomycin plus either ceftazidime or meropenem

^a Cefotaxime or ceftriaxone or cefepime

^b Add ampicillin if meningitis caused by *Listeria monocytogenes* is suspected

DURATION OF ANTIBIOTIC THERAPY



Microorganism	Duration of therapy
Neisseria meningitidis	7
Haemophilus Influenzae	7
Streptococcus pneumoniae	10-14
Streptococcus agalactiae	14-21
Aerobic gram negative bacilli -a	21
Listeria monocytogenes	> 21

a Duration in the neonate is 2 weeks beyond the first sterile CSF culture or > 3 weeks, whichever is longer

Chemoprophylaxis Regimens for Meningococcal Disease

Age Group	Antibiotic Regimen for Chemoprophylaxis
Infants aged 1 month or less	Rifampin 5 mg/kg q12h for 2 days
Children and infants older than 1 month	Rifampin 10 mg/kg q12h for 2 days
Children less than 15 years of age	Ceftriaxone 125 mg intramuscularly once
Adults	Ceftriaxone 250 mg intramuscularly once <i>or</i> Ciprofloxacin 500 mg once* <i>or</i> Rifampin 600 mg PO BID for 2 days

Bacterial Meningitis

Pyogenic Meningitis

SUMMARY

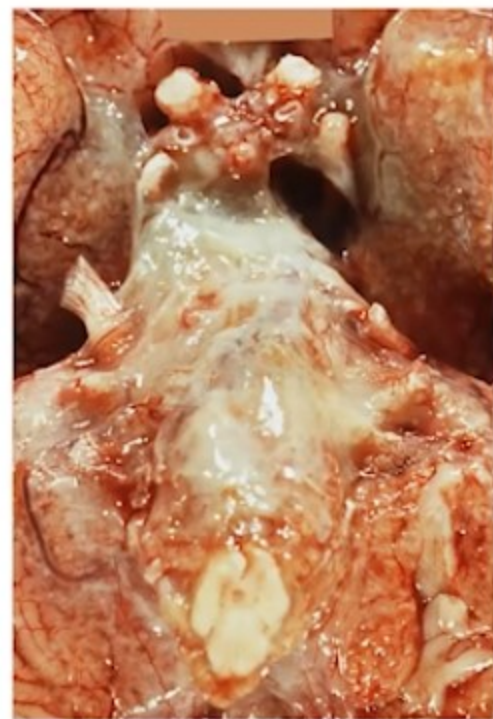
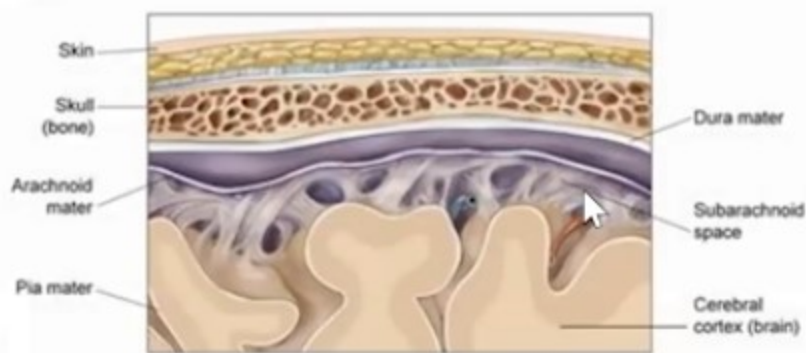
Case 5

- Fever on and off x 3 months
- Associated with weight loss, decreased appetite
- Headache x 1 month
- Behavioural disturbances x 3 days followed by 1 episode of seizure and altered sensorium
- O/E: GCS – 9; opens eyes to pain, talking irrelevantly, paucity of left side, kernigs+

Tubercular Meningitis

Pathogenesis

- TB Bacilleamia (primary or late reactivation) → subependymal tubercles → rupture into the subarachnoid space → meningitis
- Dense gelatinous exudate develops at the base of the brain → surround arteries and CN at the base of the brain → hydrocephalus, vasculitis → infarction, hemiplegia, quadriplegia



Clinical Presentation

- **3 Stages**

- **1 - Pts lucid at presentation w/o focal neuro signs or hydrocephalus; prodromal, lasts 2-3 wks and characterized by insidious onset of malaise, HA, low-grade fever**
- **2 – Meningitic phase -meningismus, V, lethargy, confusion, CN palsies, hemiparesis**
- **3 – Paralytic phase – advance to stupor, coma, seizure, hemiparesis.**

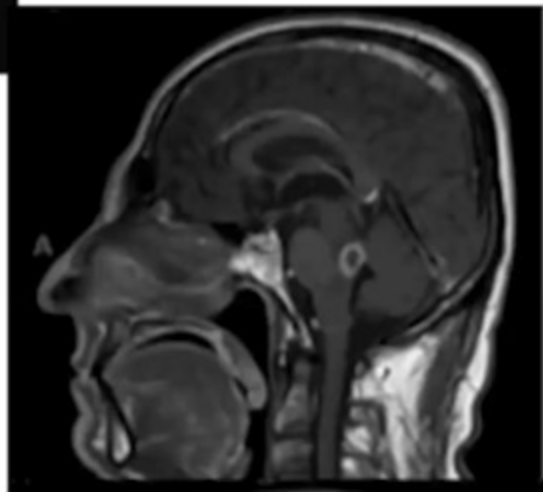
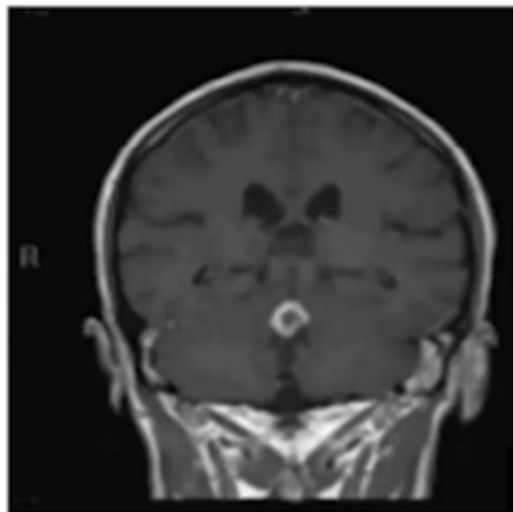
Clinical Presentation

- Most common clinical findings:
 - Fever
 - HA
 - Vomiting
 - Nuchal Rigidity
 - Altered mental status
 - CN Palsies, esp CN III

