

INTRACRANIAL CAVERNOMA

PRESENTER : Dr Shameem Ahmed

MODERATOR : Dr P.S. Chandra
Dr G.D. Satyarthee

DEPT OF NEUROSUGERY, AIIMS

INTRODUCTION

- CEREBRAL CAVERNOUS MALFORMATION (**CCM**), CAVERNOUS HEMANGIOMA, CAVERNOUS ANGIOMA, CRYPTIC VASCULAR MALFORMATION, OCCULT VASCULAR MALFORMATION, HEMORRHOID OF BRAIN.
- Developmental abnormalities that affects the blood vessels supplying the brain.
- Dilated sinusoidal channels lined by single layer endothelium without intervening brain parenchyma.
- Can occur anywhere in the CNS
- Angiographically occult vascular malformations.

EPIDEMIOLOGY

- Prevalence: 0.5%
- 5-10% of all Cerebro-vascular malformation
- 80% are supratentorial
- Familial CCM accounts around 20-30%
- Increased prevalence in Mexican American families

EPIDEMIOLOGY

- 30- 50% asymptomatic
- 20-30% of cavernomas may be a/w venous anomaly
- Bimodal presentation-
 - Pediatric:3-11 yrs.
 - Adult : 2nd to 4th decade.
- Age at first diagnosis:
 - <20 yrs: 25-30%
 - 20-40 yrs: 60%
 - >40 yrs: 10-15%

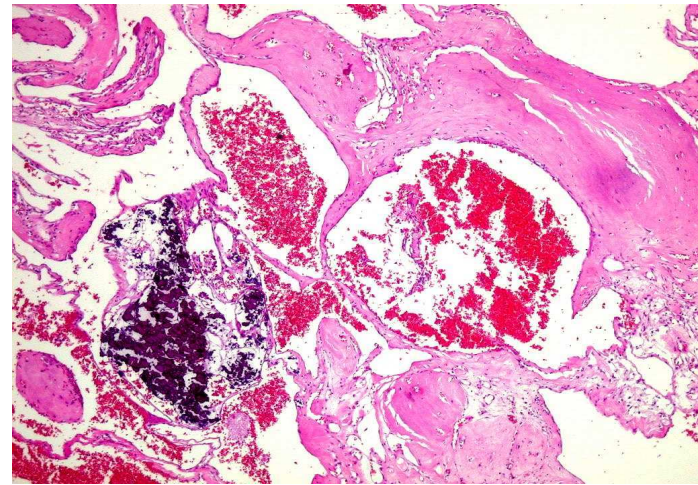
GENETICS

- Usually sporadic (80%)
- Three autosomal dominant genes (7p/7q/3q) a/w familial form.
The precise function not known :
 1. **ccm1 on 7q chromosome and expresses KRIT1**
 2. **ccm2 on 7p chromosome and expresses MGC4607**
 3. **ccm3 on 3q chromosome and expresses PCD10**
- Working model : Alteration in growth control pathway involving the regulation of Krev 1 / rap 1a by KRIT 1 protein following mutation of CCM 1

PATHOLOGY

- Mulberry appearance, soft / hard consistency, usually 1 -5 cm
- Enlarged capillaries with abnormal gap between endothelial cells with thin collagenous wall & lack of smooth muscle / elastic fibers
- Capillaries are immediately adjacent to each other, with no intervening neural tissue.
- No feeding arteries or draining veins. May be a/w venous anomaly. Blood flow is low.
- Blood degradation products (hemosiderin staining) and gliotic reaction in the adjacent brain

PATHOLOGY



CLINICAL PRESENTATION

- Approx 50% asymptomatic.
- Seizure (40 -80 %)
 - Males more commonly presents with epilepsy.
 - Chronic intractable epilepsy is found in almost half.
- Sudden onset neurological deficits caused by hemorrhage, commonly observed in thalamic and brainstem CCM.
- Prior hemorrhage, female sex and pregnancy are the risk factors for rebleed.

