Journal of Cerebrovascular and Endovascular Neurosurgery
ISSN 2234-8565, EISSN 2287-3139, http://dx.doi.org/10.7461/jcen.2013.15.3.255

Case Report

Giant Cystic Cerebral Cavernous Malformation with Multiple Calcification - Case Report

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Cerebral cavernous malformation with giant cysts is rare and literature descriptions of its clinical features are few. In this case study, the authors describe the clinical symptoms, radiological findings, and pathological diagnosis of cerebral cavernous malformations with giant cysts, reviewing the relevant literature to clearly differentiate this from other disease entities. The authors present a case of a 19-year-old male with a giant cystic cavernous malformation, who was referred to the division of neurosurgery due to right sided motor weakness (grade II/II). Imaging revealed a large homogenous cystic mass, 7.2×4.6×6 cm in size, in the left fronto-parietal lobe and basal ganglia. The mass had an intra-cystic lesion, abutting the basal portion of the mass. The initial diagnosis considered this mass a glioma or infection. A left frontal craniotomy was performed, followed by a transcortical approach to resect the mass. Total removal was accomplished without post-operative complications. An open biopsy and a histopathological exam diagnosed the mass as a giant cystic cavernous malformation. Imaging appearances of giant cavernous malformations may vary. The clinical features, radiological features, and management of giant cavernous malformations are described based on pertinent literature review.

Keywords Cavernous malformation, Giant cyst

J Cerebrovasc Endovasc Neurosurg. 2013 September;15(3):255-259
Received : 26 June 2013
Revised : 16 July 2013
Accepted : 22 August 2013

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INTRODUCTION

The cavernous malformation (CM), also known as cavernous angioma or cavernoma, is a vascular malformation characterized by the presence of sinusoid-like capillary vessels containing blood with poor circulation.[4] CMs vary in size from a few millimeters to a several centimeters. However, unlike giant aneurysms, defined as having diameters of 25 mm and over, no threshold dimension has been accepted for a giant CM (GCM).[8] Kim et al.[12] studied a variety of CMs sized between 1 mm and 75 mm, and reported a mean size of 14.2 mm. The majority of CMs are small but they can occasionally reach significant size. Although arbitrary, Lawton et al.[13] defined a GCM as a CM with a diameter greater than 6 cm. CMs vary greatly in size according to the pathological definition. Although rare, if CMs are over a certain size, they may be referred to as GCMs. Attention is required for radiological differentials from large tumors. We report a case of GCM with a review of relevant studies.

CASE REPORT

A right-handed, 19-year-old male was referred to the division of neurosurgery due to right sided motor