Case 6: Tuberculoma

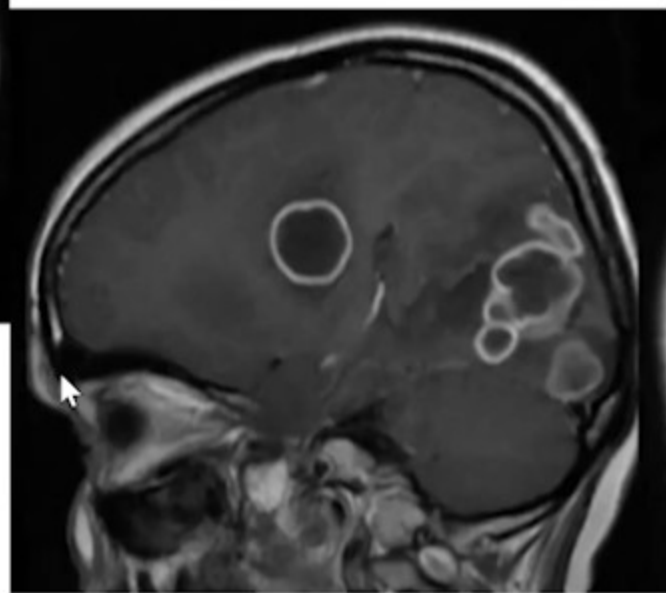
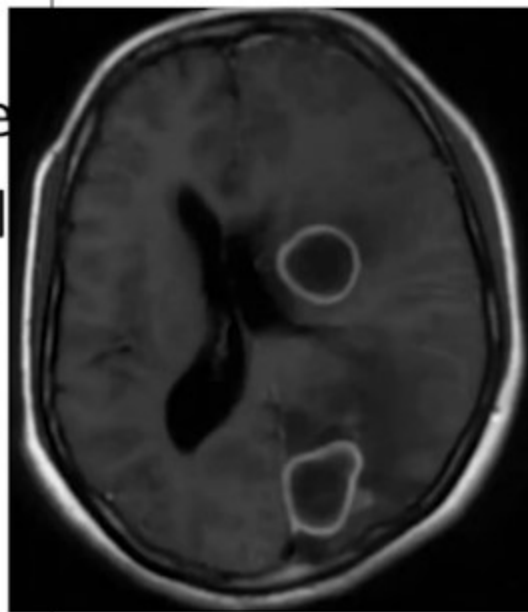
- The least common of CNS TB
- 1% of patients.
- Multiple in 15%-33%
- Seizure
- Symptom of Raised ICT – Headache, Vomiting.
- Focal neurological deficits
- Constitutional symptoms : fever, weight loss in 20-25%

Modi et al J Postgrad Med Edu Res 2013:47(4)



Case 7: Tuberculous abscess

- Single or multiple
- Common in IC status, old people
- Rapidly progressive neurological deficits
- Raised ICT – Headache, Vomiting.
- Focal neurological deficits
- Surgical exploration and drainage



Case 8: Optochiasmatic Arachnoiditis



- Important causes of vision loss in TBM
- Has important therapeutic and prognostic implication
- Exudates- interpeduncular, suprasellar and Sylvian cisterns of the brain
- Develop paradoxically with anti-TB drugs
- Treatment --challenge response-- generally unsatisfactory

Expert Rev. Anti Infect. Ther. 9(9), 719725(2011)

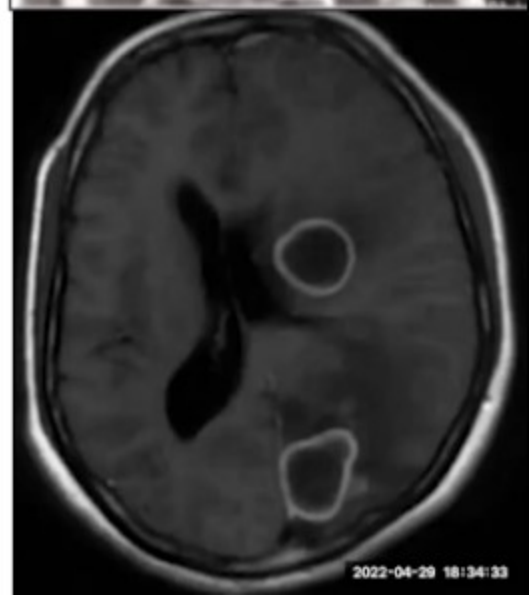
Diagnosis

- Other Studies

- Brain imaging – demonstrates hydrocephalus, **basilar exudates and inflammation**, tuberculoma, cerebral edema, cerebral infarction

- CXR

- Abnormal, sometimes miliary pattern



Diagnosis

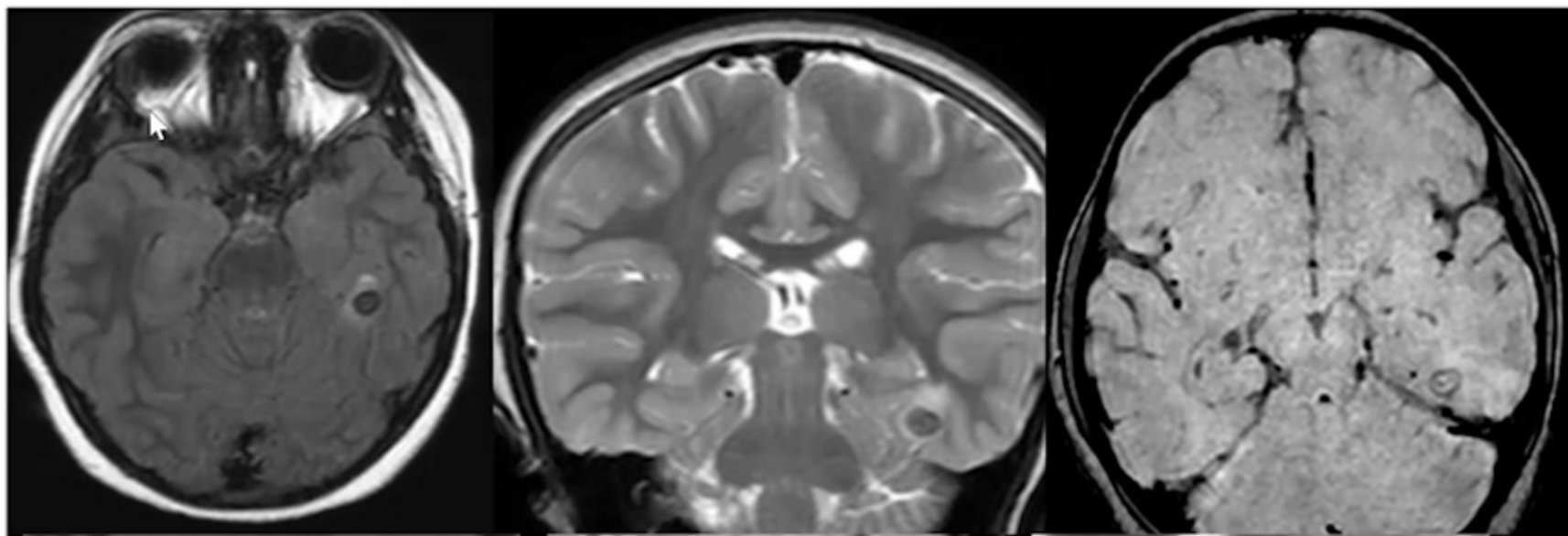
- CSF Examination
 - Usually lymphocytic pleocytosis
 - Paradoxical change from lymphocytic to neutrophilic predominance over 48 hr pathognomonic for TB meningitis
 - Elevated protein with severely depressed glucose
 - Repeated specimens for AFB culture necessary
 - ADA level

Treatment: Antimicrobial Therapy

- Start as soon as there is suspicion for TB meningitis
- Same Guidelines as those for pulmonary TB
 - Intensive Phase: 4 drug regimen of Isoniazid, Rifampin, Pyrazinamide, and Ethambutol or Streptomycin for 2 months
 - Continuation Phase: Isoniazid, Rifampin, Ethambutol for another 10 - 16 months
- Glucocorticoids Indicated with: Dexamethasone 12 mg/d x 3 weeks followed by a slow taper
 - rapid progression from one stage to the next
 - elevated OP on LP, CT evidence of cerebral edema
 - worsening clinical signs after starting antiTb meds
 - increased basilar enhancement, or moderate to advancing hydrocephalus on head CT
- Surgery: Ventriculostomy placement

Case 9

- 14 year / Male
- History of 3 episodes of right focal seizures x 3 days
- No altered sensorium
- No focal deficits



