CNS TUBERCULOSIS IMAGING AND SURGERY

Tuberculosis

- As old as recorded history
- Symptoms described in the Rig Veda (1500 BC)
- Unequivocal lesions in Egyptian mummies
- Odier, Ford described meningeal TB 1790
- Surgical excision Wernicke and Hahn 1882,

Tuberculosis

- CNS tuberculosis complicates 10% of all TB
- Never the first manifestation
- Occurs within 6-12 months
- Circle of Willis more frequently involved than the basilar system

Mycobacterium tuberculosis

- Acid fast bacillus
- Does not stain on gram stain
- Obligate aerobes
- Difficult to grow
- High lipid in cell wall
- Hominis/ Bovine/ Avium

Pathogenesis

- May develop during initial infection/ reactivation
- Haematogenous dissemination
  - Commonest
  - Focus in brain (Rich focus)
  - Rupture of focus into subarachnoid/ ventricular space
- Contiguous spread

CNS tuberculosis

- Intracranial
  - Parenchymal
  - Meningeal
  - Osseous
- Spinal
  - Parenchymal
  - Meningeal
  - Arachnoiditis
  - Osseous

Epidemiology

- Incidence varies blacks > whites
- Predominantly in the **young (50% <10**)
- Abscess in 4-8% (20% with HIV)

Pathology

- Immature lesions – multiple tubercles in oedematous brain
- Mature: avascular mass, nodular extensions, yellowish gritty casseous areas
- 60% attached to dura

Pathology (parrenchymal)

- Can be present anywhere
- Cerebellum in children
- Cerebral hemisphere and basal ganglia commoner in adults

Pathology (tuberculoma)

- Tuberculoma (classical lesion)
- Tuberculoma en plaque
- Tuberculous abscess
- Cystic tuberculoma
- Multiple grape like tuberculoma
- Microtuberculoma
- Calcified tuberculoma
- Tuberculous encephalopathy

Pathology (tuberculoma)

- Dastur described six main types
  - Parenchymal changes.
    - (1) Ventriculitis
    - (2) Border-zone encephalitis
    - (3) Infarction
    - (4) Internal hydrocephalus
    - (5) Diffuse oedema
    - (6) Tuberculoma

Pathology (meningeal)

- Classically Commonest in 6m – 3 years
- Now adults 50%
- Thick exudate encasing nerves, vessels
- HCP, tuberculoma, arachnoiditis
- Diffuse perivasculitis
- Infarcts
- Pachymeningitis

Diagnosis

- Montoux test
- Hb/ ESR
- CXR
- ELISA
- CSF
- PCR
- Imaging
- Biopsy

Imaging

- X ray
- Angiography
- CT
- MRI

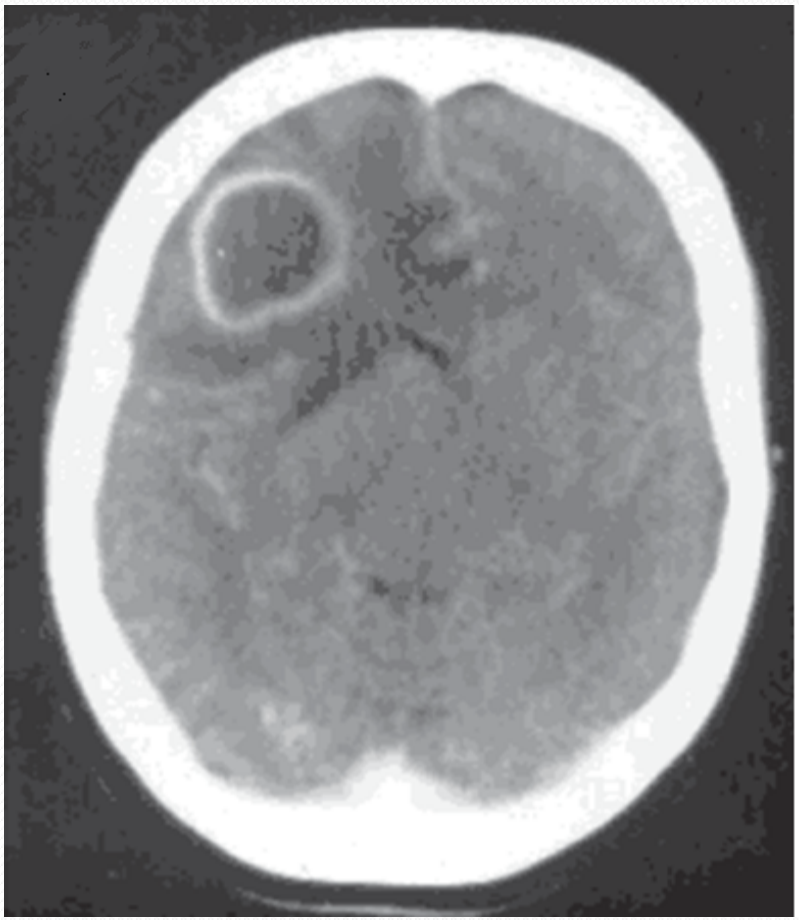
} of historical significance

Imaging

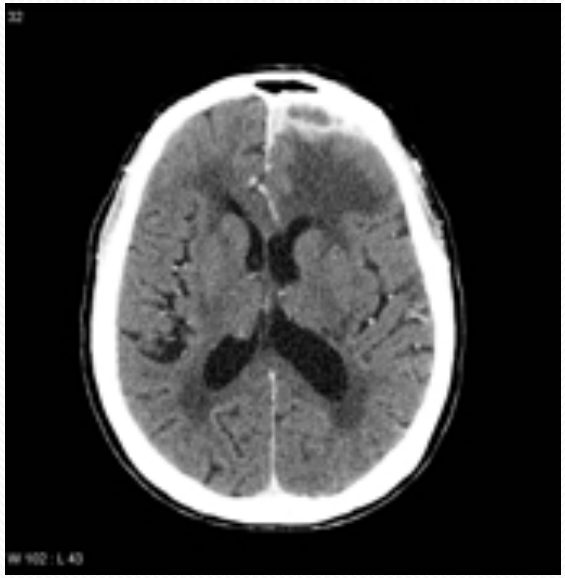
- Tuberculoma
  - Typically cortical and subcortical
  - Multiple in 10-35%
  - Milliary rare (children)
- Meningitis (commonest form of CNS TB)
  - Isolated meningitis is rare (5% in children)
  - Basal cisterns

