Giant Cerebral Cavernous Hemangiomas: A Report of Two Cases and Review of the Literature

ABSTRACT

Giant cerebral cavernous malformations (GCM) are rare vascular anomalies. They occur predominantly as solitary lesions in the supratentorial compartment. They are usually not associated with any other vascular malformations. Clinical Presentation GCM are common in the second decade, affecting females predominantly, and occur without familial association. They are all symptomatic due to their giant size and location. The GCM mimic neoplastic lesions because of their size and need to be considered in the differential diagnosis. A complete surgical extirpation is the treatment of choice. Use of intraoperative neuronavigation, diffusion tensor imaging (DTI) of fiber tracts and electrophysiological monitoring assist in safe and total excision of the lesions. A complete surgical excision of GCM is possible without significant surgical morbidity and results in long term cure.

KEYWORDS: Cavernous malformation, Cavernoma, Cavernous angioma, Giant cerebral angioma

INTRODUCTION

Cavernous malformations (CMs), also known as cavernous angioma, cavernous hemangioma or cavernoma, are well circumscribed, multilobulated, angiographically occult vascular malformations composed of sinusoidal vascular channels (caverns) lined by single layer of endothelium separated by collagenous stroma devoid of elastin, smooth muscle, or other mature vascular wall elements. The lack of intervening brain parenchyma is a characteristic pathological marker. CMs range in size from 0.1 to 9 cm, with a mean of 1.4 to 1.7 cm (6, 9, 14, 18, 19, 22, 29, 40). Few data can be found about the size of these malformations. The majority of CMs are small but they may reach significant size. Unlike giant aneurysms, defined as having a diameter of at least 25 mm, no threshold dimension has been defined for giant cavernous malformation (GCM). We have defined a GCM to measure at least 6 cm in one dimension, as has been previously described by Lawton et al. (20). In this report, we review our experience of treatment of two cases of GCM and the available literature on clinical presentation, radiological features, surgical management and outcome of GCM.

CASE REPORTS

Case 1

A 24-year-old right handed female presented with generalized tonic clonic convulsions since 3 months. On examination she did not have any neurological deficit. The patient’s Magnetic Resonance (MR) images showed a heterogeneously enhancing 6.0x5.4x4.2 cm. mass lesion in right parieto-occipital region showing areas of hemorrhages and cysts with altered blood (Figure 1A). A peripheral hypointense rim seen on T2 weighted image was highly suggestive of a GCM (Figure 1B). A 4-vessel digital subtraction angiogram (DSA) demonstrated an avascular mass. The patient underwent a right parieto-occipital craniotomy. The lesion, which was seen on the cortical surface, was noted...
to have yellowish discoloration and was a conglomerate of multiple cysts containing altered blood interspersed with areas of calcification. The lesion was well demarcated from adjacent gliotic brain and was excised circumferentially. There were no significant arterial feeders, however a large venous channel was noted in relation to the mass. The patient had uneventful post operative recovery. The histological examination of the lesion showed multiple dilated vascular spaces lined by endothelium and containing red blood cells, and showing a cluster of thin walled vascular spaces (Figure 1C, D). There was no intervening brain parenchyma within the lesion. A diagnosis of GCM was thus confirmed. The patient was asymptomatic at one year of follow up. A postoperative MR scan showed a complete extirpation of the right parieto-occipital cavernoma (Figure 1E, F).

**Case 2**

A 25-year-old right-handed female presented with focal convulsions involving right sided limbs followed by secondary generalization for 8 months. Since 3 months she also noticed weakness of right sided limbs. On examination she had Grade 3 right hemiparesis. MR scan of the brain showed a large left fronto-parietal parasagittal cavernous hemangioma with features of subacute hemorrhage. The lesion measured 6.5x5.0x5.0 cm (Figure 2A, B). The patient underwent left frontoparietal parasagittal craniotomy under neuronavigation guidance with white fibre tracking (Diffuse Tensor Imaging). The posterior part of superior frontal gyrus was stained yellowish. A gliotic plane surrounding lesion was identified and the mass was excised circumferentially. Postoperatively the patient recovered uneventfully with no additional deficit. Histological examination of the lesion showed multiple dilated vascular spaces lined by endothelium and containing red blood cells. There was a cluster of thin walled and hyalinised vascular spaces with recent and old hemorrhages in the stroma (Figure 2C). During follow up at six months the patient was seizure free and the right hemiparesis was gradually improving. A postoperative neuroradiological evaluation confirmed a complete excision of the left frontoparietal cavernoma.