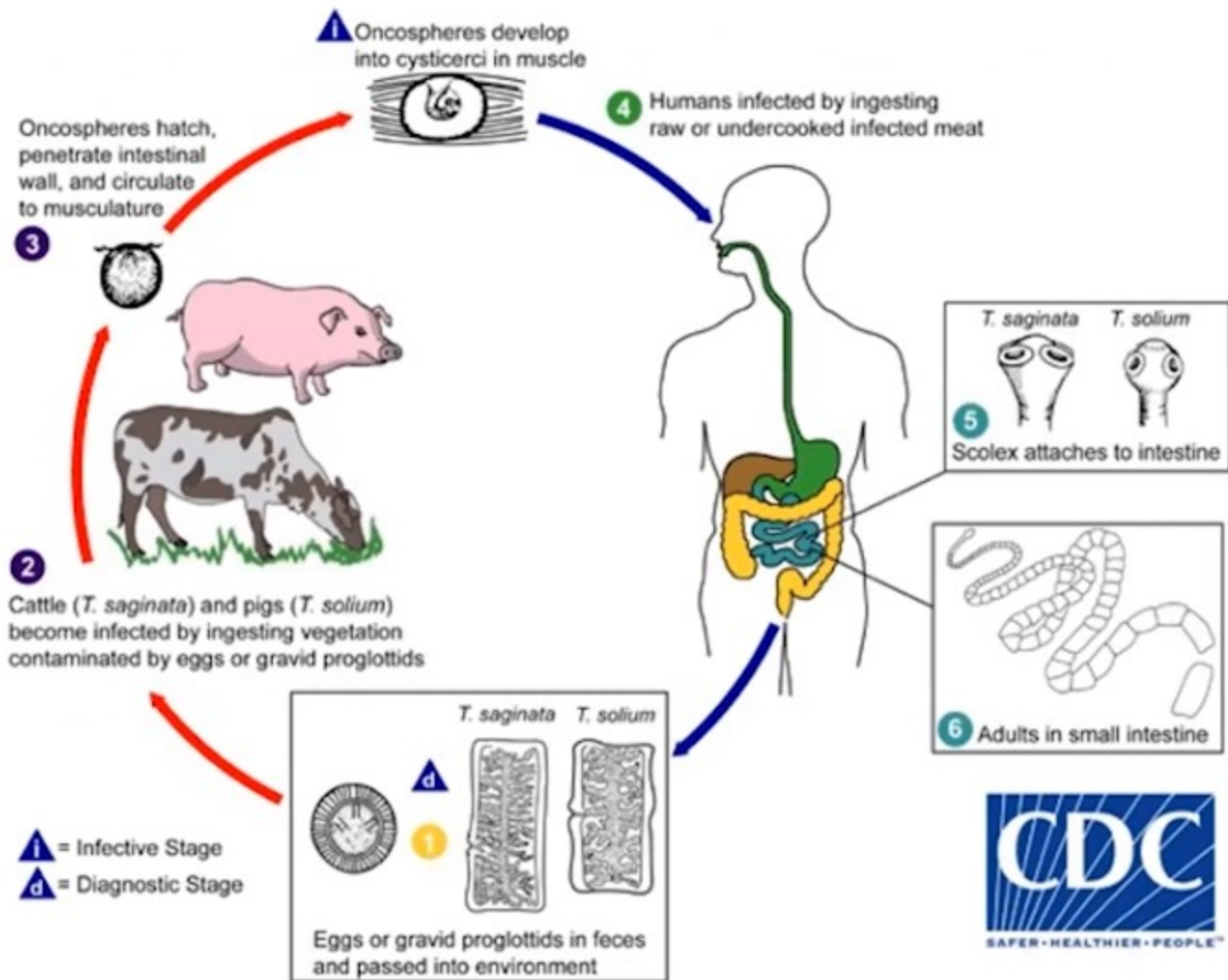
NEUROCYSTICERCOSIS



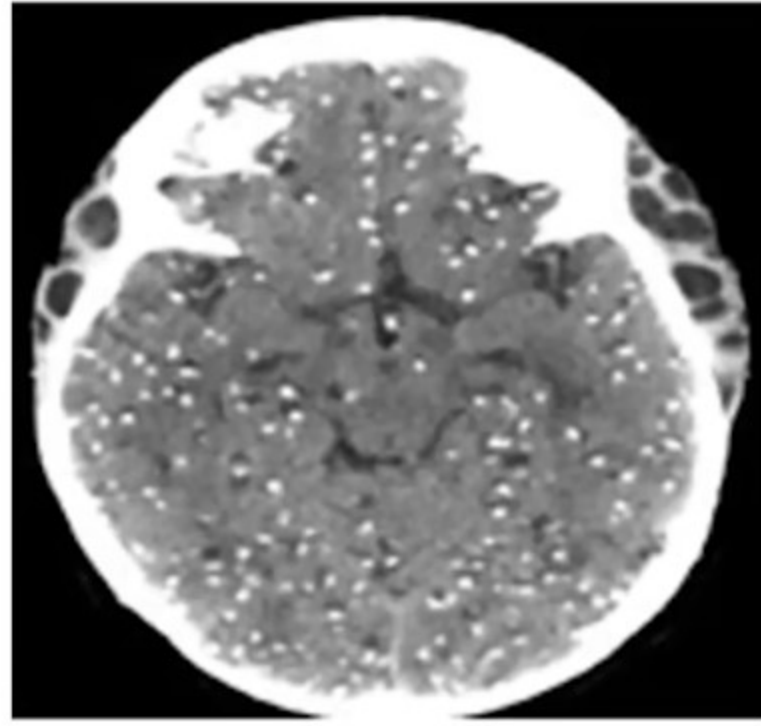
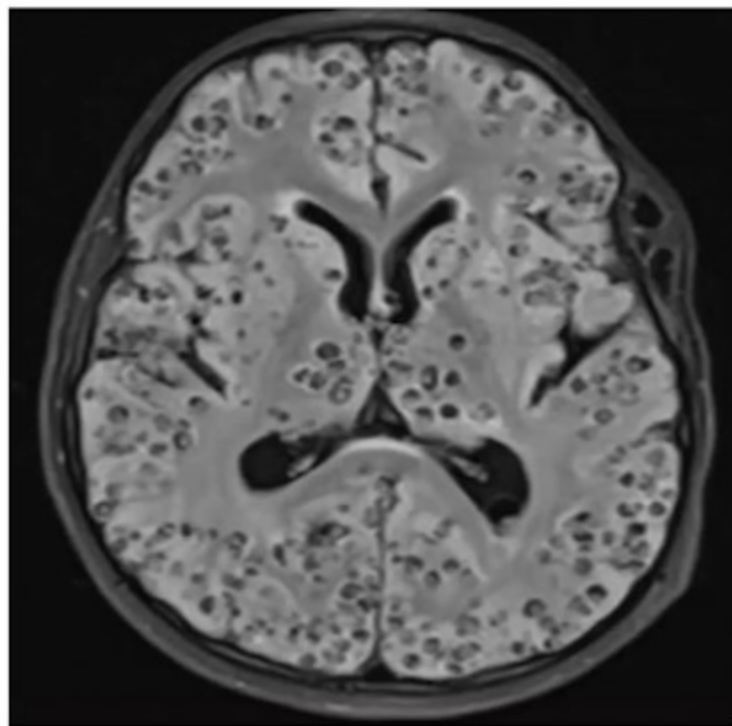
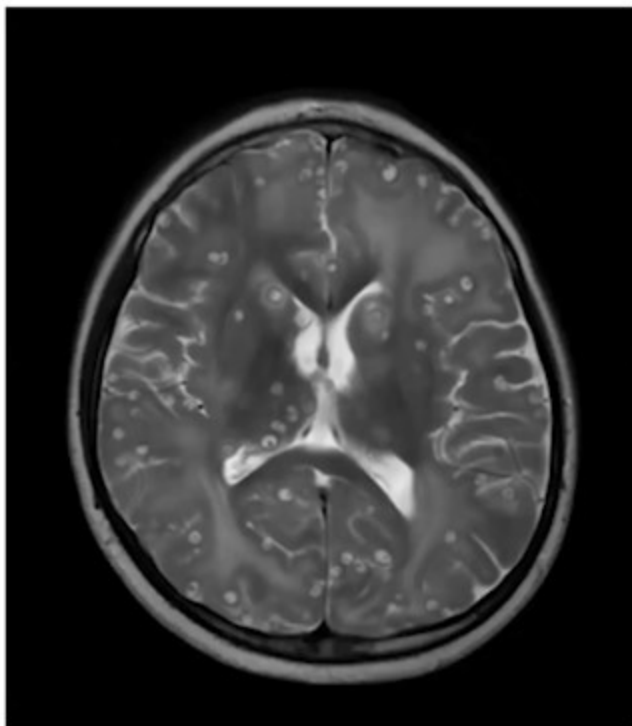
INTRODUCTION