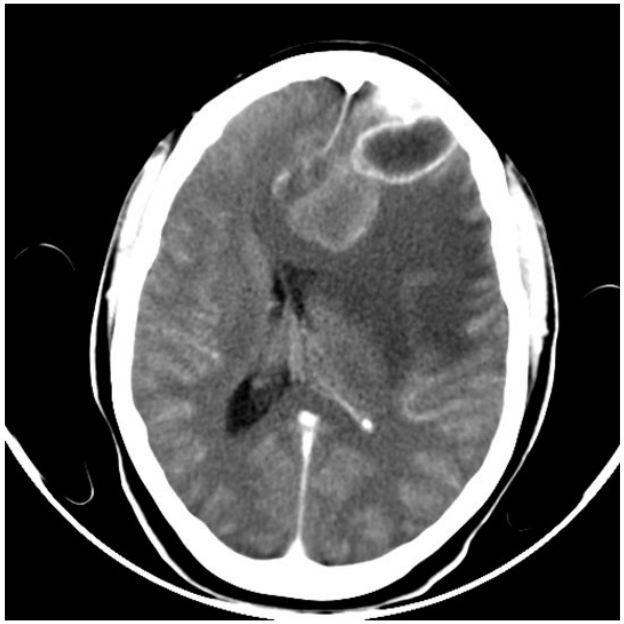
Imaging (CT tuberculoma)

- Cerebritis: hypodense areas
- Perilesional oedema out of proportion
- Early tuberculoma: iso to slightly hyper dense , ring enhancement
- Evolved : well delineated ring enhancing mass, target sign (central enhancement or calcification)
- Healed: often calcify
- Manifestations
  - Small disc/ rings
  - Large rings with central lucency
  - Large nodular mass with irregular outline
  - Multiple lesions in 15-20%



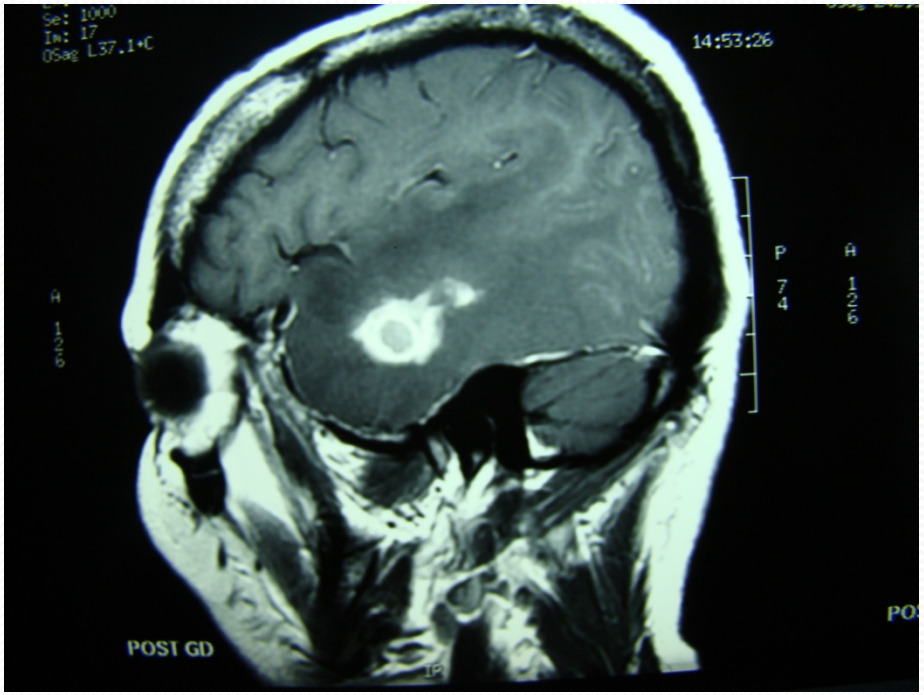
Caseating tuberculosis granuloma involving the right frontal lobe. CECT shows a rim-enhancing lesion in the right frontal lobe consistent with a caseating tuberculosis granuloma