**DISCUSSION**

Cavernous malformations (CMs) are amongst the common vascular malformations. The prevalence of CMs is estimated...
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CMs accounts for approximately 5% to 10% of all intracranial vascular malformations (9, 22, 28, 29, 42). Patients with CMs typically present between second and fourth decade (6, 14, 33, 38, 40). The majority of CMs are supratentorial (6, 29, 43) and most commonly located in parietal lobe and thalamus (3, 34). Intracranial extra axial cavernomas are relatively rare (39). Giant cavernomas are usually found in the gastrointestinal tract, especially in the liver and spleen and also in the subcutaneous region. Giant intracranial extra-axial cavernomas are reported in the scalp, pericranium, parietal convexity, pituitary gland, middle cranial fossa and cavernous sinus (11, 16, 31, 35, 36). Giant intra-cranial, intra-axial cerebral parenchymal cavernomas are extremely rare. GCM are very rare and usually not considered in the differential diagnosis of large tumour. Our literature search could locate only 16 cases of GCM (1, 4, 5, 7, 8, 12, 13, 15, 20, 23, 37) including the two cases in the present report, fulfilling our definition of GCM (Table I).

Growth of GCM

The cause of development and growth of CMs is uncertain. CMs grow over time and can develop de novo. CMs are considered dynamic lesions which grow and change their size over time. There are several theories regarding mechanism of growth. The universally accepted theory suggests that processes of bleeding and thrombosis within the lesion leads to an increase in the size of the CMs. There is a transient rise in venous pressure, causing a self limiting seepage of blood from the lesion also called erythrocyte diapedesis (21). This leads to an increase in the size of the CM. A second theory proposes that CMs expand by the same mechanism as chronic subdural hematoma. There is evidence to show that CMs endothelialize small hematomas that they create (32). Another theory suggests expansive growth of CM that mimics a neoplasm. Pozzati et al. suggest that the lesions are either induced to produce or spontaneously produce angiogenic factors that allow gradual progression of vessels. This theory describes a proliferative vasculopathy, hemorrhagic dysangiogenesis or hemorrhagic angiogenic proliferation (2, 25).

Epidemiology

Cerebral CMs rarely attain large size. Patients with cerebral CMs typically present between second and fourth decade (6, 14, 33, 35, 38, 40) whereas majority of GCMs occur in children and young adult. Of the 16 cases of GCMs, half are below the age of 18 years (Table I). The age ranges from 7 months (5) to 45 years (1). The mean age of the patients was 16.8 years. The overall prevalence among male and female is equal for CMs (6, 18, 22, 28) whereas there is clear female preponderance for GCM, with 9 patients being females out of 16 cases (37). Familial cases account for 20-50% of patients presenting with CMs (18), but there is no familial association reported for GCM. The majority of CMs are supratentorial (6, 28, 43) but around 9-35% occurs infratentorially (18, 33). Multiple CMs are also not uncommon and may occur in up to 10-30% of sporadic cases and 84% of familial cases (9, 43). However all reported cases of GCMs are supratentorial and solitary. Most common location for GCMs was frontal or fronto-parietal region, but also been reported from other locations like occipital lobe (4), pineal region (12), and within the intraventricular septum pellucidum (1).