- Parasitic infection caused by *Taenia solium* or *pork tapeworm*
- Cause “*Taeniasis*” or “*Cysticercosis*”
- Life cycle comprises of oncospheres (soil), cysticerci(pigs), adult stages(humans).
- *Humans – definitive host- reproductive stage*
- *Pigs – intermediate host*

LIFECYCLE



Starry Sky pattern



TREATMENT

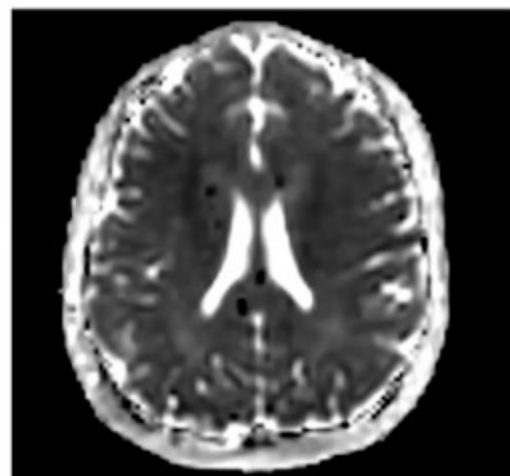
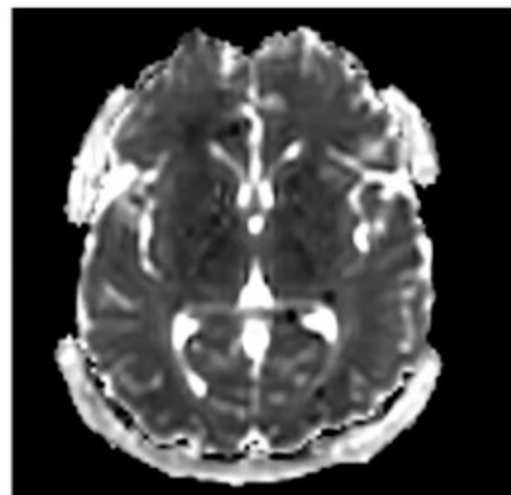
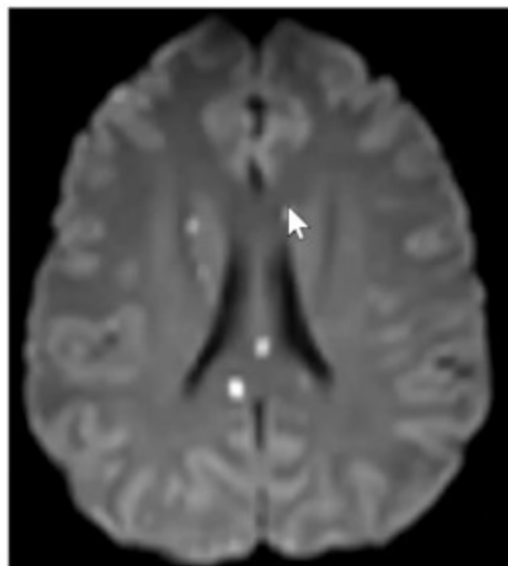
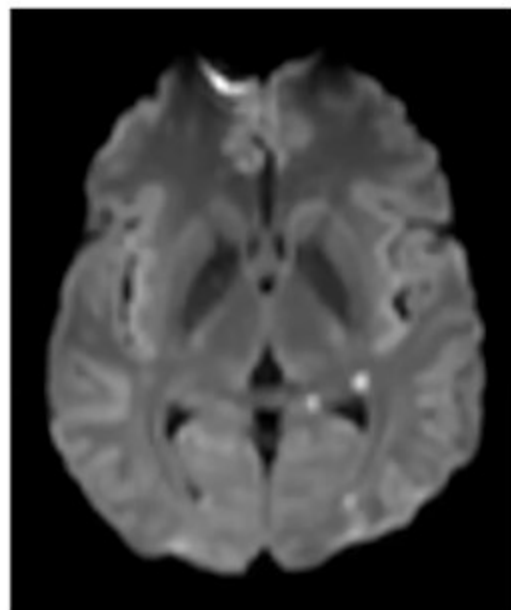
- Antiparasitic
 - Albendazole (15 mg/kg/day divided into two daily doses for 10– 14 days with food)
 - Praziquantel (50 mg/kg/day)
 - Based on the location, stage and number of the vesicle
- Symptomatic
 - Seizures
 - Raised intracranial pressure associated symptoms

CASE 10

- 38/M
- h/o fever, headache, vomiting for 8 days, altered sensorium for 3 days
- O/E- Insight absent, anterograde amnesia, Neck rigidity +
- CSF- 19 cells (12-lympho, 7-poly), Protein- 52, Glucose- 61
- **Weil felix- OX 2- 1:160, OX 19: 1:80** (suggestive of Rickettsial infection- spotted fever group)

Rickettsial infections

- Rickettsiae are pleomorphic obligate intracellular coccobacilli
- Transmitted by arthropod vectors
- Humans are incidental hosts except in epidemic typhus (humans are reservoir host)
- CNS involvement is common in RMSF and epidemic typhus
- Present with headache, fever, myalgia and rash



