Surgical Treatment of Cerebral cavernous Malformations: Report of 6 Cases and pertinent Literature review

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ABSTRACT

Cerebral cavernous Malformation (CCM) is a rare neurovascular malformation accounting 0.5% to 4% of all intracranial vascular malformations. People harboring CCM may be symptomatic or may present with seizure, hemorrhage or progressive neurological deficit. Asymptomatic CCM needs no treatment. The symptomatic CCM may or may not require intervention. The best treatment for symptomatic CCM is microsurgical excision. Over a period of five years we have been managing I2 patients with CCM, and out of them 6 patients who were symptomatic required microsurgical excision. Here, we discuss these 6 surgically managed patients and appropriate literature related to CCMs would be reviewed.

KEYWORDS

Brain cavernoma, Cerebral cavernous malformation, microsurgical excision, surgical outcome, Vascular malformation.

INTRODUCTION

Cerebral cavernous malformation (CCM) is a rare neurovascular anomaly accounting for 0.5% to 4% prevalence in general population and about 10 -15% of all cerebral vascular malformations 1,2,3. About 60-70% of CCMs are located in supratentorial and 20-30% in infratentorial region 3. The CCM may be asymptomatic or may present with seizure and or hemorrhage and rarely with progressive neurological deficit. The risk of hemorrhage from CCM is about 0.5-1% per year and rehemorrhage rate is 4-10% per year 1. Asymptomatic CCM needs no treatment. The symptomatic CCM may require only observation with anticonvulsants or surgical intervention depending on clinical radiological scenario. Best treatment for symptomatic CCM is microsurgical excision, however, radiosurgery has been used as a primary treatment for these vascular lesions but its efficacy and longterm result is still a question mark 4,5.

Below is the description of these 6 cases of symptomatic CCMs who underwent microsurgical excision over a period of 5 years (between June 2018 and January 2022) at our institute and these patients were followed up from 14 to 60 months (Table.1).

Case 1.

A 25 year old right handed young girl, presented to Emergency Department (ER) with history of acute onset of severe headache for last five days. On arrival, she was fully conscious, oriented and had no neurological deficit. CT scan of brain showed a hyperdense area in right frontal lobe and MRI of brain was suggestive of cavernoma with hemorrhage. She underwent elective right frontal craniectomy and total excision of lesion. Postoperative period was uneventful. Histology report was suggestive of cavernoma with evidence of recent bleeding. She was discharged on 10th Postoperative day (POD) with Modified Rankin Scale (MRS) of grade 0. MRI of brain on her 14th month followed up revealed no residual lesion.

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Case no 2.

A 56 year old right-handed lady was brought to the ER with the history of Sudden onset of headache and vomiting. On examination, she was drowsy but obeying command. There was no focal neurological deficit and pupils were bilaterally equal and reacting to light. CT/MRI of the brain showed posterior fossa midline hematoma in vermian area. Cerebral CT angiography was negative. She underwent midline posterior fossa craniectomy and evacuation of ICH and excision of vascular lesion which was detected during procedure. Histopathology report was suggestive of cavernoma. She was discharged on 15th POD with MRS grade 4 and on subsequent followed up of 36 months her MRS grade improved to grade 3. MRI of brain did not show any residual lesion on her last follow-up.

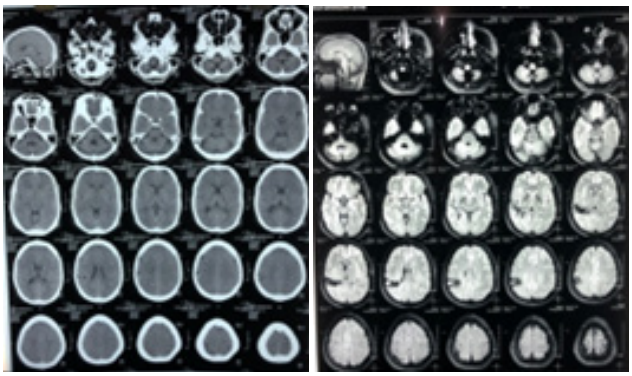
Case 3.

