



MANAGEMENT OF LEFT FRONTAL CAVERNOMA

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ABSTRACT

Cavernoma is blood vessels abnormalities where the blood vessels dilated. It may happen in various locations throughout the brain. Seizure, focal neurological deficit, haemorrhage and headache are most common symptoms of cavernoma. Cavernoma can be diagnosed using MRI, while its treatment options can either be observation, surgical excision or radio surgical depending on the natural course of the lesion, its location relative to eloquent areas of the brain, surgical accessibility and availability of surgeon skills. A 50 years old male patient having seizures was suspected to have low grade glioma after CT scan was done. However, after MRI was done, the patient was diagnosed with cavernoma on left frontal lobe. The treatment course in the hospital was mainly to treat the low grade glioma. However after low grade glioma was rule out, the treatment was stopped and treatment for cavernoma started. The treatment option to treat the patient is surgery excision. The most preferred diagnostic tool for cavernoma is MRI. The selections of treatment in management of cavernoma are observation, surgical excision or radiosurgery depending on the natural of the lesion, its location relative to eloquent areas of the brain, surgical accessibility and finally the neurosurgeon skills.

Keywords: Cavernoma, haemorrhage, cavernoma, diagnostic

INTRODUCTION

Cavernoma, also known as cerebral cavernous malformation (CCM) or cavernous angiomas (CA) are assembly of thin-walled vascular sinusoids lined by a thin endothelium lacking smooth muscle, elastin, and intervening parenchyma. They are mulberry like in shape which surrounded by hemosiderin deposits and gliosis, which may or may not be thrombosed. Cavernous malformations can be throughout central nervous system including brain, brainstem, spinal cord, cranial nerves as well as the ventricles.¹ The clinical presentation of CCM is highly variable with the most common symptoms are seizure followed by focal neurological deficits, acute hemorrhage and headache. Whereas the most widely cited risk factor for haemorrhage in CCM is family history as well as prior history of haemorrhage. Other controversial risk factors are hormonal state in pregnancy, age and location of cavernoma.¹ The common diagnostic method to identify cavernoma is magnetic resonance imaging (MRI). Despite higher specificity of MRI towards cavernoma as compared to CT scans, MRI also has greater contrast resolution and higher degree of confidence.² Treatment options in CCM depend on several aspects which are natural course of the lesion, its location relative to eloquent areas of the brain, and surgical accessibility. Surgeon skills also play roles in choosing the treatment. Three general therapeutic strategies are observation, surgical excision or radiosurgery.³

Case presentation

A 50 years-old-Malay male patient was referred to Hospital Universiti Sains Malaysia (HUSM) from Hospital Raja Perempuan Zainab (HRPZ) due to the status epilepticus episode that occurs more than 10 times in 2 hours' time, which initially starts with focal fit on the right leg and then become generalized tonic-clonic. Each episode lasted for 3 to 5 minutes and was aborted casually with intravenous (IV) Diazepam. Upon the admission, patient claimed there is no fever and head trauma. He was diagnosed with epilepsy three years ago (2009) and was on and off with his antiepileptic

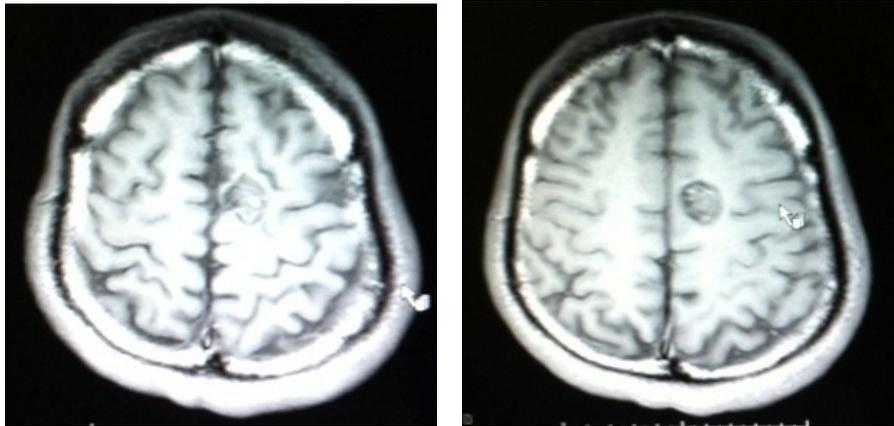
which is capsule Phenytoin 300 mg before the bedtime. On examination, the patient appeared to be alert, conscious and pink with blood pressure of 138/81 mmHg, heart rate of 76 bpm and temperature of 37°C. His percentage of oxygen saturation was 97 % and his blood glucose level is 6.3 mmol/L. His Glasgow Coma Scale (GCS) was 15/15. All his vital signs upon admission were normal and within normal range and he is fitting free at the time of admission. Upon admission, all his cranial nerve was in intact and CT scan was done to rule out low grade glioma. The scan result was reported as ill-defined, intra axial, non enhancing, heterogenous hyperdense lesion at the left frontal lobe, and calcification and gliosis at grey-white junction.