NATURAL HISTORY

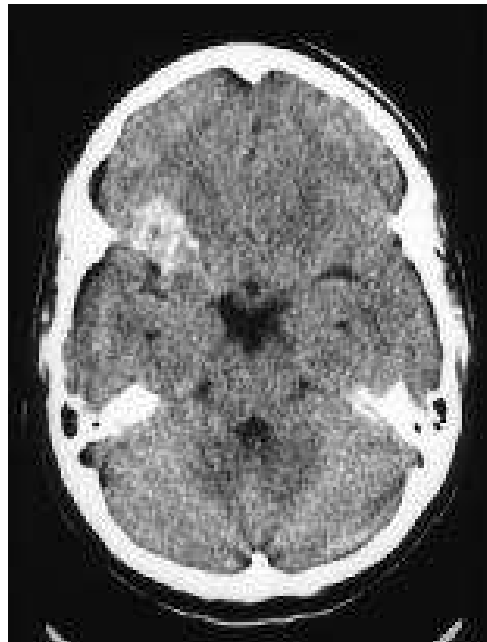
- Depends on the topography
- M.C. presentation is seizure
- Subclinical hemorrhage seen in all and clinical hemorrhage in 12.1%
- Annual hemorrhage rate 0.5 to 1 % & rebleed rate of 4.5 %
- The epileptic risk is correlated to the localization, more frequent for temporal and frontal lesions (1.5 to 2.4 % each year)
- Lesion may arise de novo, may grow / shrink / remain unchanged

NATURAL HISTORY

AUTHOR / YEAR	RATE OF SYMPTOMIC HEMORRHAGE	COMMENTS
Del Curling et al 1991	0.1 % per lesion /yr	Retrospective study based on pts recall
Robinson et al 1991	0.7 % per lesion /yr	Prospective study
Zabramski et al 1995	1.2 % per lesion /yr	Prospective MR based study. 60% episodes were symptomatic
Kondziolka et al 1995	1.3 % per lesion /yr 2.6 % per lesion /yr 0.6 % per lesion /yr 4.5 % per lesion /yr	Incidental lesion has lower rate of Hmg
Aiba et al 2005	0 % per lesion /yr 0.4 % per lesion /yr	Prospective study : low hmg rate for incidentaloma / with seizure
Porter et al 2007	4.2 % per lesion /yr	Retrospective review from 1 st hmg

RADIOLOGY

- CT scans may show focal hyperdensity, reflecting calcification or recent hemorrhage and intravenous contrast may show faint enhancement.



RADIOLOGY

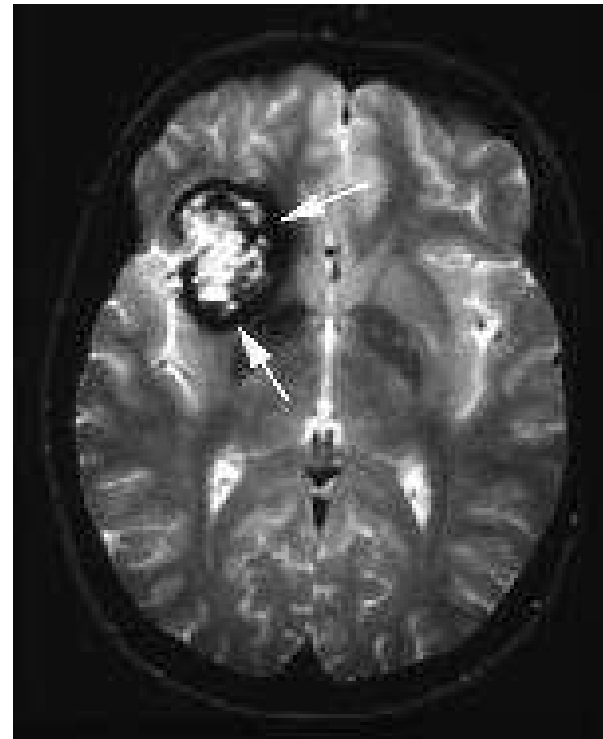
MRI

- T2WI show reticulated core of lesion “popcorn” appearance with a lucent halo surrounding a lesion.
- This pathognomonic appearance is produced due to repeated hemorrhages and hemosiderin deposition around the lesion.
- No peri-lesional edema.
- Gradient sequences are more sensitive for detection of small lesions

