INTRACRANIAL CAVERNOMA

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

CLINICAL PRESENTATION

- Approximately 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 re-bleed.

NATURAL HISTORY

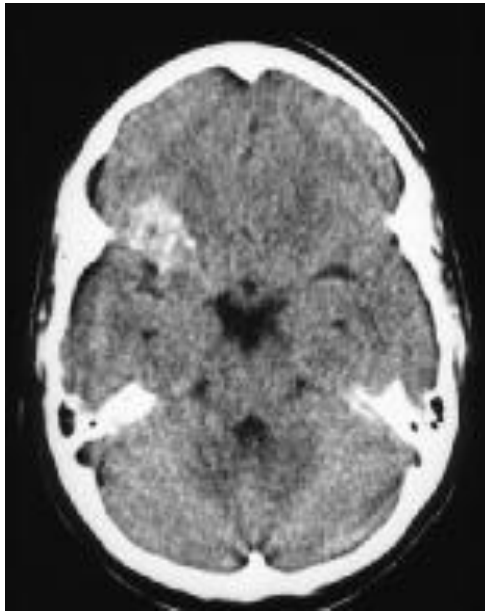
- Depends on the topography
- M.C. presentation is seizure
- Subclinical hemorrhage seen in all and clinical hemorrhage in 12.1%
- Annual hemorrhage rate 0.5 to 1 % & rebleed rate of 4.5 %
- The epileptic risk is correlated to the localization, more frequent for temporal and frontal lesions (1.5 to 2.4 % 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 1st 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

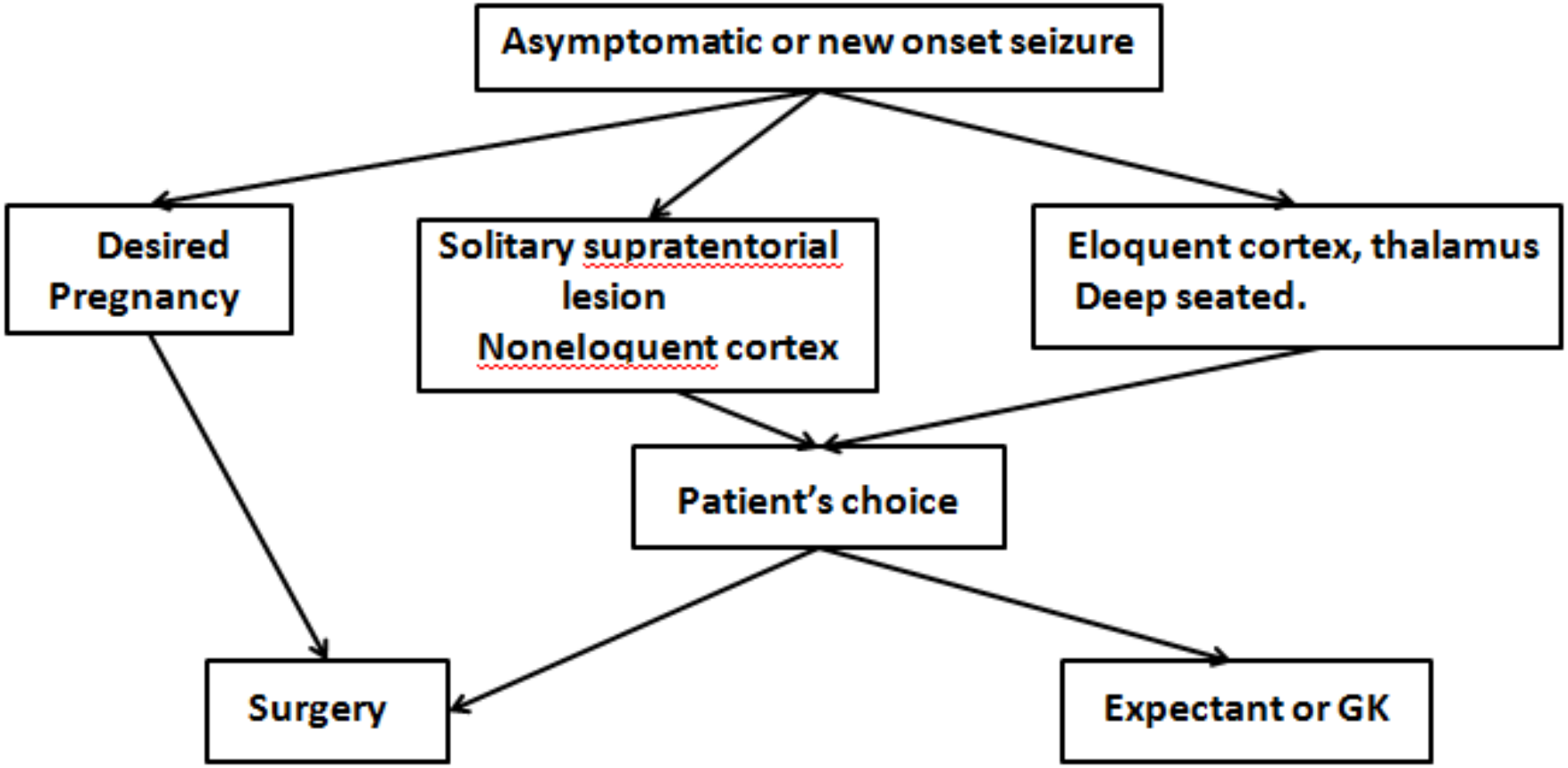
- Cerebral DSA demonstrate no vascular abnormalities. Developmental venous anomalies may be associated cavernoma and may be be seen on angiography.