CMs may be associated with other vascular malformation and other central nervous system pathologies like central nervous system tumors, visceral hemartomas and extra cerebral soft tissue tumors. Association of CMs with venous malformations, capillary telengectasia and arteriovenous malformations has been described, most common being venous malformations (2, 26, 27, 29, 40). Clinical studies estimate that 2.1%-30% of patients with CMs have venous angioms (26, 41). In present

Figure 2: A) Coronal flair MR image showing a giant cavernoma in the parasagittal left frontal parenchyma, harbouring a cystic as well as a solid component and a characteristic rim. B) Post-contrast sagittal MR image showing the heterogeneously enhancing mass in the left posterior frontal motor cortex. C) Photomicrograph showing thin walled vascular spaces with adjacent gliotic cerebral parenchyma. (Hematoxylin and Eosin, X100).
### Table I: Giant Cavernous Malformations Reported in the Literature

<table>
<thead>
<tr>
<th>S no</th>
<th>Author, Year (Ref)</th>
<th>No of cases</th>
<th>Age, Sex</th>
<th>Size (cm)</th>
<th>Location</th>
<th>Symptoms</th>
<th>CT scan</th>
<th>MR scan</th>
<th>Approach</th>
<th>Post op status</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Khosla et al., 1984 (13)</td>
<td>1</td>
<td>3 years, male</td>
<td>&gt;6</td>
<td>Lt frontoparietal</td>
<td>Enlarged head, Rt hemiparesis</td>
<td>Lt giant cystic lesion with small solid component</td>
<td>-</td>
<td>Lt frontal</td>
<td>Improved</td>
<td>4 months</td>
</tr>
<tr>
<td>2</td>
<td>Kawagishi et al., 1993 (12)</td>
<td>1</td>
<td>11 months, male</td>
<td>8</td>
<td>Rt pineal region and trigone</td>
<td>Rt hemiparesis</td>
<td>Huge multilocular lesion with hyperdense rim</td>
<td>Lt parietal</td>
<td>Improved</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>de Andre et al., 2002 (5)</td>
<td>2</td>
<td>7 years, female</td>
<td>12x14</td>
<td>Lt frontoparietal</td>
<td>Macrocephaly, convulsions</td>
<td>Large hyperdense irregular lesion</td>
<td>Lt frontoparietal</td>
<td>-</td>
<td>Improved in 4 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>7 months, female</td>
<td>&gt;6</td>
<td>Lt frontoparietal</td>
<td>Convulsions</td>
<td>Hyperdense and cystic</td>
<td>Cystic lesion with hyperdense periphery</td>
<td>Lt frontotemporoparietal</td>
<td>Rt hemiparesis</td>
<td>Improved in 3 months</td>
<td>5 years</td>
</tr>
<tr>
<td>4</td>
<td>Connelly et al., 2003 (1)</td>
<td>1</td>
<td>45 years, female</td>
<td>6.5</td>
<td>Intraventricular septum pellucidum</td>
<td>Memory disturbances</td>
<td>Intraventricular heterogeneous lesion</td>
<td>Intraventricular extending to superior parietal lobule, T2 hyperintensity at periphery</td>
<td>Superior parietal lobule along interhemispheric fissure</td>
<td>Uneventful</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>Muzumdar et al., 2003 (23)</td>
<td>1</td>
<td>18 years, male</td>
<td>6x3.5</td>
<td>Lt frontal lobe</td>
<td>Lt focal seizure</td>
<td>Large hyperdense frontal SOL</td>
<td>Rt frontal mixed intensity lesion on T1W, hypointense rim on T2W</td>
<td>Rt frontal</td>
<td>Uneventful</td>
<td>3 years</td>
</tr>
<tr>
<td>6</td>
<td>Chicani et al., 2003 (4)</td>
<td>1</td>
<td>15 years, male</td>
<td>7X5</td>
<td>Lt parieto-occipital</td>
<td>Rt homonymous hemianopia</td>
<td>Well-circumscribed rounded hemorrhagic mass</td>
<td>Well defined hemorrhagic mass</td>
<td>Lt occipital</td>
<td>Hemanopia worsened</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>Lawtow et al., 2004 (20)</td>
<td>1</td>
<td>12 years, male</td>
<td>13x7x7</td>
<td>Anterior 2/3 Rt cerebral hemisphere</td>