A 40 year old right handed gentleman was brought to Emergency complaining sudden severe headache and vomiting for last one day. On examination he was found to have GCS (Glasgow Coma Scale) of 13 without neurological deficit. MRI of brain showed right cerebellar hematoma with suspected cavernoma within vicinity of hematoma. Elective posterior fossa suboccipital craniotomy and evacuation of hematoma and excision of cavernoma was performed. Histology report was suggestive of cavernoma. Patient was discharged on 10th POD with MRS of 1. On her last followed up of 40 months there was no evidence of recurrence.

Case 4.

A 30 year old male, nonhypertensive, nondiabetic was attending at Neurosurgical OPD for last 6 months with recurrent fainting attacks which was not controlled by multi anticonvulsant therapy. MRI of brain showed right parietal 'Popcorn' like heterogenous mass with mild perilesional edema suggestive of cavernous malformation. After discussion with patient and family about pros and Cons of surgical procedure, a discission was made for surgical intervention. Right parietal craniotomy and total excision of lesion was carried out. Post operative CT/MRI did not reveal any residual mass. At the time of discharge, he had mild left sided hemiparesis which disappeared on subsequent followed up. Histopathological characters were suggestive of cavernous malformation. There was no recurrence on 60 months followed up and seizure has been controlled by single drug (Figure.1).

Figure.1



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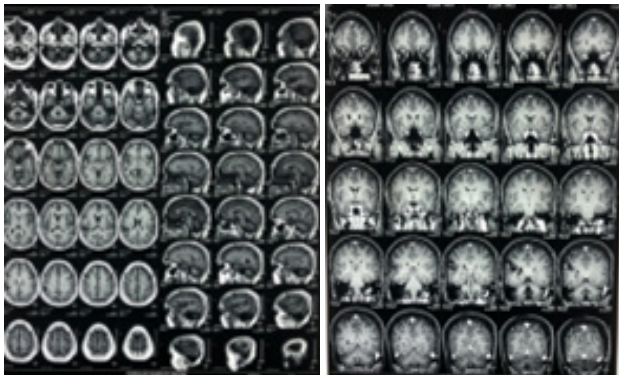

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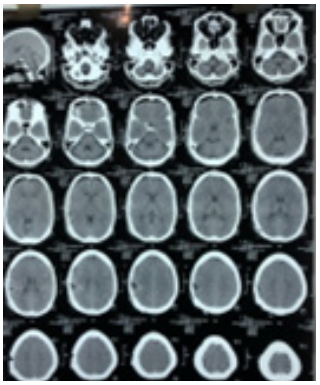

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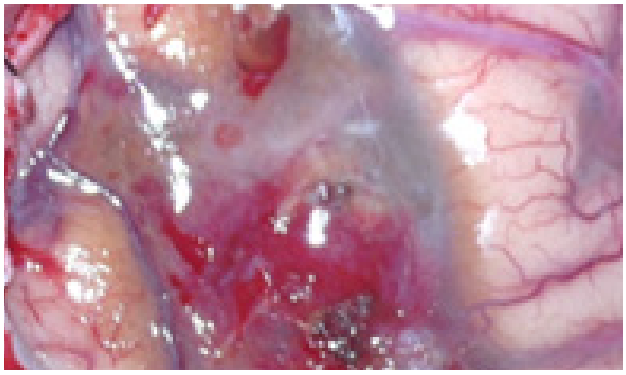

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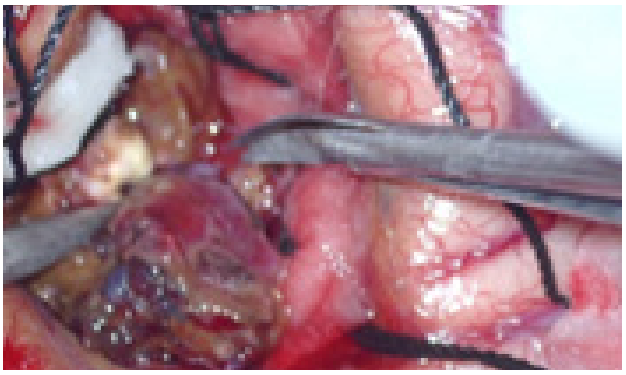