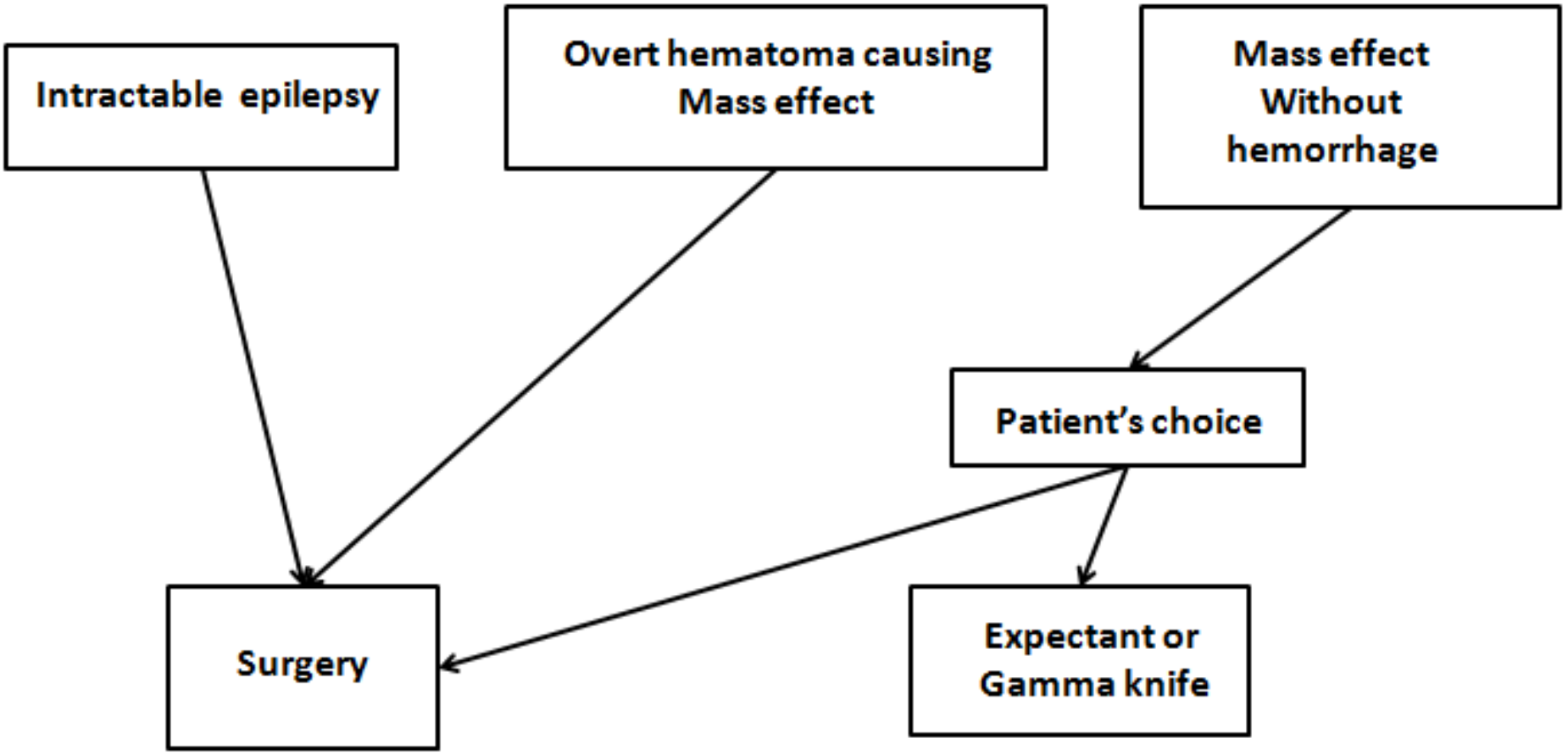
DIFFEENTIAL DIAGNOSIS

- 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).


Asymptomatic or new onset seizure
Desired Pregnancy
Solitary supratentorial lesion
Noneloquent cortex
Eloquent cortex, thalamus
Deep seated.
Patient's choice
Surgery
Expectant or GK


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

- **Anterior lesion – transcallosal route**
- **Lateral thalamic lesion – tanscortical 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 features of raised ICP , ocular symptoms , neuro-endocrine abnormalities .
- EVD / Shunt to lower ICP
- Interhemispheric transsplenial , sub occipetal 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%

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 normal veins.

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