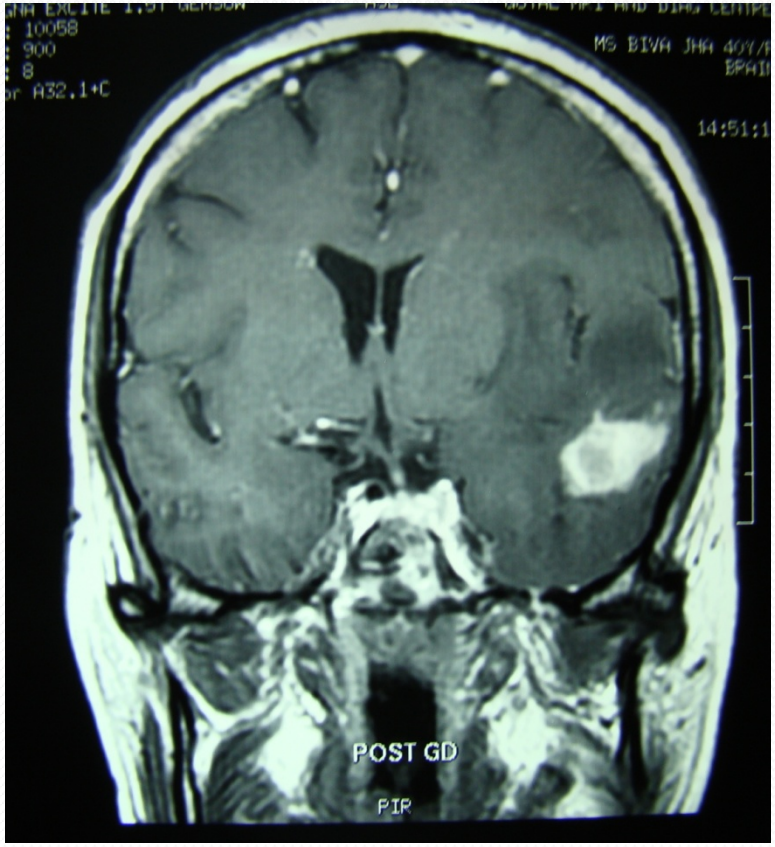




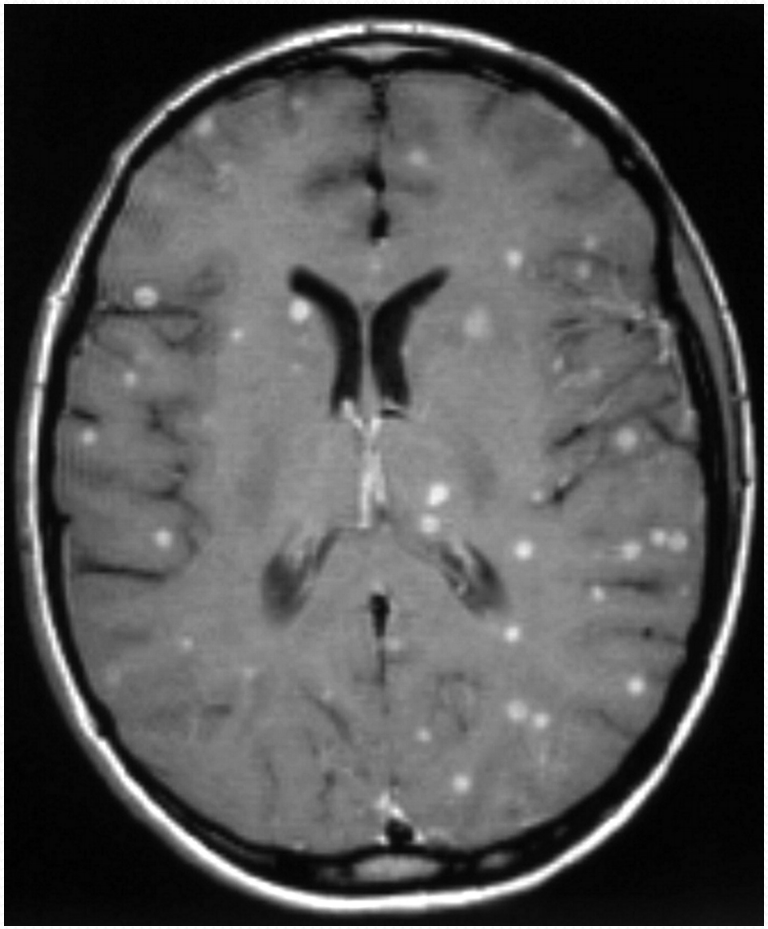
Imaging (MRI tuberculoma)

- T1 : isointence
- T2: central hyper with hypo ring
- Marked thin rim enhancement
- Hypo on T2: fibrosis, gliosis, macrophage infiltration

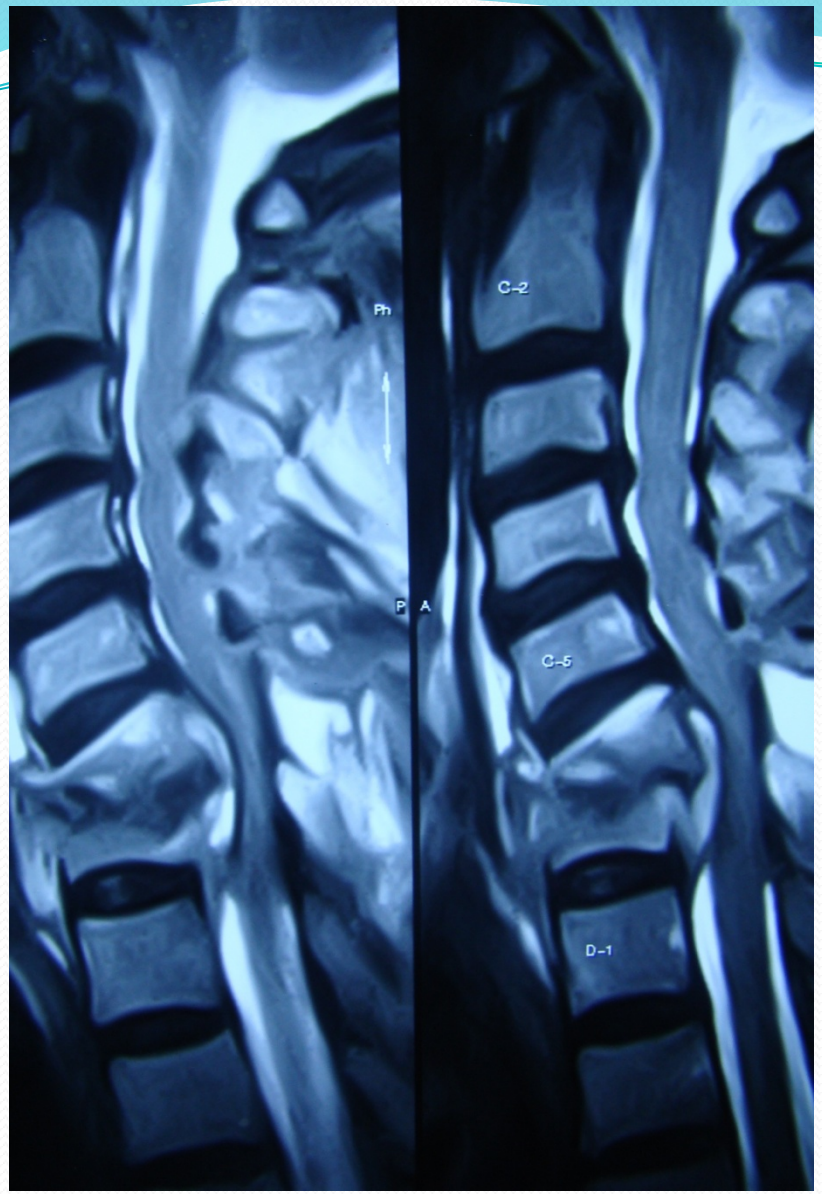




Parrenchymal tuberculosis. contrast-enhanced T1-weighted MR image demonstrates multiple enhancing caseating and non-caseating tuberculomas, predominantly within the left frontal and parietal lobes