RADIOLOGY

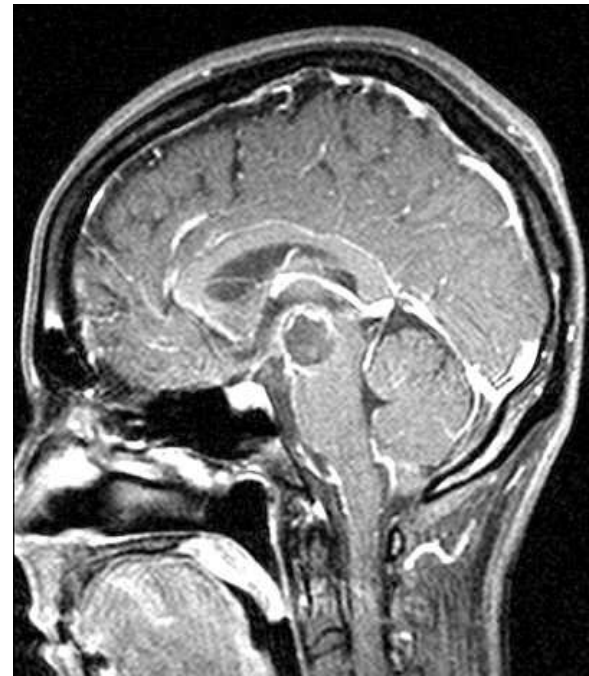


T1WI demonstrates blood products within the lesion.



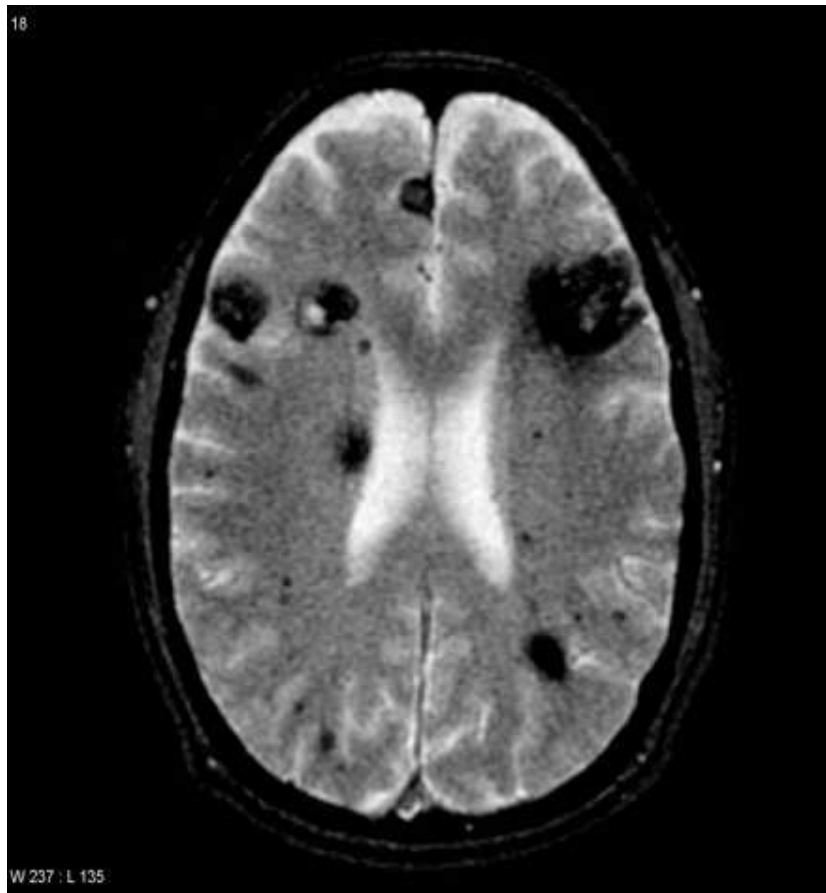
Axial T2WI shows the circumferential hemosiderin ring

RADIOLOGY



Pre- and post-contrast sagittal MR: mid brain cavernoma

GRADIENT ECHO MRI BRAIN



RADIOLOGY

- Cerebral DSA demonstrate no vascular abnormalities. Developmental venous anomalies may be associated cavernoma and may be seen on angiography.