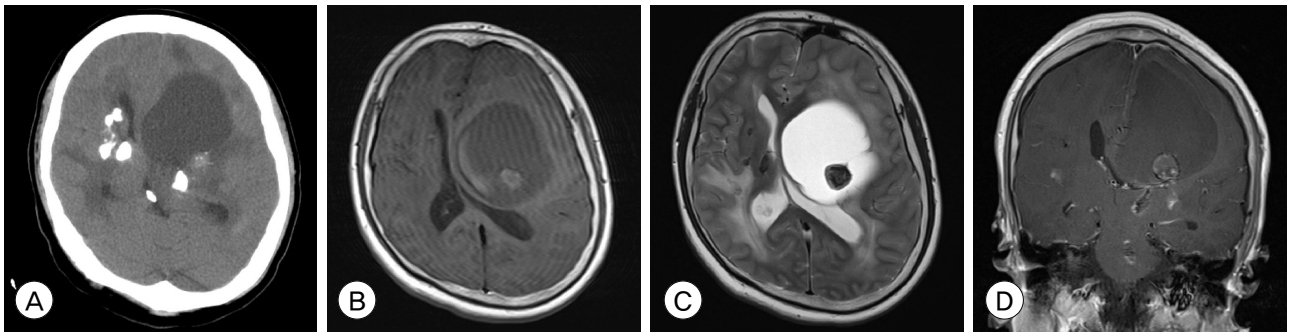

Fig. 1. *Preoperative imaging (A) Non-enhanced computed tomography scan shows a homogenous large-cystic lesion of 7.2×4.6×6 cm size in the left fronto-parietal lobe and basal ganglia. Note that there are mutliple parenchymal calcifications in both parietal lobes. (B) T1-weighted axial magnetic resonance imaging shows a large fronto-parietal hyperintense cystic lesion with local mass effect and minimal surrounding edema. (C) T2-weighted axial magnetic resonance imaging shows a heterogeneous high intra-cystic nodule, exhibited with hypodensities, suggestive of calcification. (D) T1-weighted contrast-enhanced coronal image reveals heterogeneous, slight enhancement of intra-cystic nodule, and a lack of enhancement of the cystic component.*

weakness (grade II/II) that persisted for 3 months. Since the age of 5, the patient had been clinically diagnosed with 1st grade mental retardation and epilepsy with daily prescription medication as follows: levetiracetam 500 mg 1T twice a day (bid), valproate 600 mg 1T bid, topiramate 100 mg 1T bid, clonazepam 0.5 mg 1T per day. Also, the patient had familial history of an 18-year-old sister with an astrocytoma on her left pons, diagnosed when she was 10 years old. After a surgical resection, she fully recovered. No other family members had significant clinical history.

The patient's computed tomography (CT) scan revealed a well-defined cystic mass with a size of 7.2×4.6×6 cm filled with 2 cm intra-cystic nodule on left fronto-parietal lobe. There were also multiple parenchymal calcifications in both parietal lobes (Fig. 1A). The mass was lobulated, ovoid, and bulging, and had surrounding edema with mass effect. The patient's magnetic resonance imaging (MRI) showed the mass as low signal intensity (SI) in T1-weighted images (WI), but high SI in T2WI (Fig. 1B, C). The 2 cm intra-cystic nodule was heterogeneous high SI in T1WI, low SI in T2WI and slightly enhanced, heterogeneous high SI in T1-weighted contrast-enhanced coronal image (Fig. 1B, C, D). Based on the CT and MRI findings, the lesion was diagnosed as a low-grade glioma or congenital infection such toxoplasmosis or cytomegalovirus, or even a neurocysticercosis. Surgical resection was decided upon as the course of treatment. A left frontal craniotomy was performed, followed by a transcortical approach to remove the mass. From the MRI, the T1 low SI, T2 high SI lesion in the surgical field was identified as a cyst with yellow fluid, and was removed with aspiration. The intra-cystic nodule, which was 2×2 cm in size, freely movable, relatively hard, with a yellow surface, and low vascularity, was resected en bloc. There were no significant complications or bleeding. After the operation, the patient made a rapid recovery. Motor weakness was improved to grade III/III. However, the histological exams of the mass revealed it to be a CM (Fig. 2). The follow-up CT scan showed no residual lesion (Fig. 3).

DISCUSSION

CMs are relatively rare vascular anomalies composed of abnormal cavernous endothelial-lined spaces lacking smooth muscle and intervening neural tissue.[2] These malformations have a reported prevalence rate of 0.4 to 0.9% based on autopsy and MRI series.[22] Most CMs occur sporadically as solitary lesions.[2][10] On rare occasions, CMs reach a significant size, 6 cm