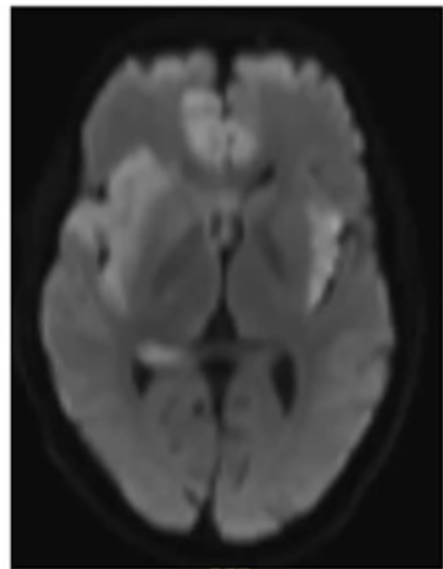
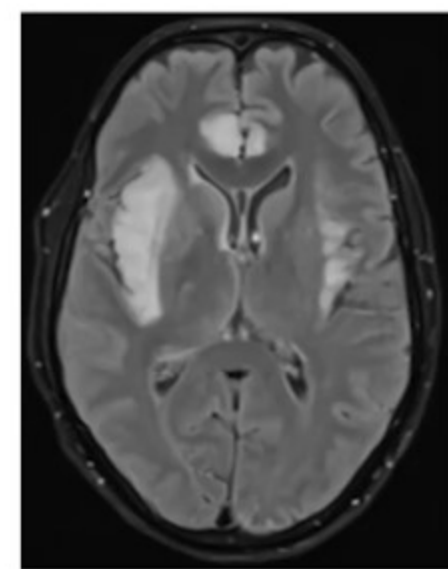
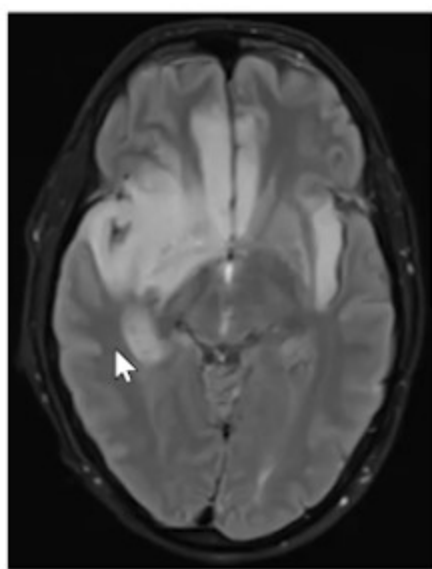
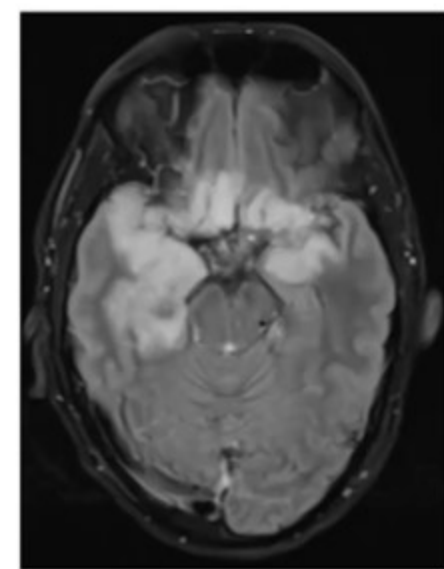
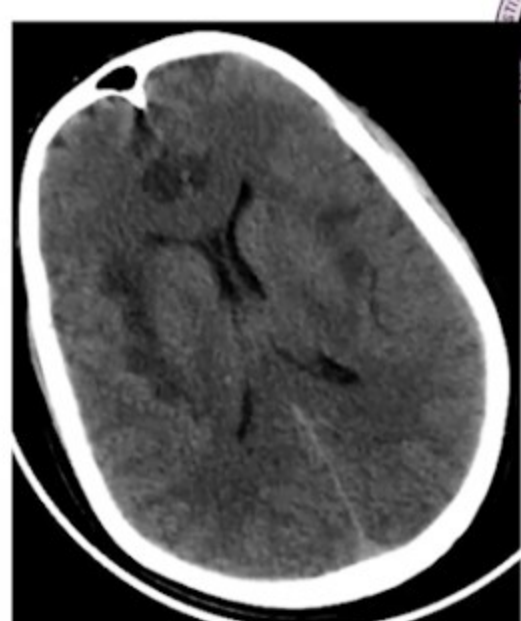
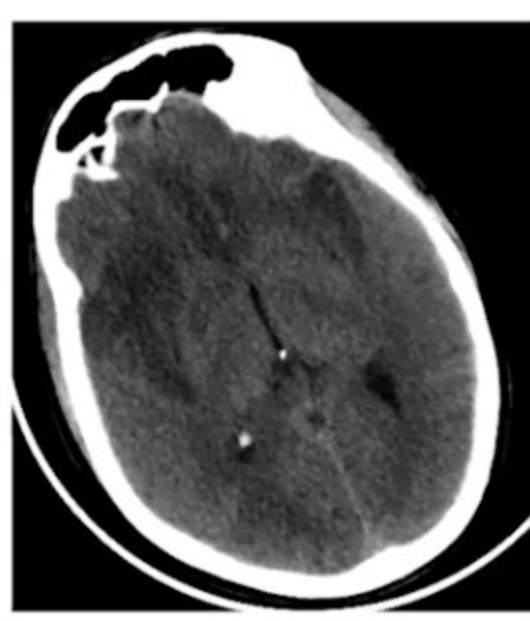
Disease	Agent	Vector	Reservoir	Rash
RMSF	<i>R. Rickettsii</i>	Tick	Rodents	Begins on ankle or wrists. Macupapular then petechial (on D5 of fever)
Epidemic typhus / Brill-Zinser disease	<i>R. Prowazekii</i>	Louse	Humans	Macupapular rash begins in axilla
Endemic typhus	<i>R. Typhi</i>	Rat flea	Rodents	Macupapular rash begins in axilla
Q fever	<i>Coxiella burnetii</i>	No animal vector	Cattle, sheep, dog, goat	Rare
HME	<i>Ehrlichia cheffeensis</i>	Tick	Deer	Maculopapular
HEE	<i>Erhlichia ewingii</i>	Tick	Deer, canines	Absent
HGE	<i>Anaplasma phagocytophilum</i>	Tick	Deer, rodents	Rare - macular

Case 11: 16 year/ male

- Fever x 4 days
- Irrelevant talk.....
- Picking clothes
- Talking towards ceiling
- Seeing people who have expired, snakes
- Seizures x morning followed by LOC.



Visual Hallucinations



HSV

- Most common cause of Viral encephalitis
 - Common in children and elderly
- Etiology: Herpes simplex virus – Type I and Type II (infants)
- Bimodal age distribution: early childhood, age > 50 yrs

- Fever (90%)
- Headache (81%)
- Psychiatric symptoms (71%)
- Seizures (67%)
- Vomiting (46%)
- Focal weakness (33%)
- Memory loss (24%)
- Alteration of consciousness (97%)
- Hemiparesis (38%)
- Cranial nerve defects (32%)
- Visual field loss (14%)
- Papilledema (14%)