Treatments

On admission, the patient was suspected to have low grade glioma and was planned for MRI and strict GCS monitoring. The patient was also planned for IV Phenytoin 100 mg three times daily, IV Diazepam 5 mg when needed, tablet Dexamethasone 4 mg three times daily and IV Pantoprazole 40 mg twice daily. According to EFNS guideline on the management of status epilepticus, the preferred treatment pathway is IV of 4 mg Lorazepam or 10 mg Diazepam directly followed by 15 to 18 mg/kg phenytoin or equivalent fosphenytoin.⁴ Thus, the treatment planned for this patient does follow the recommendation and the seizure manages to be controlled. Phenytoin was given to control epilepsy. Phenytoin acts by increasing the efflux or decreasing the influx of sodium ions across cell membranes in motor cortex during nerves impulse generation. Thus, it will stabilizes the neuronal membranes and eventually reduce seizures activity. Special precaution should be taken in patient with hepatic impairments, hypotension and severe myocardial insufficiency.⁵ Diazepam was also planned to be used when needed which is to be used if the patient is having fitting. However, throughout the days that patient stayed in the ward, he was fitting free. Diazepam acts by binding to stereospecific benzodiazepine receptor on postsynaptic

GABA neuron which will then enhance inhibitory effects of GABA on neuronal excitability. This is due to the increase in neuronal membrane permeability to chloride ion that will cause shift in chloride ion. It will result in less excitable state due to hyperpolarization of the membrane and thus cause stabilization of the membrane.⁵ One of the functions of Dexamethasone is as an anti-inflammatory agent. In low grade glioma which is one of the brain tumours, brain will be swelled and inflamed. Thus, dexamethasone was used to treat the inflammation of the brain. However since the most common side effects of dexamethasone are gastrointestinal perforation, gastric ulcer and ulcerative esophagitis, Pantoprazole was usually prescribed together with dexamethasone. Dexamethasone acts as anti-inflammatory by suppressing migration of neutrophils to the inflammation area as well as reduced the production of inflammatory mediators. It will also reverse the high capillary permeability. While Pantoprazole which is proton pump inhibitors group will prevent gastrointestinal ulcer by inhibiting H⁺/K⁺ ATP pump in parietal cell and thus will cause suppression in gastric acid secretion.⁵ Despite the planned upon admission, the patient

was only given tablet Dexamethasone 4 mg three times daily and Keppra (Levetiracetam) 500 mg twice daily throughout his days in ward. Levetiracetam is one of the newer agents of antiepileptic. Its mechanism of action was unknown exactly. However theory suggests that it may be involve one or more of inhibition of voltage-dependent N-type calcium channel, facilitation of GABA-ergic inhibitory transmission through displacement of negative modulator, reduction of delayed rectifier potassium current and binding to synaptic protein that modulate neurotransmitter release.⁵ After MRI was done and the result was reviewed, the patient was diagnosed with left frontal lobe cavernoma. Then, dexamethasone dose was reduced to 2 mg twice daily for 2 days before being stopped. The patient was also planned for magnetoencephalogram (MEG) before being discharged and scheduled for surgery in nine weeks time. The medication at discharge is tablet Levetiracetam 500 mg twice daily for one month supply. Levetiracetam was given to control his seizure before the surgery.



Images of MRI scan of the patient's brain that shows that the patient is having a left frontal lobe cavernoma

DISCUSSION

In general, there are three therapeutic strategies in management of cavernoma. If the lesion was asymptomatic or inaccessible, observation was preferred. Patients with no gross haemorrhage, seizures or other specific symptoms are clearly the candidates for clinical observation. While if the patient was presenting with symptomatic haemorrhage and lesion was in an accessible and non eloquent area of the brain, surgical resection was recommended. However in the case where the lesion is surgically inaccessible or does not present any haemorrhage, the treatment option was less clear.³ Since the patient was presenting with seizures and the lesion was accessible, thus the recommended treatment option is to have surgical resection. According to a published review, 84 % of the patients were seizure-free after surgical removal of cavernoma and 8 % of the patients were improved. While, 6 % of the patients does not have any changes in their status and only 2 % showed deterioration.³ Since the patient is having seizure as the main complaint, thus the high percentage of success for seizure-free after surgical removal of cavernoma should be taken into account in deciding the treatment option. Algorithm that developed by Department of Neurological Surgery at North Western Memorial Hospital was used to facilitate the management of cavernoma. The algorithm is as follows:¹

- Cases of suspected cavernoma should undergo MRI scan with gradient echo imaging (to exclude or define multifocal lesions and likely genetic substrate) and gadolinium-enhanced study (to exclude of define associated venous angioma).
- Observe carefully if there is asymptomatic lesion in any location with follow-up MRI at interval of one to two years. Benign nature of lesion obviates the need for immediate resection unless they grow or become asymptomatic.
- Use resection with frameless stereotactic guidance in superficial lesions in accessible non eloquent areas with haemorrhagic presentation. Lesions in eloquent areas can either be observed or resected depend on risk-benefit balance in each individual patient.
- Resection using frameless stereotaxy with functional MRI guidance recommended for progressive enlargement of cavernoma with effect-related symptoms.
- Accessible lesions with seizure disorders are strongly recommended for surgical extirpation of lesion and surrounding abnormal brain parenchyma. The threshold for intervention depends on accessibility of lesion, eloquent location, severity of seizure disorder and resistance to medical management.