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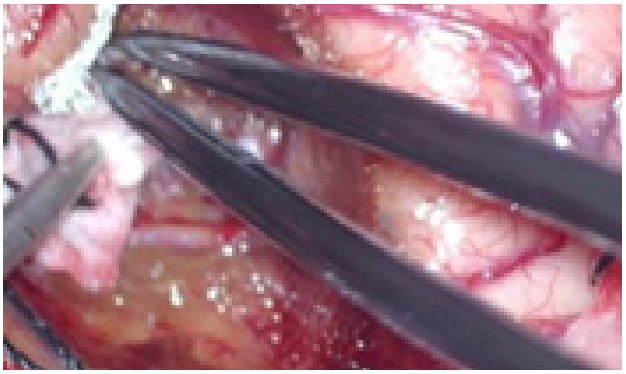


1h

Fig. 1. Pre operative CT/MRI of brain (1a, b,c & d) depicting right parietal hyperdense lesion on CT and heterogenous signal mass on MRI of different sequences; 'Popcorn' like appearance on T2 weighted image suggestive of Cavernoma. Intraoperative pictures of same patient (1e, f, g & h): 1e. Red cherry like right parietal lesion, 1f. Removal of lesion, 1g. Hemostasis of brain surface after total excision of lesion, 1h.

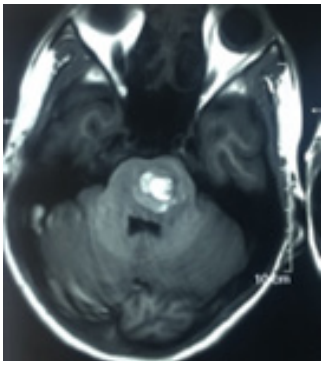
Case 5.

A 46 year old gentleman presented to ER with history of headache, vomiting and loss of consciousness for last 6 hours and he had a similar type of ictus two times in the past but was not investigated thoroughly. Clinical examination revealed his GCS of 13 without any focal deficit. CT/MRI of brain depicted large hematoma of 3.5 X 3.1 X2.5 cm in size in right basal ganglia. Cerebral CT angiography did not reveal any underlying vascular lesion. He underwent right frontal craniotomy and interhemispheric removal of hematoma. Intraoperative findings were suggestive of cavernoma with intralesional bleed. Histology also turned out to be a cavernous malformation. The postoperative period was uneventful. He was discharged on 10th POD with MRS grade I. On subsequent follow-up his MRS was grade I and had no residual on latest MRI (64 months)

Case 6.

A 19 year old boy was brought to ER with history of headache, vomiting and left-side weakness for last 2 days. He was found to have GCS of 14 with left-sided hemiparesis of grade 3 on clinical examination. MRI of brain showed pontine hematoma with the features of underlying cavernomas malformation. He underwent right suboccipital retromastoid craniectomy and excision of lesion via right posterolateral trajectory (between right 7th and 5th cranial nerve root exit/entry zones). Gross total excision of cavernoma was achieved. Postoperative recovery was gradual and he was discharged on 21st POD with mild left-sided hemiparesis. He had MRS grade I on subsequent followed up. There was no residual lesion found on follow-up MRI of brain. The histology was cavernoma (Figure.2).

Figure.2



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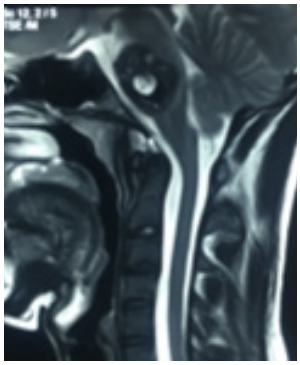

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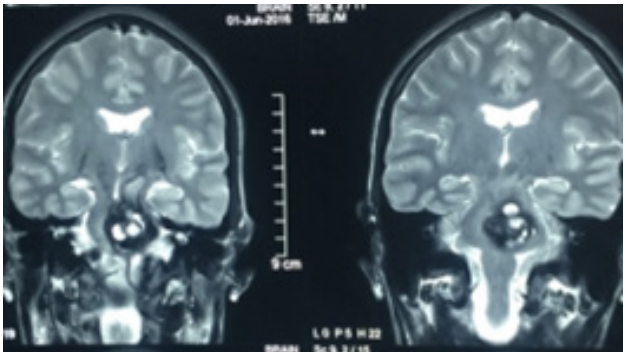

