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CASE REPORT

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CASE REPORT

Giant intraventricular and paraventricular cavernous malformations with multifocal subependymal cavernous malformations in pediatric patients: Two case reports

Suwadee Eng-Chuan, Supika Kritsaneepaiboon, Anukoon Kaewborisutsakul, Kanet Kanjanapradit

ORCID number: Suwadee Eng-Chuan (0000-0002-3047-9791); Supika Kritsaneepaiboon (0000-0002-7749-5908); Anukoon Kaewborisutsakul (0000-0001-9548-3006); Kanet Kanjanapradit (0000-0003-0591-0751).

Author contributions: Eng-Chuan S, Kritsaneepaiboon S were the radiologists reviewed the literature, interpreted imaging findings and contributed to manuscript drafting; Kaewborisutsakul A was the patient's neurosurgeon performed the operation, reviewed the literature and contributed to manuscript drafting; Kanjanapradit K interpreted the histologic tissue and contributed to manuscript; Eng-Chuan S, Kritsaneepaiboon S were responsible for the revision of the manuscript for important intellectual content; all authors issued final approval for the version to be submitted.

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Suwadee Eng-Chuan, Supika Kritsaneepaiboon, Department of Radiology, Faculty of Medicine, Prince of Songkla University, Hat Yai 90110, Thailand

Anukoon Kaewborisutsakul, Neurosugery Unit, Department of Surgery, Faculty of Medicine, Prince of Songkla University, Hat Yai 90110, Thailand

Kanet Kanjanapradit, Department of Pathology, Faculty of Medicine, Prince of Songkla University, Hat Yai 90110, Thailand

Corresponding author: Supika Kritsaneepaiboon, MD, Lecturer, Department of Radiology, Faculty of Medicine, Prince of Songkla University, 15 Karnjanavanich Road, Hat Yai 90110, Thailand. supikak@yahoo.com

Abstract

BACKGROUND

Giant cavernous malformation (GCM) is rarely found in intraventricular or paraventricular locations.

CASE SUMMARY

We present two cases of 6-mo and 21-mo boys with intraventricular and paraventricular GCMs including a literature review focused on location and imaging findings. Characteristic magnetic resonance imaging findings such as multicystic lesions and a hemosiderin ring or bubbles-of-blood appearance can assist in the differential diagnosis of a hemorrhagic intraventricular and/or paraventricular mass.

CONCLUSION

Multifocal intraventricular and/or paraventricular GCM in small children is rare. The characteristic magnetic resonance imaging findings can help to differentiate GCMs from other intraventricular tumors.

Key words: Cavernous malformation; Giant intraventricular; Paraventricular; Multifocal subependymal; Children; Case report

Core tip: We present two rare cases of multifocal intraventricular and/or paraventricular giant cavernous malformation (GCM) in small children including a literature review

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focused on location and imaging findings. The GCM is a rare entity. Intraventricular cavernous malformations are very rare and account for 2.5% of all brain cavernous malformations and are mostly found in the third ventricle. Characteristic magnetic resonance imaging findings such as multicystic lesions and a hemosiderin ring or bubbles-of-blood appearance can assist to differentiate GCMs from other intraventricular tumors/masses.

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INTRODUCTION

The overall prevalence of intracranial cavernous malformation (CM), cavernous hemangioma, cavernous angioma or cavernoma is 0.4%-0.6% and the mean age of presentation is 30.6 years[1]. Its prevalence in children is very rare at 0.37%-0.53%[2,3]. The most common location is the cerebral hemisphere[1]. Intraventricular CMs are very rare and account for 2.5% of all brain CMs and are mostly found in the third ventricle[4,5]. The size of the CMs varies between 1 mm and 75 mm (mean size 14.2 mm)[4-6]. The giant cavernous malformation (GCM) is a rare entity and there is no standard size definition, with some prior studies defining a GCM as having a diameter greater than 4-6 cm[7,8]. The most common presenting symptoms are seizure, neurological deficits, and hemorrhage[8,9]. The current standard treatment for symptomatic patient is surgical removal, particularly for lesions in noneloquent areas[8-10]. The surgical outcome is good despite the large size[10,11]. Herein we reported two cases of paraventricular and intraventricular GCMs with intraventricular hemorrhage in small children.