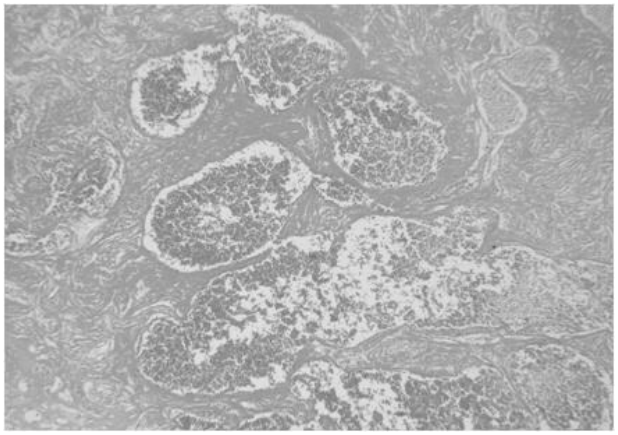

Fig. 2. Low-power photomicrographs show thromboses within the cavernous vascular spaces. Also note thin-walled vascular channels without neural tissue (Hematoxylin & Eosin, ×100).

in diameter or larger, becoming what may be defined as a GCM.[13] The pattern of growth is probably recurrent bleeding, followed by organization of the clot, pseudocapsule formation, and secondary expansion.[3]

Although CMs may occur in patients in their twenties to forties, the majority of GCMs develop in children, with the youngest reported case being 3.5 months of age.[1][3][4][20][22] The gender balance is equal in CMs, but there seems to be a female predominance in GCMs.[4][22] Familial CMs account for 20% to 50% of patients.[18] However, in review of literature for GCMs, no familial occurrence has been reported.[22] Multiple CMs may occur in 10% to 30% of sporadic cases and up to 84% in familial cases, but multiple GCMs have not been reported.[22][23]

The GCM may clinically present with symptoms ranging from headaches to catastrophic, life-threatening hemorrhages. A significant number of GCMs present with a seizure, acute-onset of a severe headache, or a new focal neurologic deficit.[8] On the other hand, large, slow-growing lesions often manifest with increased intracranial pressure from obstructive hydrocephalus or the mass occupying significant space. The subtle onset of right sided motor weakness, as seen in this case, has been reported in literature as the result of the mass growth occurring slowly and without significant hemorrhage.[3]

The causes of cystic degeneration of CMs remain unknown. Research points to recurrent minor hemorrhage of internal vascular sinuses or neocapillaries within CMs as possible factors. Bleeding episodes within a CM cause the osmotic pressure across the CM membrane to change, leading to gradual fluid accumulation within the CM, cystic degeneration, and subsequent CM growth.[15][19] Cystic degeneration within the CMs in the cerebellopontine angle is a progressive process; CMs may be at different stages. As a result, when imaging examinations are performed, the CMs may show various features of cystic degeneration. For example, multiple cysts may be seen within the solid component of the CM, as in this case, and a large cyst may be seen in combination with small nodules. In addition, cystic CMs may have different supply of blood. All of these features contribute to different enhancement patterns upon contrast-enhanced CT or MRI examination, which can vary from no enhancement at all to marked enhancement.

Diagnosis is mostly straightforward in typical cases

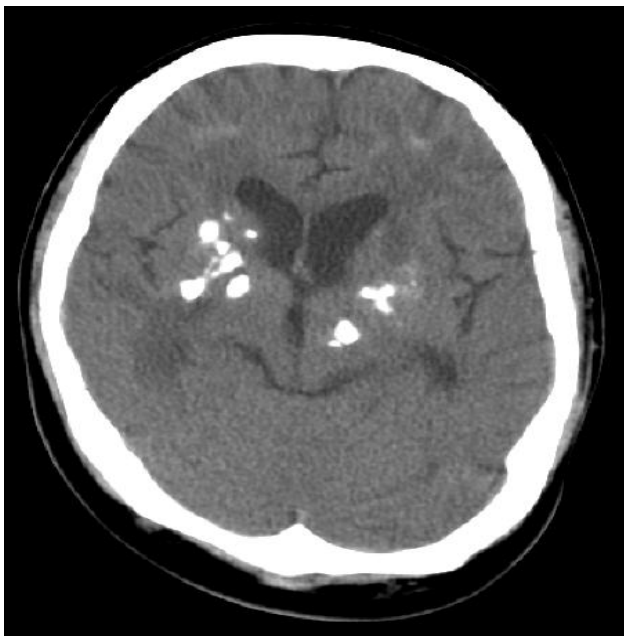

Fig. 3. Postoperative computed tomography image shows no residual cavernous malformations with intact multiple calcifications.