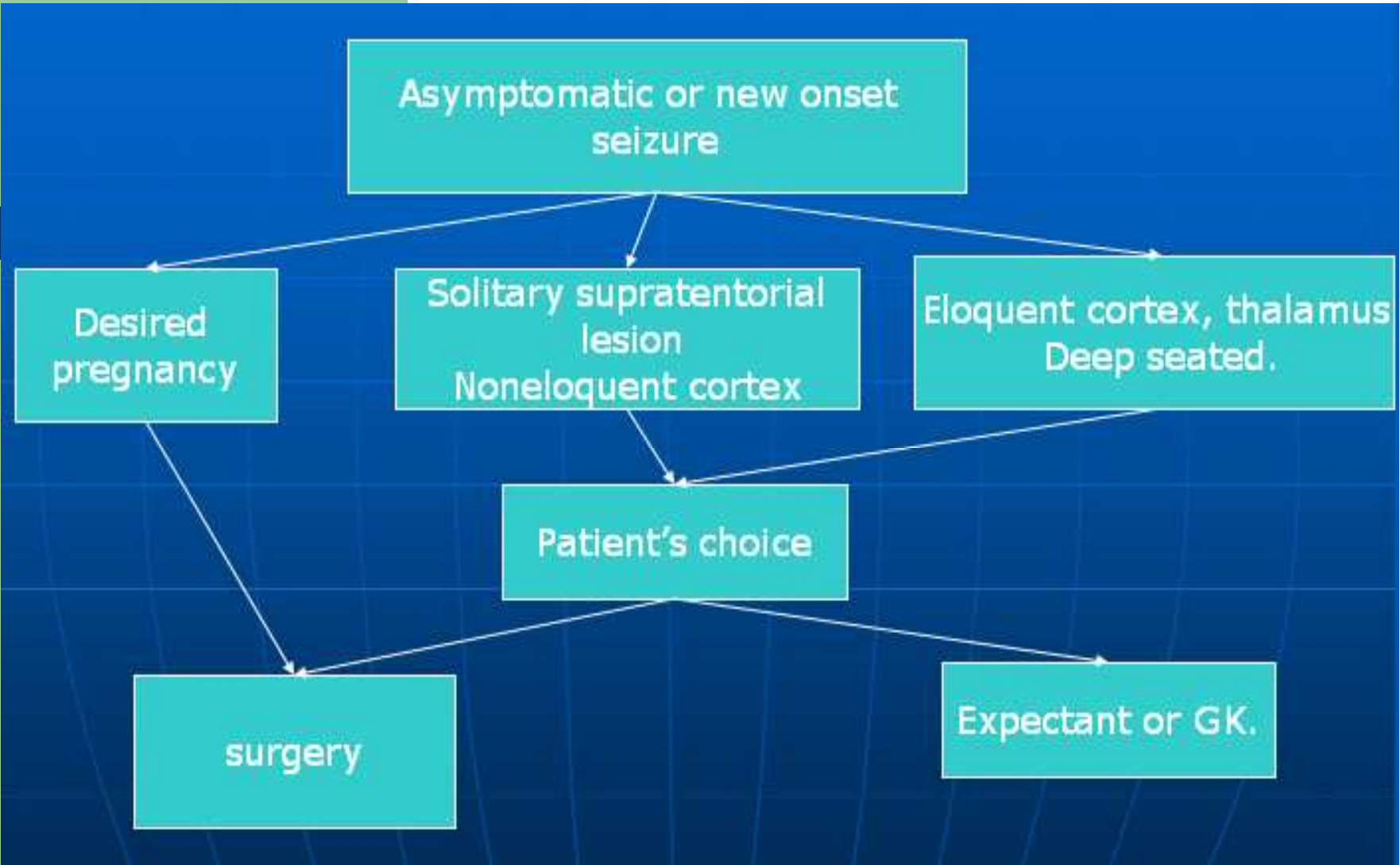


DIFFERENTIAL DIAGNOSIS

- Hemorrhagic metastasis viz melanoma
- Glioma e.g. oligodendoglioma , pleomorphic xanthoastrocytoma
- AVM – occult / overt
- Hemorrhagic telangiectasia (Osler Weber Rendu disease) / multiple metastasis

Management Options

- Medical treatment.
- Stereotactic radiotherapy or gamma knife.
- Surgical resection (gold standard).