<td>Convulsions, Lt hemiparesis</td>
<td>-</td>
<td>Majority of Rt Hemisphere with speckled areas</td>
<td>Rt hemicraniectomy</td>
<td>Lt hemiparesis</td>
<td>Improved over 2 years</td>
</tr>
<tr>
<td>8</td>
<td>Hong et al., 2006 (15)</td>
<td>1</td>
<td>22 years, female</td>
<td>5x6</td>
<td>Rt frontal</td>
<td>Convulsions</td>
<td>Well-defined with calcifications</td>
<td>Rf falx, hyp on T1W mixed on T2W</td>
<td>Lt frontal</td>
<td>Improved</td>
<td>-</td>
</tr>
<tr>
<td>9</td>
<td>van Lindert et al., 2007 (37)</td>
<td>3</td>
<td>36 years, female</td>
<td>6-7</td>
<td>Rt temporo-parieto-occipital</td>
<td>Headache, vomiting, ataxia</td>
<td>Circumscribed enhancing</td>
<td>Lt frontal hyperdense</td>
<td>Lt frontal</td>
<td>Improved</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>35 years, female</td>
<td>6-7</td>
<td>Lt frontal</td>
<td>Generalized seizure</td>
<td>Lt fronto-temporal multicystic paraventricular</td>
<td>-</td>
<td>Lt frontal</td>
<td>Improved</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 months, female</td>
<td>6-7</td>
<td>Lt fronto-temporal</td>
<td>Generalized seizure</td>
<td>Lt fronto-temporal multicystic paraventricular</td>
<td>-</td>
<td>Lt frontal</td>
<td>Improved</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Gezen et al., 2008 (8)</td>
<td>1</td>
<td>10 months, male</td>
<td>6x4x4.5</td>
<td>Lt parietal</td>
<td>Focal seizure</td>
<td>-</td>
<td>Lobulated Lt paraventricular parietal, acute and subacute hemorrhages</td>
<td>Lt parietal</td>
<td>Rt hemiparesis</td>
<td>Improved over 2 years</td>
</tr>
<tr>
<td>11</td>
<td>Dong et al., 2008 (7)</td>
<td>1</td>
<td>20 years, female</td>
<td>7x5x5</td>
<td>Lt frontal lobe and basal ganglia</td>
<td>Seizures</td>
<td>Mixed density Lt frontal and basal ganglia</td>
<td>Multilocular lesion with low signal rim on T2W</td>
<td>Lt frontal</td>
<td>Uneventful</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>Present study</td>
<td>2</td>
<td>29 years, female</td>
<td>6x5.5x4.5</td>
<td>Rt parieto-occipital</td>
<td>Generalized seizure</td>
<td>-</td>
<td>Heterogeneous lesion with hypointense rim on T2W</td>
<td>Rt parietooccipital</td>
<td>Uneventful</td>
<td>1 year</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25 years, female</td>
<td>6.5x5x5</td>
<td>Lt motor area</td>
<td>Focal seizure with weakness</td>
<td>-</td>
<td>Lt fronto-parietal parasagittal lesion with subacute bleed</td>
<td>Lt frontoparietal parasagittal</td>
<td>Improved in Rt Hemiparesis</td>
<td>6 months</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** S no, Serial number; Ref, Reference; Cm, Centimetre; CT, Computerised Tomography; MR, Magnetic Resonance; Post op, Post operative; Rt, Right; Lt, Left; T1W, T1 weighted; T2W, T2 weighted.
review of literature only one case of GCMs was found to be associated with venous angioma (7). In Case 1 of the present report, a large venous channel was noted in relation to the GCM.

**Clinical Presentation**

A high incidence of asymptomatic CMs has been reported in some autopsy series (24, 42). With the advent of MR studies, 11-44% of patients were discovered to harbour CMs, when they were investigated for unrelated symptoms (28, 29). GCMs have never been detected incidentally or have been asymptomatic except in one of the earliest report of GCM by Sansone et al. (22). A 72 year female with metastatic breast carcinoma had a dumbbell shaped cavernous lesion in the pituitary region detected incidentally on post-mortem examination. However since the size of the CM was less than 6 cm, this case was not included in our literature survey, and the case did not qualify as a GCM by our definition.