Milliary CNS tuberculosis. Axial contrast-enhanced T1-weighted MR image shows multiple small high-signal-intensity foci within both cerebral hemispheres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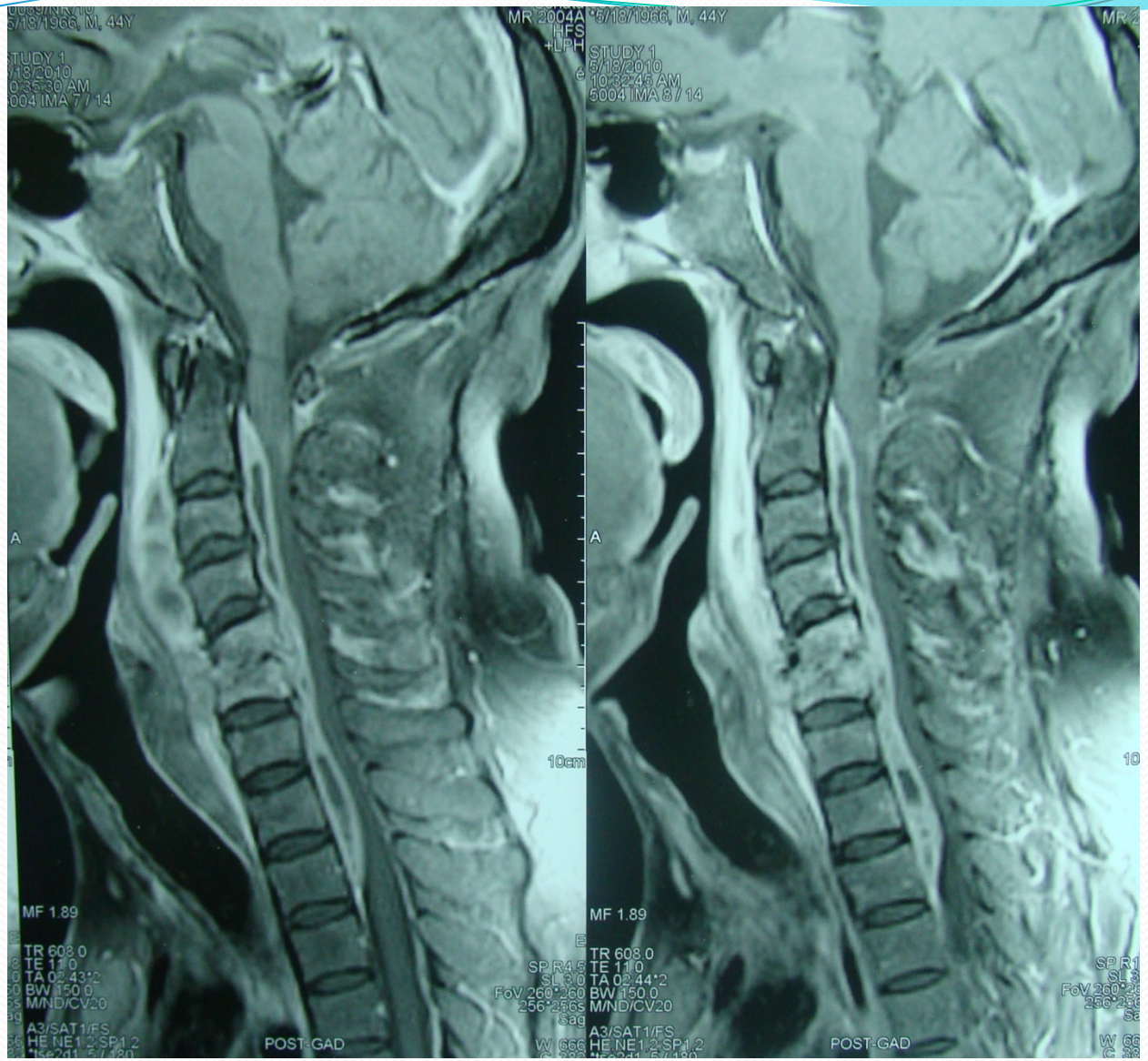
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STUDY 1
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STUDY 1
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HE NE1 2 SP1.2
POST-GAD

	CT	MRI
Noncaseating granuloma	NECT: hypo-/isodense CECT: homogenous enhancement	T1WI: low SI T2WI: high SI T1WI Gd: homogenous enhancement
Caseating granuloma with a solid center	CECT: heterogenous enhancement centrally Ring enhancement of the capsule	T1WI: low/intermediate SI T2WI: intermediate/low SI T1WI Gd: rim enhancement
Caseating granuloma with a liquid center	NECT: hypodense CECT: rim enhancement	T1WI: hypointense SI T2WI: hyperintense SI + rim hypo T1WI Gd: rim enhancement

A. Bernaerts, F. M. VanhoenackerTuberculosis of the central nervous system: overview of neuroradiological findings. Eur Radiol (2003) 13:1876–1890

Imaging (meningitis)

- Active
- Sequelae
  - Hydrocephalus
  - Ischemia and infarction
    - Medial lenticulostriate
    - Thalamoperforating

    75%
    - Cortex 25%
    - Bilateral 70%
  - Atrophy
  - Calcification

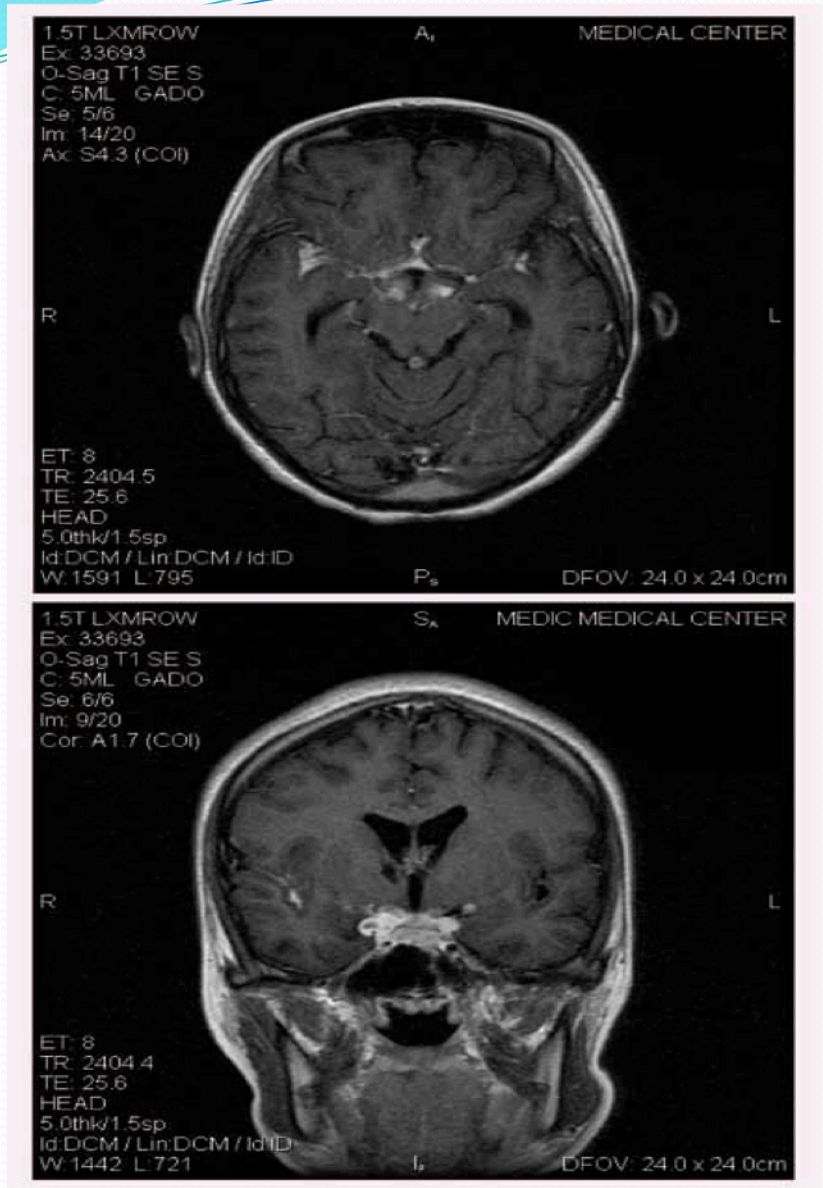
Imaging (CT meningitis)