Intractable epilepsy

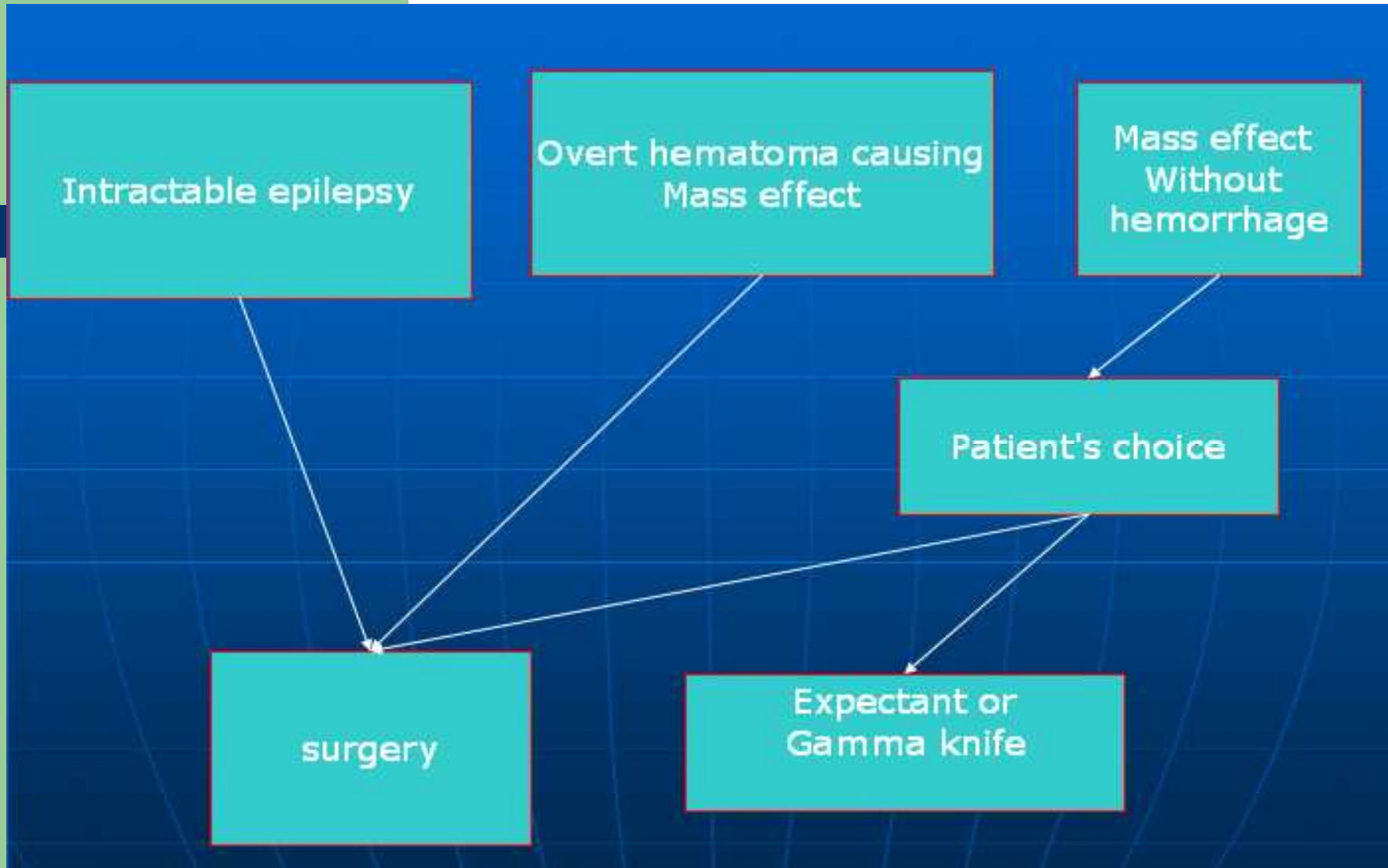
Overt hematoma causing
Mass effect

Mass effect
Without
hemorrhage

Patient's choice

surgery

Expectant or
Gamma knife



Medical Management

- Offered to asymptomatic, incidentally detected lesions, surgically inaccessible lesions and unfit for surgery
- Regular follow up MRI to assess increase in size or new hemorrhages.
- Medical treatment is limited to control of seizure activity.
- Patients are refrained from strenuous exercises, anticoagulant use, avoid pregnancy

Surgical Treatment

Merits:

- Reduction of mass effect.
- No rebleeding from completely excised CCM.
- 75-88% of patients become seizure free after complete resection.
- Intractable epilepsy may become well controlled.
- Complete cure can be assured.

Surgical Treatment

Demerits:

- In brainstem and thalamic CM, surgical treatment may lead to neurological deficits.
- Standard surgical mortality and morbidity