The usual symptoms of CMs are seizures, focal neurological deficit and overt hemorrhage (6, 9, 14, 18, 28, 29, 34, 38, 40, 43). GCMs are more likely to present with seizure and mass effect causing progressive neurological deficit and rarely present with overt haemorrhage. In the current review of 16 cases of GCMs, 11 cases presented with seizure episodes and in 5 cases, the GCM had mass effect. The deficits included hemiparesis (12, 13, 20), homonymous hemianopia (4), memory disturbances with behavioural changes (1). Two children presented with enlarged head (5, 13).

**Neuroradiology**

The imaging characteristics of CMs which are known to be angiographically occult are well defined. MR imaging is currently the most sensitive and most specific method of diagnosing CMs (21). Gradient echo (GRE) imaging is much more sensitive than conventional MR imaging for detecting small CMs. The characteristic finding on MR images include variable hyperdense signal intensity centrally with a reticulated pattern on T2 weighted images representing degrading haemorrhages of various ages. A surrounding hypointense ring corresponds to the hemosiderin containing region around the CMs. The central portion is said to have popcorn or honeycomb appearance and should enhance with contrast administration. On T1 weighted MR, the region of low intensity signal also is seen, along with a heterogeneous signal centrally (27, 43). Angiography is typically of little value in assessing CMs, which show no vascular blush and no feeding arteries or draining veins. The lesion is typically angiographically occult.

The neuroradiological diagnosis of GCMs is challenging as they are rare lesions. The imaging appearance of GCMs may be variable ranging from completely cystic lesion (13) to those resembling neoplasm with striking contrast enhancement and mass effect (5, 32). Neoplastic lesions may closely mimic the appearance of GCMs most notably hemorrhagic metastases, especially from melanoma and some glioma, like oligodendrogioma and pilocytic astrocytoma, with calcifications or hemorrhages. Overt hemorrhages may totally obscure typical MR features of underlying pathology, especially CMs and the true cause of hemorrhage may be missed. Hence, a follow up imaging at an interval of six weeks, after complete lysis of the blood is advisable. The MR appearance of sub acute hematoma and thrombosed AVMs may closely resemble CMs.

**Treatment**

A microsurgical complete excision of CMs or GCMs is considered the gold standard of treatment. The current well established indication for surgical excision for CMs is recurrent hemorrhages, intractable epilepsy, and progressive neurological deficit unless location is associated with unacceptable high surgical risk (6, 7, 29). GCMs are excised to relieve their mass effect and to establish a histological diagnosis of the lesion. Despite their size, a good surgical outcome has been reported in various reports of surgical extirpation of GCMs, including our two cases. Gross total excision was achieved in all, including our cases, except in one case where near total excision was achieved, as two-third of the cerebral hemisphere was diffusely infiltrated (20). Surgical extirpation is safe and possible without significant blood loss inspite of their giant size. A complete excision results in a long term cure with near complete recovery of pre-existing neurological deficits. The presurgical planning includes functional MR imaging and fiber tracking imaging (Diffuse tensor imaging) especially for lesions adjacent to eloquent areas of the brain (44). Intraoperative neuronavigation and cortical mapping of motor areas enable a precise localization and safe excision (30). No adjuvant therapy has been considered in any case of GCM. The role of radiosurgery and stereotactic radiotherapy for deep seated, surgically inaccessible CMs remains controversial (10, 17).

**CONCLUSIONS**

GCM are a distinct type of vascular malformation. They are solitary and occur in the supratentorial compartment. These lesions are more common in children and young adults without any familial association. They occur predominantly in females. GCM are unlikely to be associated with other vascular malformations. Their presentation is with mass effect and seizures, and hemorrhagic manifestations are rare. GCM need to be considered in the differential diagnosis of neoplastic mass lesions. Surgical excision is feasible without significant morbidity and offers complete long term cure.

**REFERENCES**