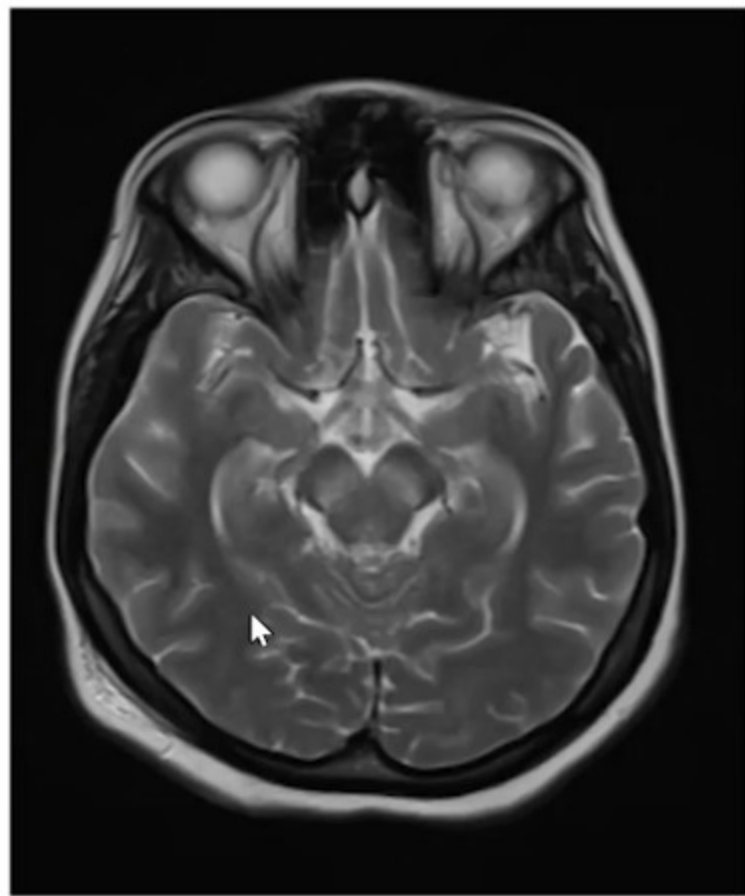
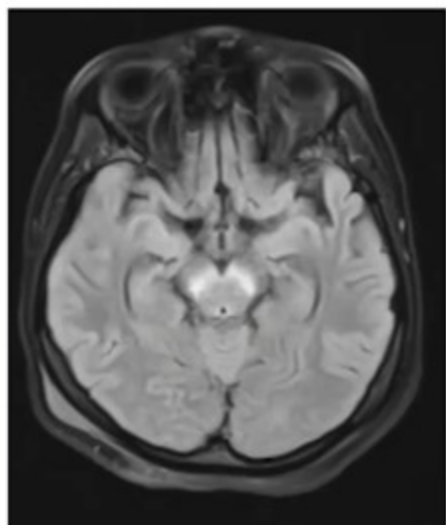
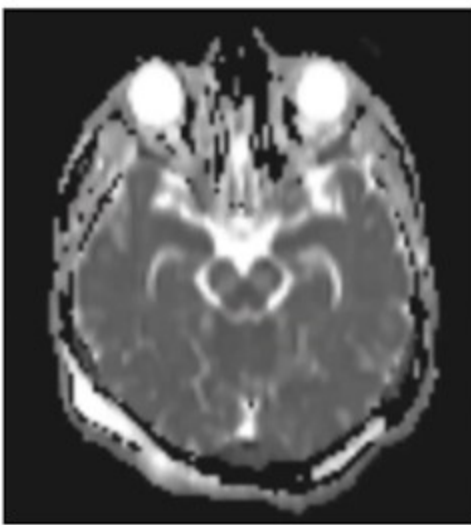
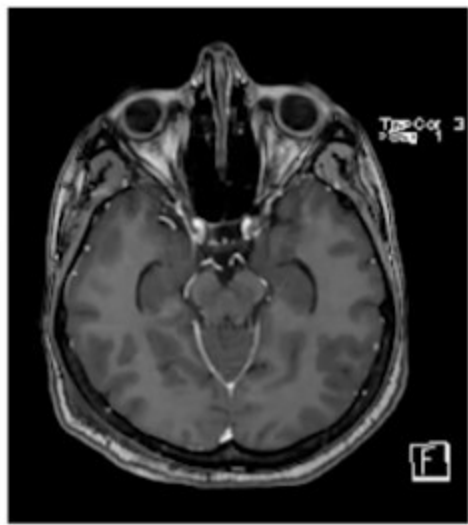
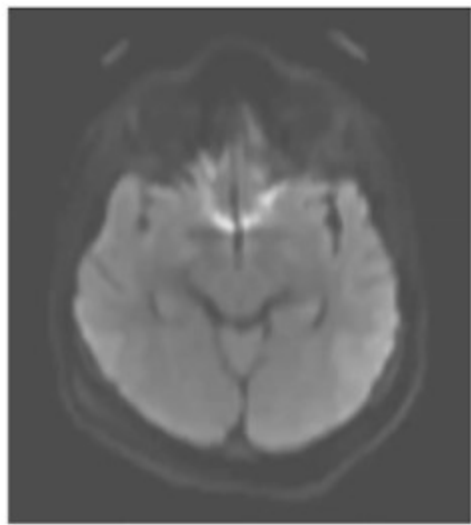
Fp1-F3
F3-C3
C3-P3
P3-O1
Fp1-F7
F7-T3
T3-T5
T5-O1
Fp2-F4
F4-C4
C4-P4
P4-O2
Fp2-F8
F8-T4
T4-T6
T6-O2
Bg-Rf



Case 12: 15y/Male

- Fever x 2 weeks
- Headache, myalgia
- Decreased interaction and not verbalising x 4 days
- O/E:
 - Decreased blink rate
 - Drooling of saliva
 - Rigidity of all limbs



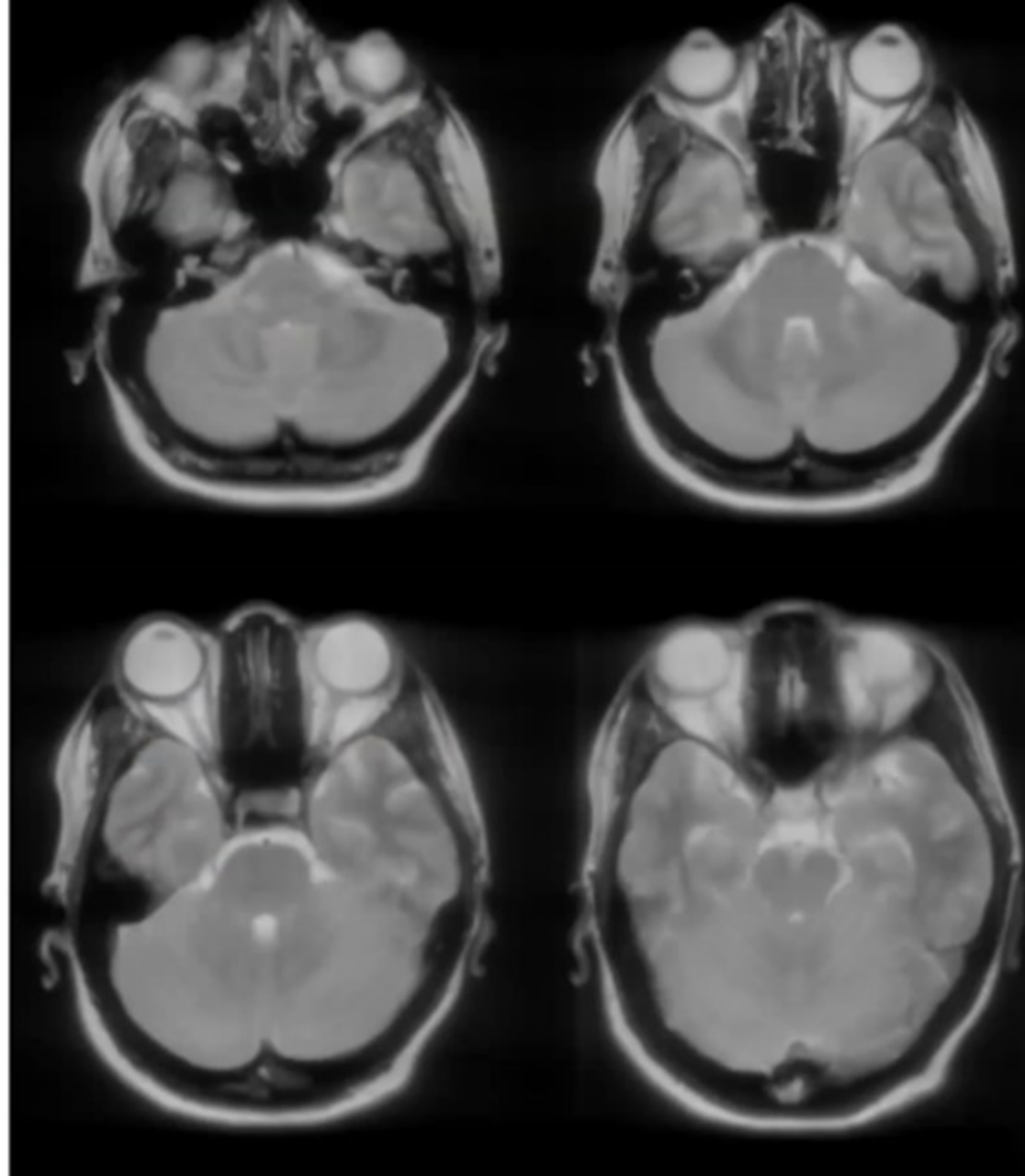


Case 13: 42 year/Male

- Fever x 2 days
- Altered sensorium x 2 days
- O/E:
 - drowsy, mute, opening eyes spontaneously and localizing to pain
 - terminal neck stiffness.
 - Fundus and pupillary response were normal.
 - Patient had complete supranuclear gaze palsy with restricted doll's eye movement in horizontal gaze and ocular bobbing with bifacial weakness and dysphagia.
 - There was spasticity of all four limbs, spontaneous limb movements with brisk deep tendon reflexes and withdrawal plantars.