Planning

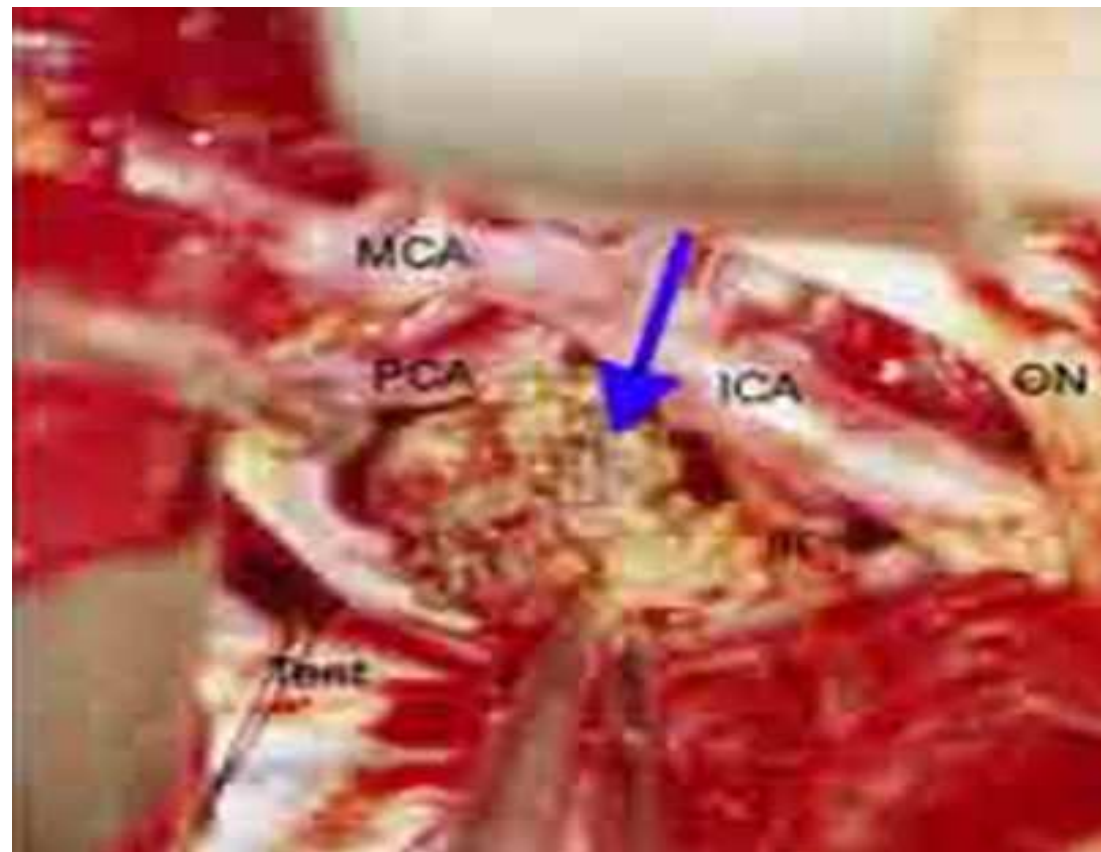
- T1WI, T2WI & contrast MRI with GRE / FLAIR sequences
- Venous malformations should be looked for
- If lesion is in the eloquent area, then functional imaging along with cortical mapping should be done.
- Frameless stereotaxy is considered in small and deep seated lesions & dot localizing CT for superficial polar lesion

Surgical Technique

- Surgical technique depends on the location of lesion, presence of associated venous malformations and presence of overt hematoma.
- Position and approach based on location , trans sulcal approach is preferred .
- Lesion should be localized after opening the dura.
- Intraoperative sonography, or stereotaxy can be used.
- Surface lesion appear as purple-blue mulberry like structure surrounded by area of hemosiderosis

Surgical Technique

- The cortical venous drainage pattern should be inspected.
- Lesion is initially shrunk with bipolar coagulation.
- The surrounding gliotic brain (pseudo capsule) offers a plane of dissection.
- Cotton patties are used for preservation of plane of dissection.
- Complete resection is to be attempted .
- Resection bed to be inspected for satellite lesion



Associated Venous Anomalies

- Approx. 24% patients of CCM
- These venous anomalies are the normal veins draining brain
- Every effort is made to preserve them
- These may be the only veins supplying the brain
- Coagulation of these may result in venous infarcts and increases the morbidity of surgery



Surgical Excision Options



- Lesionectomy alone.
- Lesionectomy and excision of abnormal tissues.
- Lesionectomy and removal of abnormal area remote from the cavernoma.

Special Considerations

INTRACTABLE EPILEPSY :

- Pre op. work up to localize source of seizure.
- If the location non eloquent, surrounding hemosiderin stained brain may be resected because of possible epileptogenicity
- Pre op evaluation detect epileptogenicity is remote from CM or multiple CM = ECOG guided surgery.
- Pre op evaluation detect epileptogenicity is dual pathology (eg-temporal lobe CM with MTS) = resection of both foci.