- NCCT:
  - scans may be normal
  - Obliteration of basal cisterns by hypo/ iso dense exudate
  - en plaque dural thickening
  - Popcorn calcification
  - Hydrocephalus
  - Sequelae of chronic meningitis
    - Infarcts

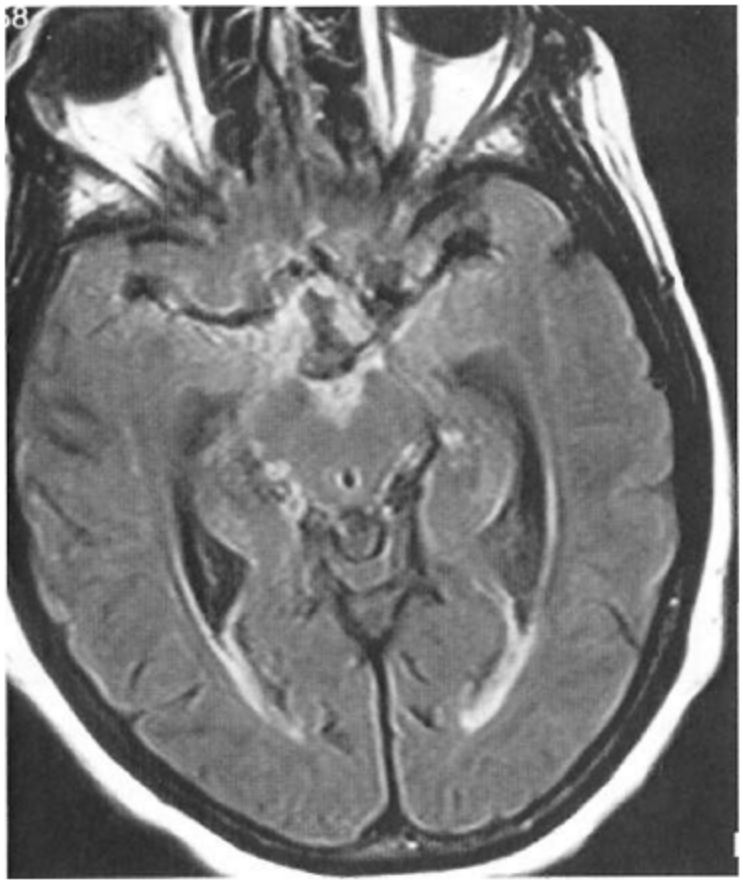
- CECT:
  - Abnormal meningeal enhancement (may persist)
  - Leptomeningeal enhancement sylvian fissures, tentorium
  - Granulomas in the basal meninges
  - Ependymitis

Imaging (MRI meningitis)

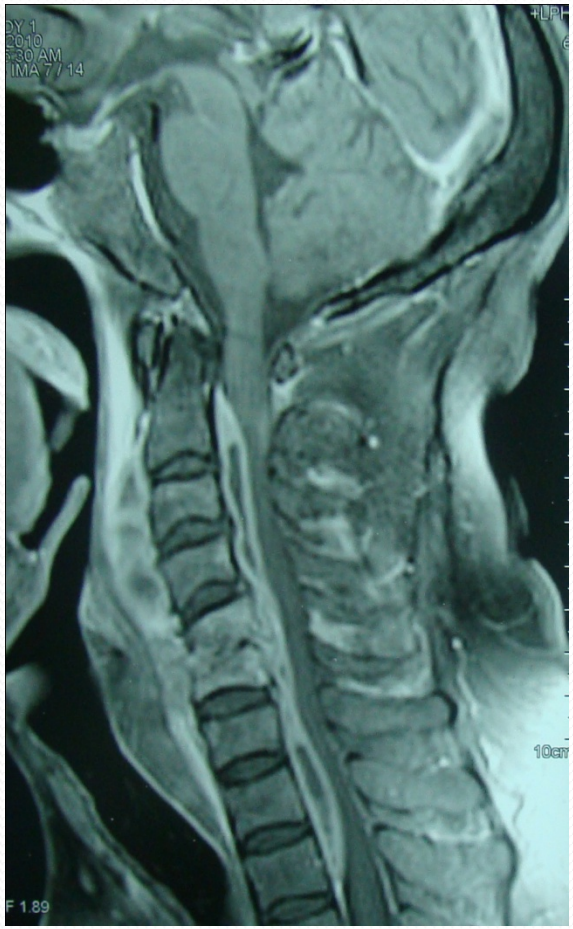
- Unenhanced scan: does not show active meningitis
  - Spine
    - CSF loculations
    - Obliteration of arachnoid space
    - Loss of cord outline in cervicodorsal cord
    - Thickening and clumping of roots in the lumbar cord
- Contrast T1 : basal meningeal enhancement
  - spine
    - Linear enhancement of cord/ roots