Case 14: 32 year/Male

- Fever with eye pain x 4days
- Difficulty in walking x 3 days
- O/E:
 - bilateral nystagmus
 - Dysarthria
 - Bilateral cerebellar signs

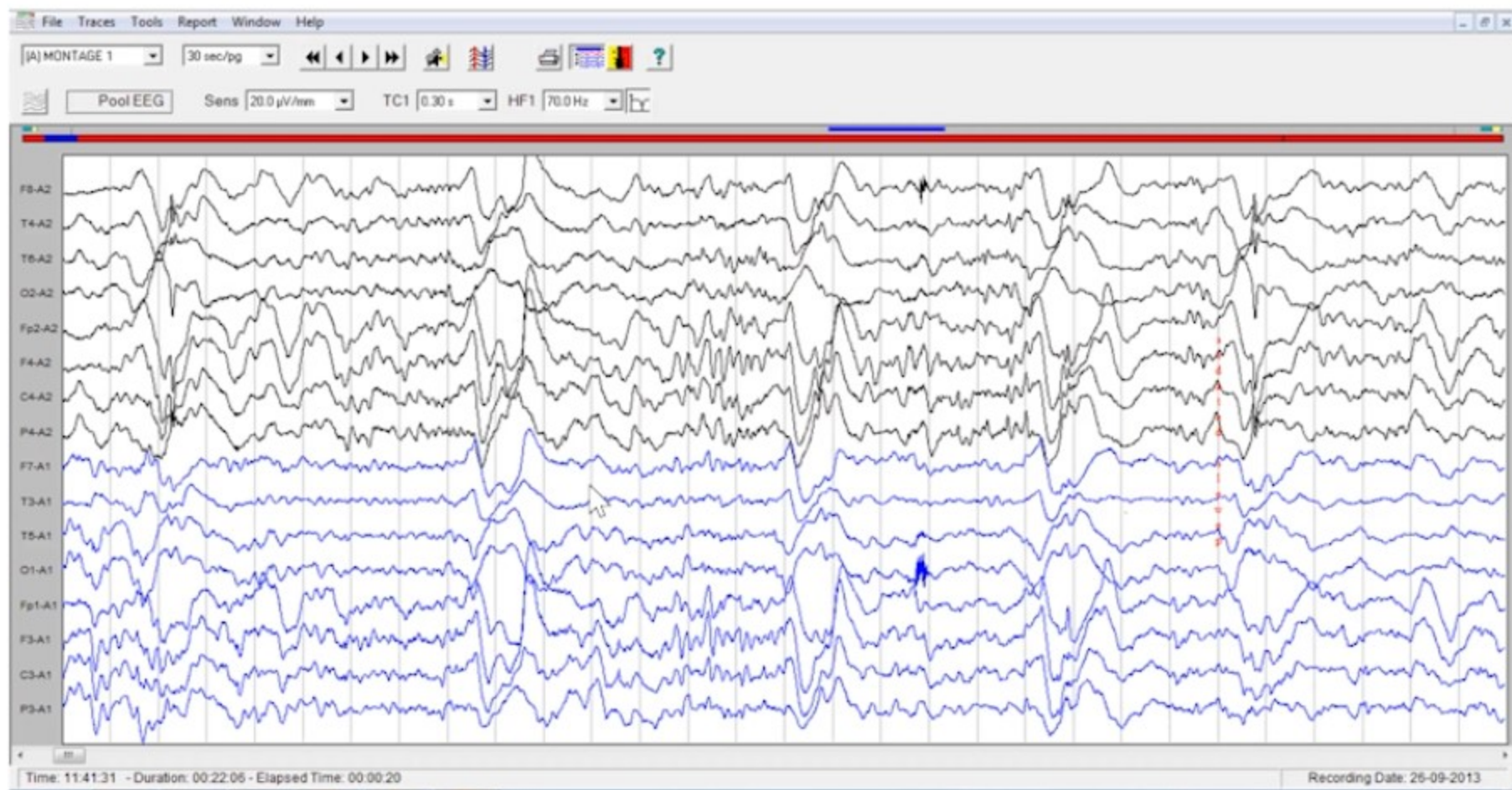
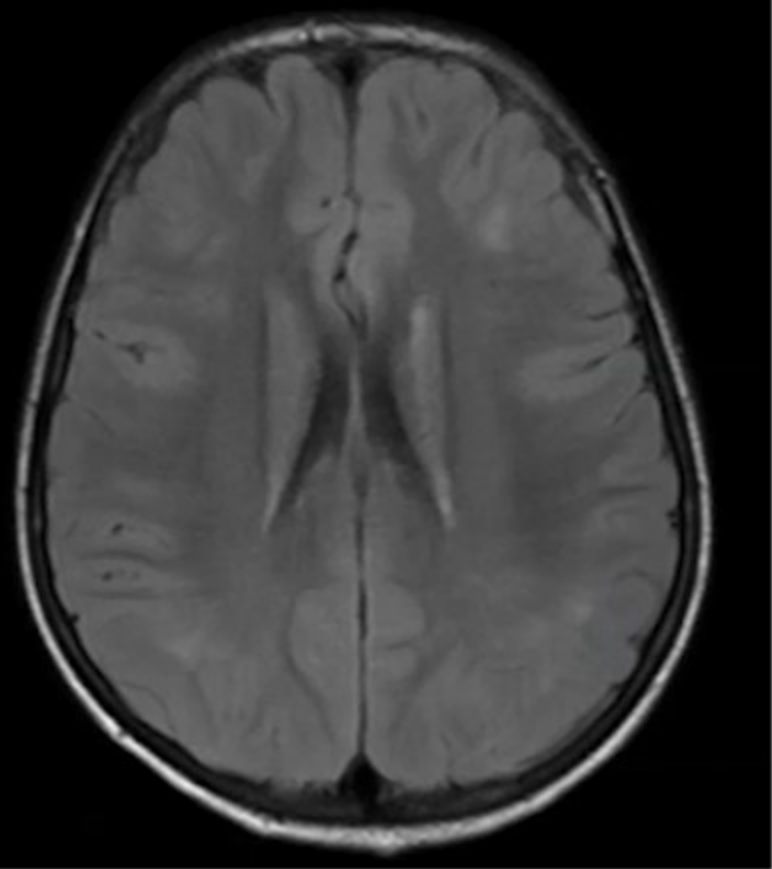


Dengue Encephalitis

- 2nd most common mosquito-borne disease affecting humans after malaria
- Vector - mosquito-borne
- Etiology: one of the four dengue virus (DENV) serotypes.