Special Considerations

CAPSULAR AND THALAMIC CAVERNOMA :

- Resection carries greater morbidity
- Resection attempted to those lesions that reach pial or ventricular surface.
- Frameless image guidance helpful

- **Anterior lesion – transcallosal route**
- **Lateral thalamic lesion – transcortical route through superior parietal lobule**
- **Medial posterior lesion – posterior interhemispheric approach**

Special Considerations

OPTIC PATHWAY CM :

- May present with acute / subacute visual disturbances
- May mimic SAH on CT
- Urgent decompression for chiasmal apoplexy ([Maitland et al](#))
- Pterional or subfrontal route
- CM may affect any part of optic pathway , lesionectomy is attempted

Special Considerations

PINEAL CM :

- < 1 % of CCM (Slavin et al)
- Present with f/o raised ICP , ocular symptoms , neuro endocrine abnormalities
- EVD / Shunt to lower ICP
- Interhemispheric transsplenial , sub occipital transtentorial & supra cerebellar infra tentorial approach depending on location of CM

Special Considerations

MULTIPLE CM :

- Multiple in 50 % cases
- Treatment at addressing symptomatic lesion
- Large sized , hemorrhage, FND , seizure focus
- Familial CM are at risk for the formation of de novo CM

Special Considerations

DURAL BASED CM :

- Commonly found in middle fossa, CP angle , tentorium and convexity
- Present with headache
- Rarely bleed
- May mimic meningioma
- Enhance strongly and homogenously on Gd MRI
- Pre op embolizaion / SRS or EBRT is advisable for highly vascular middle fossa CM
- Post op morbidity as high as 38%

Special Considerations

Brain Stem CM:

- Of all CNS cavernoma, 9-35% are found in brain stem
- Acute onset focal neurological deficits are the most common presentation
- The waxing and waning of symptoms mimic multiple sclerosis.
- Hemorrhage rate is 30 times more than that for supratentorial CCMs.
- Rebleeding rate is as high as 35%.

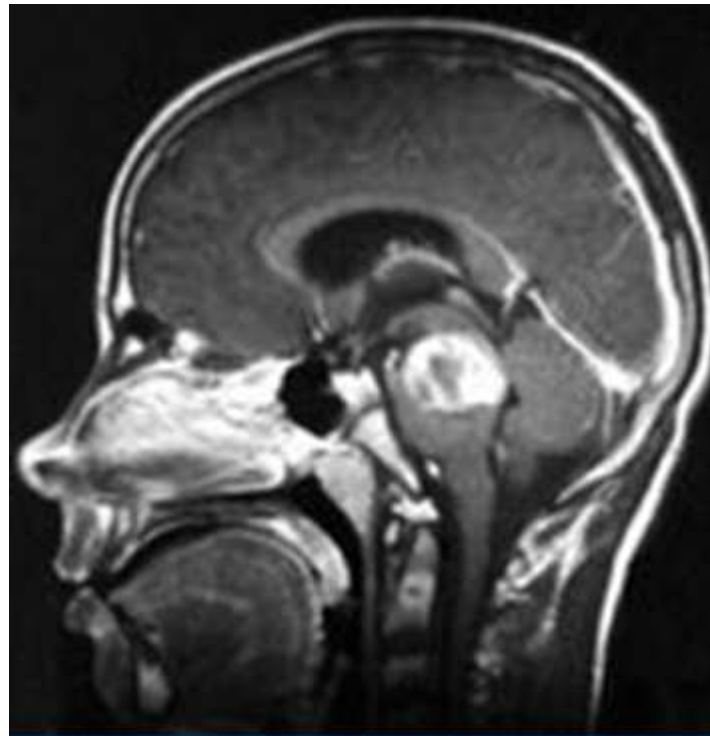
REVIEW OF LITERATURE

Brain Stem Cavernoma

Angelo Franzini, Neurosurgery 56:1203-1214, 2005 :

- 52 patients undergone micro neurosurgery for brainstem cavernoma.
- Rebleed rate was 34%.
- 29 developed temporary neurological deficits which persisted in 10 pts.
- Mortality was 1.9%

Brain Stem CM



Surgical Indications

Brain Stem CM

- Exophytic lesions reaching pial surface.
- Rapid progressive neurological deterioration.
- Hemorrhage outside the lesion capsule.
- Significant mass effect.
- Multiple debilitating hemorrhages.

Brain Stem CCM

- Lesions are considered for surgical resection only if they reach pial surface.
- Patient can be followed till they suffer one or more hemorrhages.
- Waiting for 3-5 days for hematoma to liquefy is good practice.
- Threshold of intervention should be high for pediatric population.