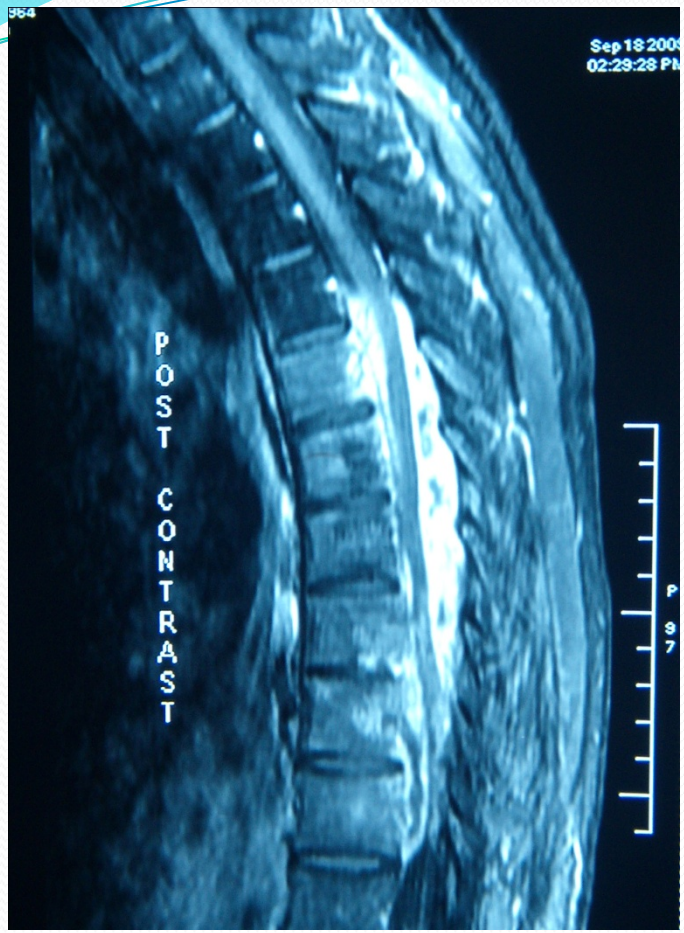
Tuberculous meningitis. Axial contrast-enhanced T1-weighted magnetic resonance (MR) image shows florid meningeal enhancement.

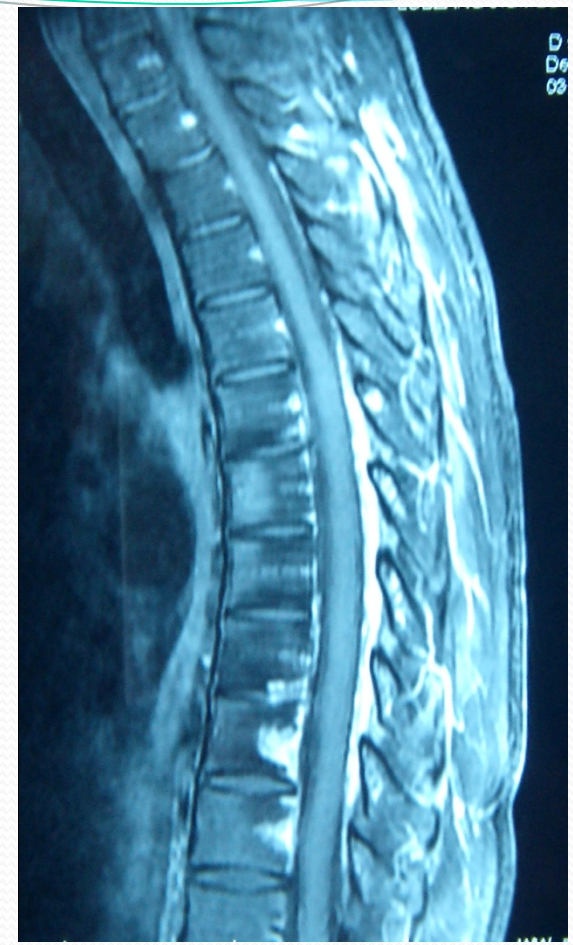


Tubercular meningitis. Axial FLAIR-MR] showing marked hyperintensity of the basal cisterns and prominent temporal horns in a patient with mild communicating hydrocephalus



Tubercular spondylitis with epidural and retroabscess





Enhanced T1-weighted magnetic resonance imaging with fat suppression show intense enhancement of the subarachnoid space indicating arachnoiditis

Tuberculous pachymeningitis

- Rare
- Common sites of involvement are cavernous sinus, floor of middle cranial fossa and tentorium.
- **Radiographic features**
- **CT**

  hyperattenuating solid plaque like densities (calcification may be seen)
- **MRI**
  - **T1** : hypo intense thickened duramater.
  - **T2** : hypo intense thickened meninges.
  - **T1 C+ (GAD)** : intense homogenous enhancement of thickened meninges.

Management

- Medical therapy

- Surgery
  - indications
    - Vision or life threatened by mass effect
    - Failure of response to medical therapy
    - Paradoxical increase in lesion size with therapy
    - Diagnosis in doubt

Medical therapy

Drug	Recommended dose			
	Daily		3 times per week	
	Dose and range (mg/kg body weight)	Maximum (mg)	Dose and range (mg/kg body weight)	Daily maximum (mg)
Isoniazid	5 (4–6)	300	10 (8–12)	900
Rifampicin	10 (8–12)	600	10 (8–12)	600
Pyrazinamide	25 (20–30)	–	35 (30–40)	–
Ethambutol	15 (15–20)	–	30 (25–35)	–
Streptomycin[a]	15 (12–18)		15 (12–18)	1000

[a] Patients aged over 60 years may not be able to tolerate more than 500–750 mg daily, so some guidelines recommend reduction of the dose to 10 mg/kg per day in patients in this age group (*2*). Patients weighing less than 50 kg may not tolerate doses above 500–750 mg daily (*WHO Model Formulary 2008*, www.who.int/selection_medicines/list/en/).

Intensive phase treatment	Continuation phase
2 months of HRZE[a]	4 months of HR

[a] WHO no longer recommends omission of ethambutol during the intensive phase of treatment for patients with non-cavitary, smear-negative PTB or EPTB who are known to be HIV-negative. In tuberculous meningitis, ethambutol should be replaced by streptomycin.