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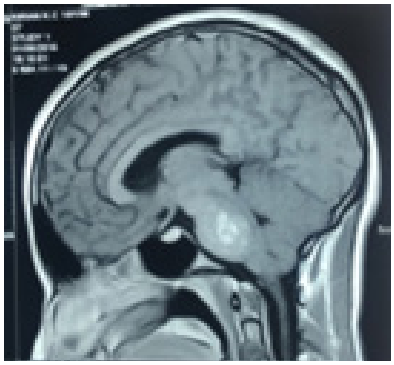

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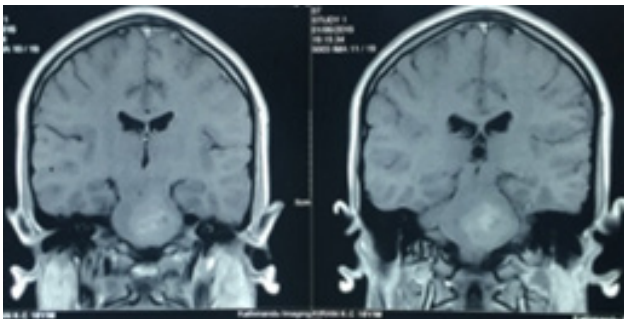

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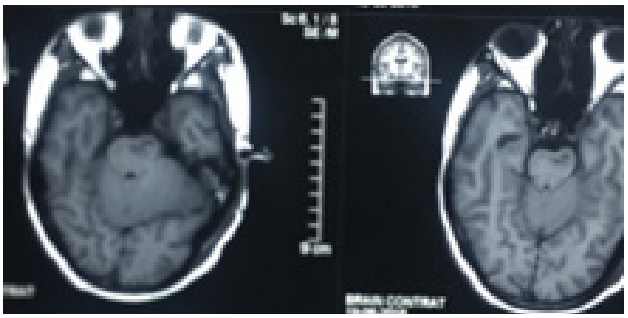

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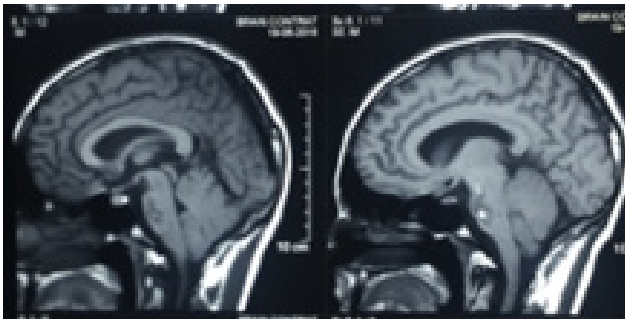

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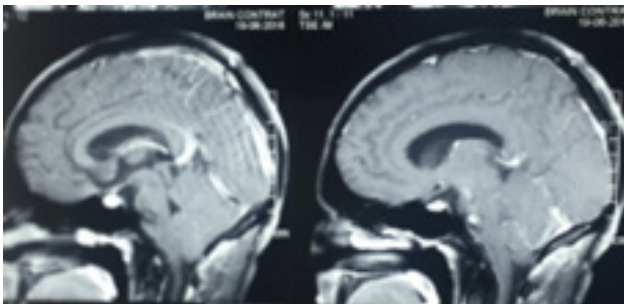


2h

Fig 2. Preoperative MRI of brain (2a, b, c, d & e) showing pontine mass of different intensities and 'Popcorn' appearance on T2 weighted image suggestive of pontine cavernoma. Post operative MRI of same patient (2f, g &h) showing no evidence of remnant.

RESULT

These 6 symptomatic patients with CCMs were operated within a span of 5 years (between June 2018 and Jan 2022) and all of these patients were adult (age ranged from 19-46 years). Four patients were male (66.7%) and two (33.3%) were female. One patient (16.7%) was presented with seizure and five patients (83%) with hemorrhage. Three cavernomas (50%) were located supratentorially and three (50%) infratentorially. Four cavernomas (66.7%) were at the eloquent area and two (33.3%) at non eloquent area. The diagnosis was made by MRI of different sequences. Intraoperative Neuro navigation, ICG videography, NPM were used whenever necessary. Total excision was achieved in all cases. Postoperative complications included transient focal deficit (2), Pseudomengingocele (I) and gait ataxia (I). Excellent functional recovery (MRS > 2) was achieved in five cases (83.3%) and good recovery in one (MRS 3). There was no surgery related mortality. Follow-up MRI of all patients did not reveal any residual and rebleeding was not observed on 14-60 months followed up.