- Lesionectomy is suggested for cases with single lesion and temporal lobe seizure. If lesionectomy failed to control seizure disorder, detailed cortical and electrode encephalographic mapping followed by possible epilepsy surgery such as amygdalohippocampectomy should be performed.
- Deep located lesion should only be observed unless there is any repetitive haemorrhage occurs and ventricular presentation is noted. Pial surface or ventricular presentation provides surgical access to the lesion.
- Case of multifocal lesions should generally be followed expectantly, with intervention reserved for expanding lesions with new symptoms. Cases with epilepsy and refractory multiple lesions should be studied extensively to decide either one or more lesions are responsible for intractable seizures.
- During surgery for cavernoma, associated venous anomalies should be spared.

Stereotactically guided microsurgical excision of lesion located deep within the brain had achieved excellent results. The lesions are difficult to be removed and became a great challenge in neurosurgeon practices. However with stereotactic microsurgery, most cases showed neurological improvement. While in radio surgical treatment, there are various serious complications in many patients. In a case series of 23 patients by Gamma Knife, 27 % of patients required microsurgical extirpation due to postoperative haemorrhage or radiation-induced mass effect and 41 % of patients found to have neurological deterioration after the treatment. Thus, stereotactic microsurgery is more preferred over radio surgical treatment.¹ Cavernoma was diagnosed efficiently using MRI as compared to the CT scan. CT scan findings are compatible with low-grade gliomas, hematomas, granulomas, and inflammatory conditions such as tuberculomas and sarcoidomas. Thus, it is relatively lack of specificity in the diagnosis of cavernous angiomas. CT images also may miss small lesions and thus may not be detected by using non enhanced CT scanning. Whereas in MRI, its sensitivity to flowing blood and blood products of varying ages, as well as the greater contrast resolution, greatly increases the specificity of MRI compared with that of CT scanning. CT scanning and MRI can be used in the follow-up monitoring of patients with known cavernous angiomas, particularly when hemorrhagic events are suspected. MRI is the method of choice for the long-term

follow-up of patients with cavernous angiomas and for the assessment of family members in whom similar lesions are suspected. In addition, MRI is extremely helpful in presurgical planning to assess the extent of the lesion, define borders, and plan the surgical approach and exposure.² As conclusion, MRI is more preferred in diagnosis of cavernoma as compared to CT scan. Magnetoencephalography (MEG) was used to identify the epileptic zone in patients with cavernoma. In a study, 6 over 8 patients were found to have co-localization from cavernoma and epileptic zone. In cases of focal seizures due to a single cavernoma, MEG may precisely delineate the epileptogenic tissue bordering the lesion. While in cases with multiple cavernomas or dual pathology, magnetic source imaging (MSI) can be used to reveal the complexity of the cases and contribute to treatment decision. MEG is a promising method for prediction of epileptic zone in cavernoma related to epilepsies and thus it can contribute to decision making about and planning of epilepsy surgery.

CONCLUSION

Diagnosis of cavernoma is most preferred to be done using MRI over other scanning diagnostic methods. The selection of treatment options of cavernoma should be based on the natural of the lesion, its location whether at eloquent areas or at non eloquent areas of the brain, surgical accessibility and finally the neurosurgeon skills. In management of cavernoma, health providers may do an observation, a surgical excision or a radiosurgery.

REFERENCES

1. Raychaudhuri R, Batjer HH, Awad IA. Intracranial Cavernous Angioma: A Practical Review of Clinical and Biological Aspect. *Surgical Neurology* 2005; 63: 319–328. <http://dx.doi.org/10.1016/j.surneu.2004.05.032>
2. Jacobsen JC, Smirniotopoulos JG. *Brain Imaging in Cavernous Angiomas*; 2011. p. 1994–2012.
3. Kuker W, Forsting M. *Intracranial Vascular Malformations and Aneurysms* Springer Berlin Heidelberg: Medical Radiology; 2006.
4. Meierkord H, Boon P, Engelsen B, Goeke K, Shorvon S, Tinuper P, Holtkamp M. *et al* EFNS Guideline on the Management of Status Epilepticus. *European Journal of Neurology* 2006; 13: 445–450. <http://dx.doi.org/10.1111/j.1468-1331.2006.01397.x>
5. Lacy CF, Armstrong LL, Goldman MP, Lance LL. *Drug Information Handbook with International Trade Names Index*. 18th Ed. Lexi-Comp Inc.; 2009.
6. Stefan H, Scheler G, Hummel C, Walter J Ramstock, J Buchfelder, M Blumcke I. *et al* Magnetoencephalography (MEG) Predicts Focal Epileptogenicity in Cavernomas. *J Neurol Neurosurg Psychiatry* 2004; 75: 1309–1313. <http://dx.doi.org/10.1136/jnnp.2003.021972>

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