Case 15: 14 Y/M

- H/O: anger outburst x 3 months
- Decreased attention in school x 3 months
- Frequent falls x 2 weeks
- One episode of seizures – GTCS – 1 day prior to presentation
- Jerky movements as depicted in the video

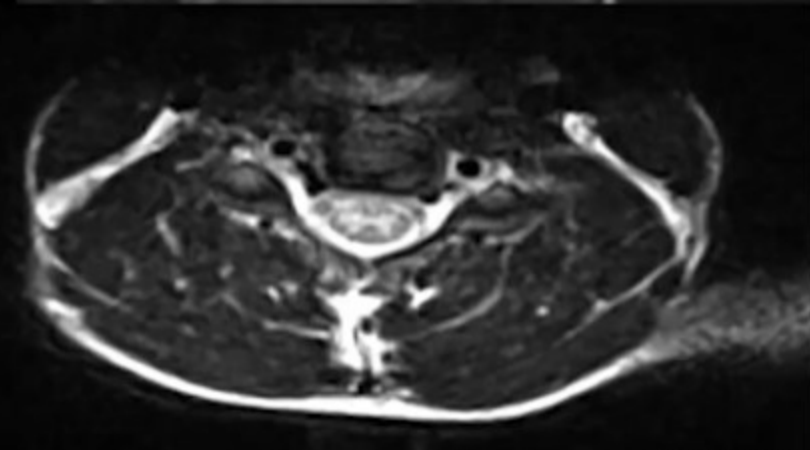
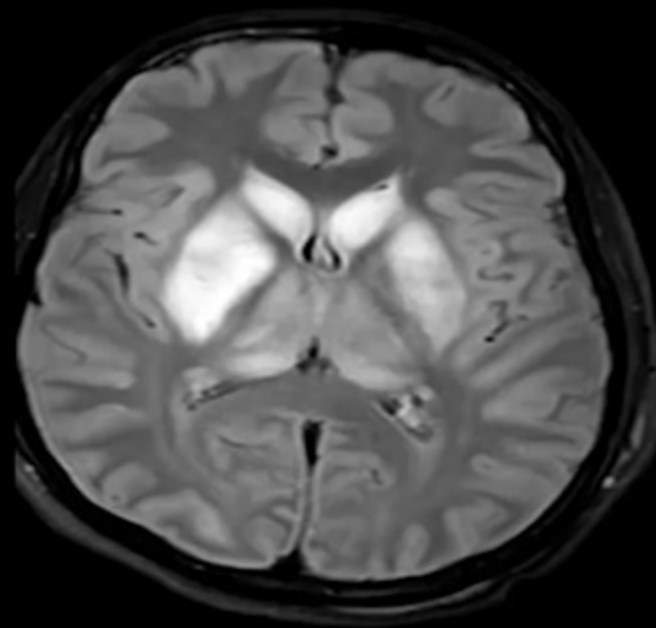
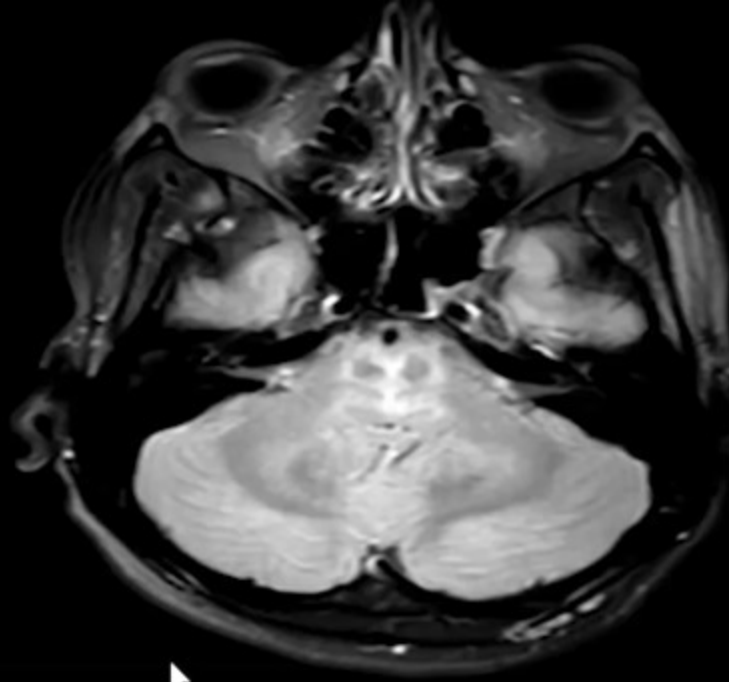
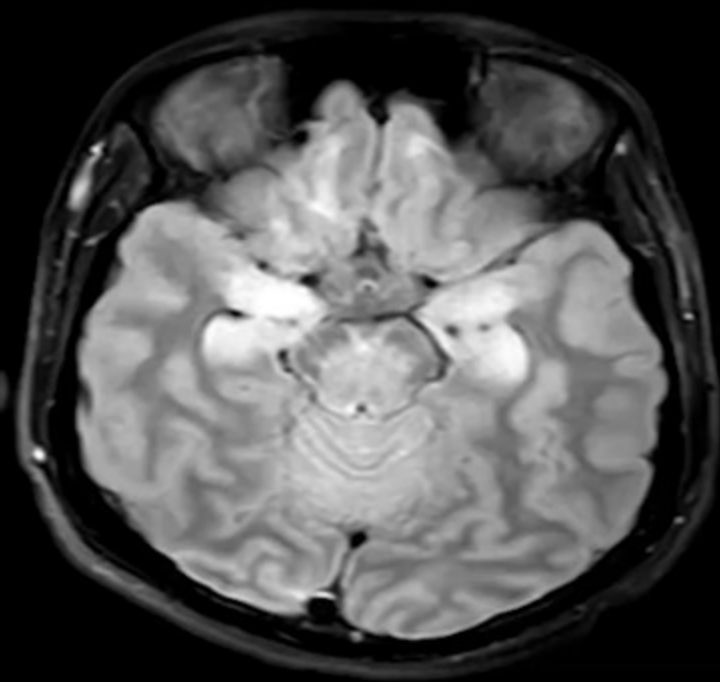


SSPE

- Late Complication of Measles virus
- Age: 5-52 years; (Average: 6-8 years).
- Median interval between acute measles infection and SSPE: 8 years (range 2 to 12 Years).
- Clinical Features: 3 Stages:
 - Stage 1- Behavioral changes, decline in scholastic performance .
 - Stage 2- Motor disturbance, spasticity, weakness, myoclonic jerks, seizures, ataxia, retinopathy, optic atrophy, dystonia.
 - Stage 3- Stupor, coma, autonomic failure.

Case 16: 21 y/M

- Fever x 2 weeks back for 2 days
 - Associated with headache
- 2 days later backache and bladder retention
- Gradual progressive quadriparesis x 1 day
- Past H/O:
 - pet dog bite at left leg 2 months back.
 - no typical history of pain, tingling, numbness at the site of the bite, hydrophobia, or behavioral changes
 - He took only two doses of purified chick embryo cell (PCEC) antirabies vaccine.



CSF for rabies neutralising antibody
titre by Rapid Fluorescent Focus
inhibition test (RFFIT): 64



He succumbed to his illness after 77days of hospital stay



Rabies Viral Encephalitis

- An acute, fatal encephalitis
 - Etiology: Highly neurotropic RNA virus
 - Genus Lyssavirus, family Rhabdoviridae.
 - Mortality:
 - Worldwide: 50,000 human deaths every year
 - 60 % of these cases – India
 - Human rabies - Endemic in India
- World Health Organization (WHO)**

Rabies Encephalitis

ENCEPHALITIC/FURIOUS FORM

- This form starts with fever, malaise, pharyngitis, and paraesthesia at the site of the bite
- Classical neurological symptoms of hydrophobia, aerophobia, agitation, hypersalivation, and seizures.

PARALYTIC /DUMB FORM

- This is Guillain-Barré-like, is characterized by progressive paralysis without an initial furious phase.
- 20–30% of rabies victims present in this manner.

Take Home Messages.....

- History is Crucial in Diagnosis
- Apart from neurological involvement try to ask history regarding the possible etiologies
- Imaging crucial for diagnosis and ruling out contraindications for LP
- Treatment at the earliest –
 - Pyogenic / TBM / Others