DISCUSSION

Cerebral cavernous malformations (CCMs) are rare, angiographically occult neurovascular anomaly with a prevalence rate of 0.5-4 % in general population 1,2,3. Synonyms of CCMs are cavernoma, cavernous angioma and cavernous hemangioma. CCMs are bunch of abnormal hyalinized capillaries surrounded by hemosiderin deposits and gliotic tissues with thrombosed clots of different ages in the center (Figure.3). About 40-60% of patients having CCMs are familial autosomal dominant and they are usually multiple 6. The sporadic CCMs, other form, are usually single and do not run into the family. Approximately 25 % of CCMs occur in children and 75% in adult 6. About 70% of CCMs are located at supratentorial and 30% at infratentorial region 3. About 20% of CCMs are found at brainstem 7,8,9.

The Clinical presentation of CCMs ranged from asymptomatic to seizure, hemorrhage and progressive neurological deficit. 40-70% patients with seizure will have supratentorial CCMs and out of them 10-20% of CCMs are located in temporal lobe and they have high risk of producing seizure than in other areas 1.

The risk of hemorrhage from CCMs is about 0.5-1% per year and re hemorrhage rate is about 4-10%. Brainstem cavernoma may present with progressive neurosurgical deficit due to increased risk of symptomatic bleeding 7,8,9.

Risks of re-hemorrhage of CCMs are previous bleeding, multiplicity, male gender, deep and subcortical location. Risk of re bleeding is also increased during pregnancy 4.

Since CCMs are angiographically occult vascular

malformation, there is no role of cerebral angiography. MRI is the best choice of investigation to diagnose CCMs. Previous literatures have shown that detection rate of CCMs has been dramatically raised after the introduction of MRI in 1990s 10. T1 and T2 weighted sequences are useful to diagnose CCMs which are surrounded by a ring of hypo intensity due to hemosiderin deposits from recurrent micro hemorrhages and classical 'Popcorn' appearance seen on T2 weighted images; some advanced techniques like gradient echo sequence, high field MRI, diffusion tension imaging and function MRI may be further useful for accurate diagnosis of CCMs 2,11.

Management of CCMs vary from case to case depending on clinical presentation, age, location of lesion. Asymptomatic patients detected incidentally, can be observed closely, however, recently B- blockers like Propanolol which acts as an antiangiogenic agent, have been used prophylactically to lower the risk of hemorrhage or progressive neurological deficit 12.

The 60% of patients with CCMs who present with seizure are treated with anticonvulsants 3. About 40% of seizure patients with CCMs are drug resistant and require other modality of treatment 13.

Surgical excision is the best treatment option for symptomatic CCMs. Single or multiple rehemorrhage, large brainstem CCMs causing progressive neurological deficit and drug resistant epilepsy with CCMs are some of the important indications for surgery 1,3,14. These days with advanced technologies like DTA and fMRI intraoperative neuro navigation 14, Neurophysiological monitor (NPM) neurosurgeons can excise deep seated lesions of an eloquent area with minimum morbidity and mortality 15. Hence, there is no word 'inoperable' for CCMs surgery.

Main aim of surgery for CCMs are to achieve complete excision and to avoid further neurological damage. However, some large deep seated or CCMs of eloquent area may not be amenable to complete excision and these remnant part may be the source of rebleeding and seizure in future 11.

Surgical strategies and surgical outcome are quite different in case of deep seated and eloquent CCMs like in basal ganglia or brainstem than other CCMs at lobar location. After the surgical resection of CCMs about 80% of patients are seizure free 13.

CCMs of basal ganglia are rare deep seated lesions that often produce significant neurological deficit. CCMs of these areas can be approached either via transfrontal transcortical or transsylvian transinsular approach. Long term good outcome can be achieved in 74% of cases 16.

Brainstem CMs can be approached via posterolateral or posteromedial approaches depending upon the location of lesion 7. These brainstem CMs can be excised via 'safe entry zone' into the brainstem avoiding important neural structures 17. The 6.6% rate of recurrence of brainstem CMs requiring reoperation and annual risk of rehemorrhage in these recurrent brainstem CMs is about 5.9% which is similar to unoperated cases 8.