H = isoniazid, R = rifampicin, Z = pyrazinamide, E = ethambutol, S = streptomycin

WHO recommendations

- PULMONARY AND EXTRA PULMONARY DISEASE SHOULD BE TREATED WITH SAME REGIMENS. NOTE THAT SOME EXPERTS RECOMMEND 9-12 MONTHS OF TREATMENT OD TB, MENINGITIS (2,3)GIVEN THE SERIOUS RISK OF DISABILITY AND MORTALITY, AND 9 MONTHS OF TREATMENT FOR TB OF BONES OR JOINTS, BECAUSE OF DIFFICULITIES OF ASSESING TREATMENT RESPONSE (3).UNLESS DRUG RESISTANCE IS SUSPECTED, ADJUVENT CORTICOSTERIODS TREATMENT IN RECOMMENDED FOR TB MENINGITISAND PERICARDITIS(1-4). IN TUBERCULOUS MENINGITIS, ETHAMBUTOL SHOULD BE REPLACED WITH STREPTOMYCIN.

2. National collabrating centre for chronic conditions. Tuberculosis : clinical diagnosis and management of tuberculosis, measures of its preventions and control. London royal college of physicians, NICE, 2006.
3. American thoracic society , CDC, infectious disease society of America. Treatment of tuberculosis morbidity and mortality weekly report: recommendations and reports,2003, 52(R-11):1-77.

WHO Treatment of tuberculosis: guidelines – 4th ed

Duration of treatment

6 months

van Loenhout-Rooyackers JH, Keyser A, Laheij RJ, Verbeek AL, van der Meer JW. Tuberculous meningitis: Is a 6-month treatment regimen sufficient? Int J Tuberc Lung Dis 2001;5:128-35.

12 months

Thwaites GE, Hein TT. Tuberculous meningitis: Many questions, too few answers. Lancet Neurol 2005;4:160-70

18 months or Longer

Santosh Isac Poonnoose, Vedantam Rajashekhar: Rate of Resolution of histologically verified intracranial tuderculomas. Neurosurgery 53:873-879, 2003

Treatment

Rate of radiological resolution of intracranial tuberculoma

Series	duration of ATT	residual lesions %
Wang 1996 (16)	6	20
Rajeshwari 1995 (6)	9	12
Awada 1998 (2)	12	0
Poonnoose 2003 (28)	18	69.2

Santosh Isac Poonnoose, Vedantam Rajashekhar: Rate of Resolution of histologically verified intracranial tuderculomas. Neurosurgery 53:873-879, 2003

Medical management

- 4 drugs x 3-4 months
- 2 drugs x 14-16 months occasionally longer
- Regression of size from 4-6 weeks
- Most resolve in 12-14 months

R Patir, R Bhatia, Tandon PN. Surgical management of tuberculous infections of the nervous system. Schmidek and Sweet operative neurosurgical techniques 5th edition; 1617-1631

- AED to continue
- INH blocks phenytoin metabolism
- Steroids in all irrespective of age and stage

Prasad K, Singh MB. Corticosteroids for managing tuberculous meningitis. Cochrane Database Syst Rev 2008;1:CD002244.

Resistant tuberculosis

- MDR : resistant to INH and Rifampicin
- EDR/ XDR : MDR + resistance to Quinolones and injectable second line drugs

SECOND LINE DRUGS

GROUP	DRUGS(ABBREVATIONS)
GROUP 1:- FIRST LINE ORAL AGENTS	• PYRAZINAMIDE(Z) • ETHAMBUTOL (E) • RIFABUTIN (Rfb)
GROUP 2:- INJECTABLE AGENTS	• KANAMYCIN (Km) • AMIKACIN (Am) • CAPREOMYCIN (Cm) • STREPTOMYCIN (S)
GROUP 3:- FLUOROQUINOLOLES	• LEVOFLOXACIN (Lfx) • MOXIFLOXACIN (Mfx) • OFLOXACIN (Ofx)
GROUP 4:- ORAL BACTERIOSATIC SECOND LINE DRUGS	• PARA-AMINO SALICYLIC ACID (PAS) • CYCLOSERINE (Cs) • TERIZIDONE (Trd) • ETHIONAMIDE (Eto) • PROTIONAMIDE (Pto)
GROUP 5:- AGENTS WITH UNCLEAR ROLE IN TREATMENT OF DRUG RESISTANT-TB	• CLOFAZIMINE (Cfz) • LINEZOLID (Lzd) • AMOXICILLIN/CLAVUNATE (Amx/Clv) • THIOACETAZONE (Thz) • IMIPENUM/CILASTATIN (Imi/Cin) • HIGH DOSE ISONIAZID (High dose H) • CLARITHROMYCIN (Cir)

Use atleast 4 drugs

- Use any first line of oral agents (group-1) that are likely to be effective.
- Use an amino glycoside or polypeptide by injection. (group-2)
- Use a fluoroquinolones. (group-3)
- Use the remaining group-4 drugs to complete the regimen of at least 4 drugs.
- For regimen with fewer than four effective drugs, consider adding 2 group-5 drugs. The total number of drugs will depend upon degree of uncertainty, and regimens often contain five to seven.

Surgery

- Severe elevation of ICP
- Threatening life or vision
- Do not respond to drugs clinically/ radiologically
- Diagnosis in doubt
- Obstructive hydrocephalus

R Patir, R Bhatia, Tandon PN. Surgical management of tuberculous infections of the nervous system. Schmidek and Sweet operative neurosurgical techniques 5th edition; 1617-1631

- Aim diagnosis/ relieve pressure

Surgical management

- Biopsy of the mass lesion
- Hydrocephalus
  - Communicating (commoner)
  - Non communicating

Surgery principles

- Non eloquent areas total excision (small lesion)
- Subtotal/ partial excision (large lesion/ eloquent cortex)
- Conservative excision around vital structures
- Evacuation of central liquifactive portion in deep seated lesions
- Residual lesions may respond to medical therapy
  - **R Patir, R Bhatia, Tandon PN. Surgical management of tuberculous infections of the nervous system. Schmidek and Sweet operative neurosurgical techniques 5th edition; 1617-1631**
- Hydrocephalus

MRC GRADING FOR HYDROCEPHALOUS

STAGE	
1	FULLY CONSCIOUS, NO PARESIS
2	DECREASED LEVEL OF CONSCIOUSNESS,LOCALIZING PAIN
3	DEEPLY COMATOSE ± GROSS PARESIS