Goals Of Treatment.. Brain Stem CM

- Minimize amount of normal brainstem traversed.
- Complete excision of the tumor.

Surgical technique.. Brain Stem CM

- Position and approach differs with location of lesion.
- If it doesn't reach pial surface, then intra operative sonography or stereotaxy can be used along with hemosiderin staining.
- Dark bluish red area or mulberry appearance is classical for cavernoma

Surgical technique.. Brain Stem CM

- Hemosiderin stained area should be considered a normal tissue.
- Internal decompression should be done followed by careful dissection from surrounding tissues.
- Every possible attempt is made to save the venous anomalies.

Surgical technique.. Brain Stem CM

- Complete excision may not be possible due to technical limitations.
- Better to stage the procedure than to risk the functionality

Post Operative Management.. Brain Stem CM

- Patient usually kept intubated for at least 24 hours.
- Demonstration of gag and cough reflexes guides extubation.
- MRI / CT on early post op days for assessment of extent of excision if patient's condition permits.

OUTCOME

- When CCM are completely removed , risk of further growth and hemorrhage is essentially permanently eliminated
- More than 80% of patients were same or better after surgery while few worsened in various series.
- Cranial nerve deficits, motor deficits, meningitis, CSF leak, tracheostomies are the usual complications of brainstem CM

FOLLOW UP

- Post op MRI scan
- First degree relative with more than 1 family member having a cavernoma should have CECT or MRI brain to be done along with genetic counseling

REVIEW OF LITERATURE

Shih YH, Pan DH, Clin Neurol Neurosurg. 2005 Feb;107(2):108-112

- 46 patients (16+30) were treated with surgery and GK.
- 79 % (11/14) vs. 25 % (4/16) of patients became seizure free after surgery and GK ($p < 0.002$).
- 100 vs. 67 % patients- no rebleed (NS).
- Concluded that surgery is better option for supratentorial CM in terms of seizure control and rebleed rates.

Gamma Knife Therapy...**IN CCM**

PRINCIPLE :

- Radiation injury to endothelial cell causes release of growth factors and fibroblast proliferation.
- This causes hyperplasia of smooth muscles cells and occlusion of lumen.
- Coagulation necrosis of cavernoma and obliteration of vessels were also a proposed mechanism.

Gamma Knife Therapy

Indications:

- Surgically inaccessible lesions like thalamic, brainstem or deep seated lesion.
- Lesions presented with minor hemorrhages
- Multiple lesions.
- Patients choice.

Gamma Knife Therapy

- **Merits:**

- Reduction of rebleed rates.
- Halting of growth of lesion.
- Volume control.
- Seizure control.

- **Demerits:**

- Radiation edema and transient or permanent deficits
- Lower efficacy of treatment.

Gamma Knife Therapy

MORBIDITY-

- Perilesional edema was found in 27% with transient morbidity of 20.5% with permanent morbidity of 4.5%.
- Rebleed common in patients who presented with bleed, larger lesion volume and prescription dose less than 13 Gy.
- Edema was common with prescription dose > 13 Gy.

REVIEW OF LITERATURE

Lie AL, Wang CC. Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 2005 Feb;27(1):18-21

- **92 patients with mean follow up of 2-8 yrs.**
- **43 patients of them were primarily treated for epilepsy, 83% seizure control achieved**
- **Radiological rebleed rate was 9.8%**
- **Radiation edema developed in 7 patients**
- **Gk is effective in controlling the seizures and bringing down the rebleed rate.**
- **Recommend GK therapy for surgically unfit cases.**

REVIEW OF LITERATURE

Kim MS and Pyo SY, J Neurosurg. 2005 Jan;102 Suppl:102-6.

- 42 patients with deep seated cavernoma located at thalamus, brainstem and 8 patients with multiple cavernomas were treated by GK. Mean margin dose of 14.55 Gy was given
- Tumor size decreased in 29 patients.
- Seizure control by drugs is achieved in 88% of patients.
- Clinically significant rebleed occurred in 7.1%.
- Recommended GK for deep seated and brainstem lesions as well as multiple ones.

CONCLUSION

- Surgery still remains gold standard for intracranial cavernoma
- Conservative therapy is appropriate for cavernoma that are asymptomatic and for those who had one non devastating episode of hemorrhage
- Complications can occur and extensive informed consent should be obtained
- Meticulous radiography and clinical follow up necessary to monitor residual or recurrent disease