Gross et al reported an overall 90 % complete resection rate in his meta analysis of 1390 cases of brainstem CMs with ranged from 85-100% in large series 18.

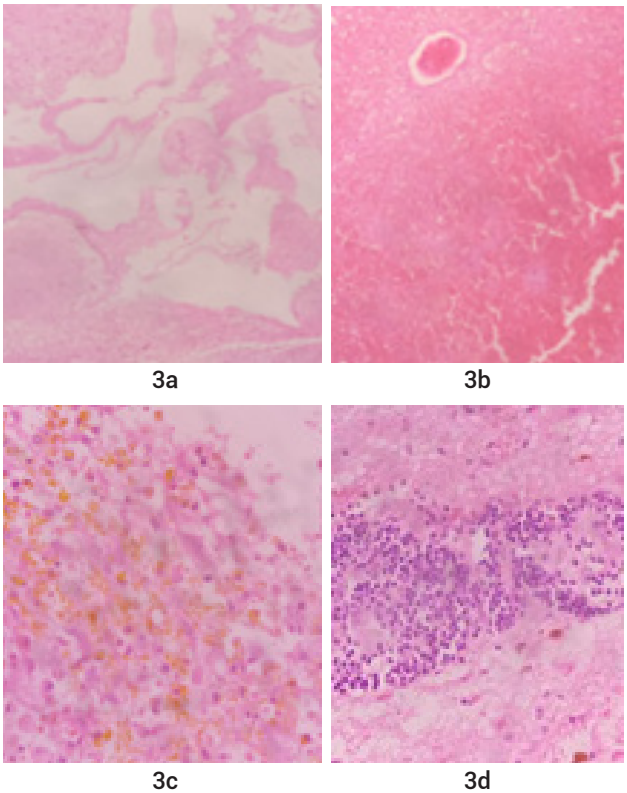
In a large series of brainstem CMs Garcia et al reported Unchanged or improved in 69-91% patients with surgical mortality of 3.5% 8.

Radiosurgery as a treatment for symptomatic CCMs is still controversial and data on long term results are not available.

Stereotactic radio surgery (SRS) has been advocated for CCMs located in deep, eloquent or inoperable areas 4,5, however, with advanced neurosurgical armamentarium there is no such "inoperable" areas in neurosurgery.

Few literatures have been published on SRS as a treatment of CCMs. The rationale of SRS use in CCMs is to prevent subsequent Hemorrhage like its utilization in AVMs 4.

Figure.3



3a **3b** **3c** **3d**

Fig 3. Histological pictures of brain cavernoma (H&E x 4 &10). Congested and dilated vascular spaces lined by hyalinized walls (3a) are associated with hemorrhage (3b) and scattered areas of hemosiderin deposits (3c). Reactive features in the form of foam cells and focal perivascular lymphocytic collections are present in neuroparenchyma (3d). All these features are suggestive of brain cavernoma.

CONCLUSION

Gold standard treatment for symptomatic CCMs is microsurgical excision. Recent advancement in imaging and technologies have allowed us to remove CCMs safely even if they are deep seated and in eloquent areas. Asymptomatic CCMs are best treated conservatively with regular clinical and radiological monitoring.

Table 1. Demographic, Clinical, Radiological, Surgical and outcome of six patients operated for Cerebral Cavernous Malformations (CCMs).

S.N.	Age/sex	Clinical presentation	Location	Surgical Approach	Complications	Outcome (MRS)	Follow up period (Months)
1	25/Female	Hemorrhage	Right frontal	Frontal craniectomy	-	0	14
2	56/Female	Hemorrhage	Posterior fossa(vermix)	Suboccipital craniectomy	Pseudomeningocele, gait ataxia	3	36
3	40/Male	Hemorrhage	Left cerebellar	Mid-line suboccipital	-	0	38
4	30/ Male	Seizure	Right parietal	Parietal craniotomy	Transient hemiparesis	1	48
5	46/Male	Hemorrhage	Right caudate nucleus	Interhemispheric, Transcallosal	-	1	48
6	19/Male	Hemorrhage	Pontine	Right Retromastoid	Mild left sided hemiparesis	2	60

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