of CM. Surrounding edema and mass effect appear only rarely.[18] CMs in the form of a cystic growth with a well-defined capsule are unusual.[18] On the other hand, in existing reports of GCMs, the radiographic appearances vary widely from completely solid to primarily cystic, or heterogeneous masses composed of both components.[11] Also, the presence of contrast enhancement is highly inconsistent, ranging from nonexistent to intensely enhancing. A number of studies report CM lesions that mimic the appearance of high-grade glial neoplasms such as oligodendrogliomas, because they appear tumefactive on MRI, having an infiltrative pattern, as well as significant perilesional edema.[13][22] Initially, in this particular case, the mass was diagnosed as a glioma, perhaps oligodendroglioma or anaplastic astrocytoma, due to visible calcifications, perilesional edema and mass effect.[6][13][22] Considering the multiple parenchymal calcifications, a well defined cystic mass, and an intra-cystic nodule, we suspected a congenital infection, such toxoplasmosis or cytomegalovirus infection, or even a neurocysticercosis.[14][21][22] Therefore, we carried out a serologic test for cytomegalovirus antibody Immunoglobulin M, cysticercus antibody, but the serology was negative. During the histopathological biopsy, we found hemosiderin depositions, necrotic tissues, microvasculatures, and an absence of neural tissue, leading to the conclusion that the mass was a CM.[1] In a retrograde analysis, the hemosiderin depositions in gradient-echo view and the absence of infiltrative pattern in MRI support the likelihood that the mass is a CM rather than a glioma.[1]

Calcifications around GCMs have been previous documented.[16][20] However, diffuse multiple calcifications co-occurring, such as this case, is unprecedented. Diffuse multiple calcifications may be formed separately from GCMs, by diseases such as toxoplasmosis, rubella and cytomegalovirus as congenital infections.[5][7][21] In our case, the patient was diagnosed with 1st grade mental retardation and epilepsy when he was 5 years of age. However, at the time, no study was done for brain imaging or congenital infections. It is highly probable that seizure and mental retardation could be congenital infections but it cannot be conclusively identified.[5][7][9]

Genetically cerebral intraparenchymal CMs are associated with 3 cerebral CM (CCM) genes, CCM-1, CCM-2 and CCM-3. The disease is autosomal dominant and almost all mutations in the CCM genes result in loss of function. It has been suggested that a 'second hit' in a patient with an existing embryonal nonfunctioning CCM gene results in complete loss of function and proliferation of endothelial cells.[17] We did not investigate genetic implications in this case.

The current neurosurgical management of CMs, when indicated, consists of image-guided surgical resection of the entire mass, regardless of the size. Standard surgical indications include recurrent hemorrhage, progressive neurologic deterioration, and medically refractory epilepsy.[4] When resection may have an unacceptably high risk, such as CMs located in eloquent cerebral parenchyma, stereotactic radiosurgeries have been attempted with varying degrees of success and increased risk of postoperative hemorrhage. Many cases report favorable outcomes with surgical resection of GCMs.[1] Our surgical approach was different from the typical GCM resection, since the lesion was almost entirely cystic. We took a transcortical approach, followed by cyst aspiration, and intra-cystic nodule removal. Our approach showed no difference in the postoperative outcome. The postoperative CT was almost entirely clear of the mass, and the patient's right-sided motor weakness improved with no complications.

CONCLUSION

In this case, a GCM with a large cyst was examined and treated by a surgical resection to alleviate the patient's neurologic deficit. This report serves to broaden the differential diagnosis of large cystic supratentorial intracranial masses. Since the imaging char-

acteristics, clinical presentations and natural history of GCMs are variable, the possibility of GCMs should be considered in differential diagnosis of intracranial mass lesions.

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