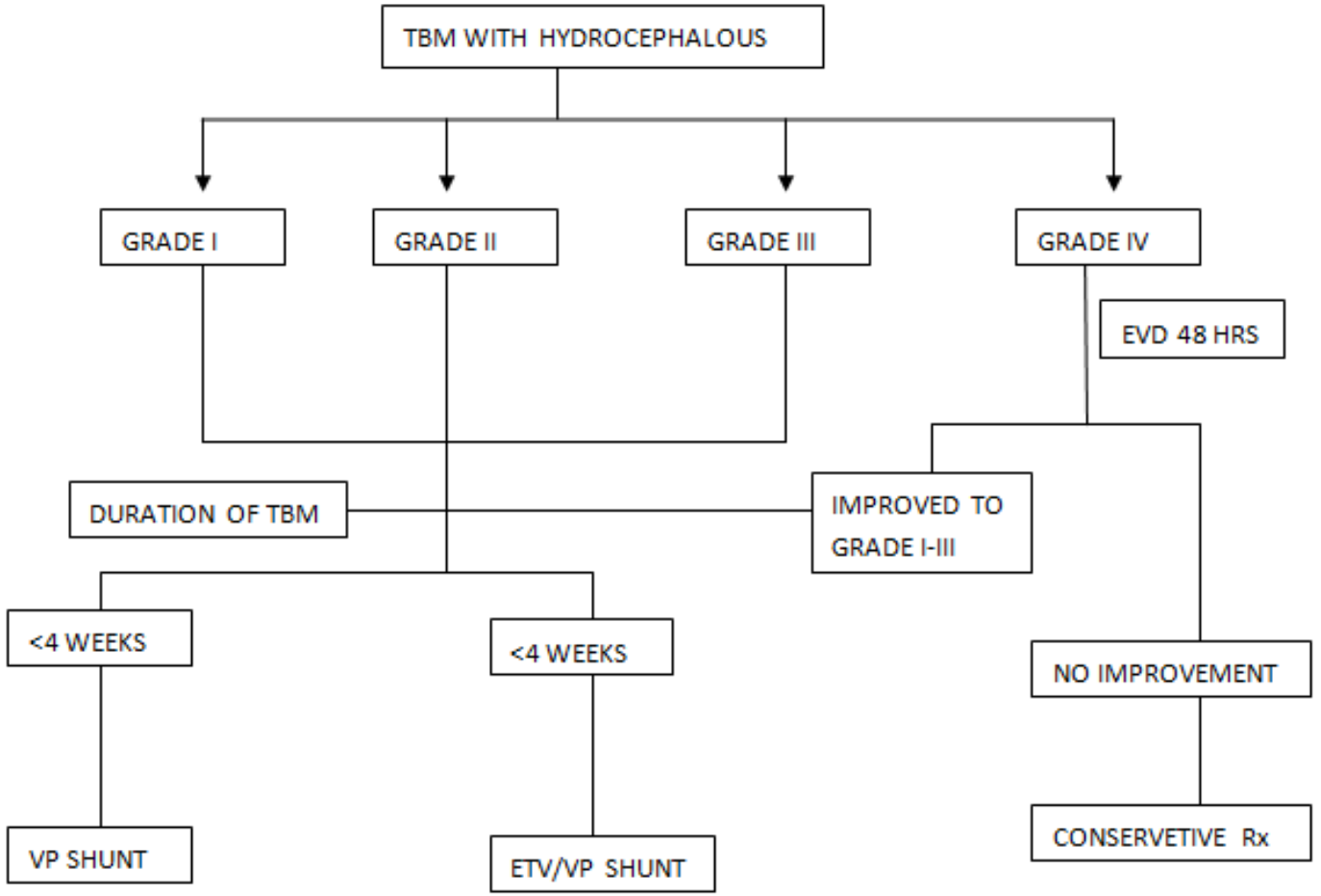
GRADING OF HYDROCEPHALOUS

VELLORE GRADING

GRADE	
1	HEADACHE, VOMITING, FEVER± NECK STIFFNESS NO NEUROLOGICAL DEFICIT NORMAL SENSORIUM
2	NORMAL SENSORIUM NEUROLOGICAL DEFICIT PRESENT
3	ALTERED SENSORIUM BUT EASILY AROUSABLE DENSE NEUROLOGICAL DEFICIT MAY OR MAY NOT BE PRESENT
4	DEEPLY COMATOSE DECEREBRATE OR DECORTICATE POSTURING

MODIFIED VELLORE GRADING

GRADE	
1	GLASS GOW COMA SCALE 15 HEADACHE, VOMITING, FEVER± NECK STIFFNESS NO NEUROLOGICAL DEFICIT
2	GLASS GOW COMA SCALE 15 NEUROLOGICAL DEFICIT PRESENT
3	GLASS GOW COMA SCALE 9-14 NEUROLOGICAL DEFICIT MAY OR MAY NOT BE PRESENT
4	GLASS GOW COMA SCALE 3-8 NEUROLOGICAL DEFICIT MAY OR MAY NOT BE PRESENT


TBM WITH HYDROCEPHALOUS
GRADE I
GRADE II
GRADE III
GRADE IV
EVD 48 HRS
DURATION OF TBM
IMPROVED TO GRADE I-III
<4 WEEKS
<4 WEEKS
NO IMPROVEMENT
VP SHUNT
ETV/VP SHUNT
CONSERVETIVE Rx

Hydrocephalus

- Inevitable in those who survive 4-6 weeks
- Mortality 20-100%
- Grade at admission significant
- Early shunt for grade I,II

- ETV
  - 73.1% success rate for ETV in TBM with hydrocephalus
    - *A chugh, M hussain et al. Surgical outcome of tuberculous meningitis hydrocephalus treated by endoscopic third ventriculostomy: prognostic factors and postoperative neuroimaging for functional assessment of ventriculostomy: J Neurosurg Pediatrics 3:000–000, 2009*
- Endovascular revascularization for ischemia
- STA MCA bypass
  - The left superficial temporal artery–MCA bypass was found to be capable of preventing new ischemic events in the 21-month follow-up period
    - Martin misch, Ultrich- wilhelm et al. Prevention of secondary ischemic events by superficial temporal artery–middle cerebral artery bypass surgery after tuberculosis-induced vasculopathy in a 5-year-old child:Neurosurg Pediatrics 6:000–000, 2010

AIIMS DATA (1975-1992)

SUPRATENTORIAL	78
PARIETAL	28
FRONTAL	26
TEMPORAL	15
BG / THALAMUS	4
SELAR/SUPRASELLAR	4
ORBITAL FISSURE	1
INFRATENTORIAL	**50**
CEREBELLUM	44
CP ANGLE	3
TENTORIUM	1
BRAINSTEM	2

Thank you