CASE PRESENTATION

Case 1

Chief complaints: A 6-mo-old boy presented with increased head circumference and delayed development.

History of present illness: Delayed gross motor development started a month ago with increased head circumference for 1 wk.

History of past illness: The patient had no previous medical history and uneventful perinatal and postnatal periods. He had no underlying disease or family history of brain tumor.

Physical examination: The patient had bulging anterior fontanel sized about 4 cm and his head circumference is about 48.5 cm (> P97).

Laboratory examinations: The patient's routine laboratory investigations were within normal limits.

Imaging examinations: Brain computed tomography (CT) showed a mixed solid-cystic intraventricular tumor with multiple internal calcifications involving the body and trigone of the lateral ventricle and third ventricle with severe hydrocephalus (Figure 1A). Magnetic resonance imaging (MRI) of the brain revealed a large mixed minimal heterogeneous enhancing solid cystic intraventricular mass with internal calcification and perilesional brain edema mainly located at the left trigone and body of the left lateral ventricle resulting in moderate hydrocephalus, subfalcine and left descending transtentorial herniation. Two other small subependymal nodules at the posterior bodies of the left and right lateral ventricles were seen. Associated intraventricular hemorrhage and subarachnoid hemorrhage were found (Figure 1B-F). The provisional diagnosis from the MRI findings was choroid plexus papilloma.

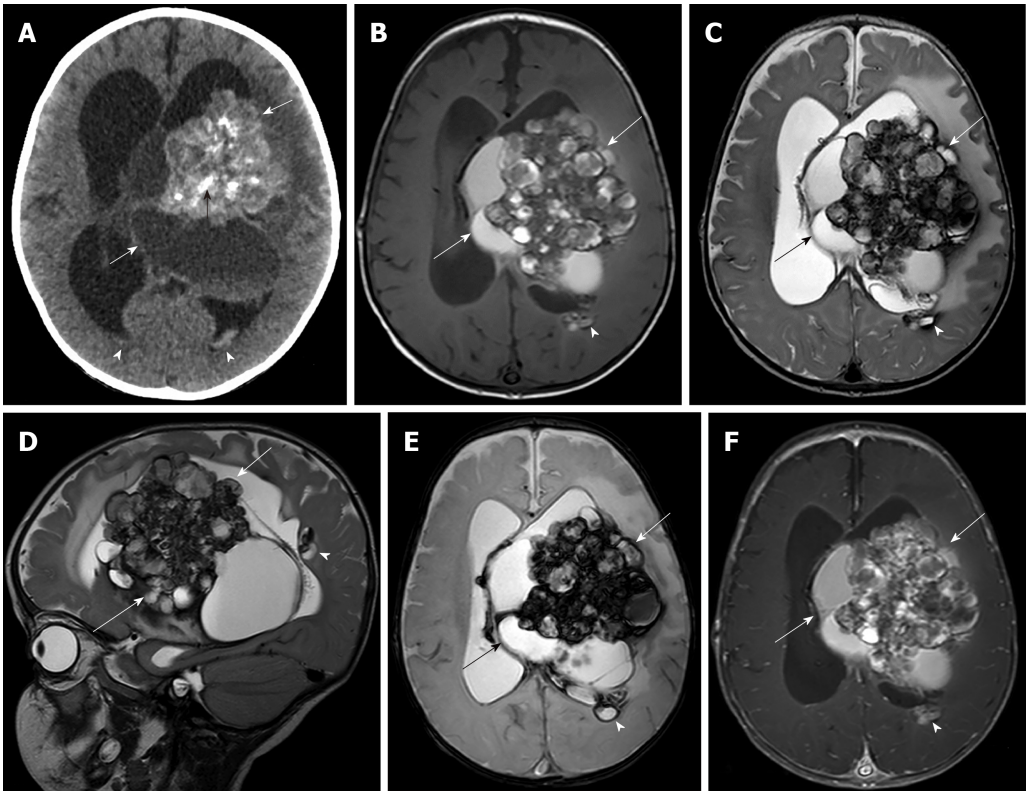

Figure 1 Pre-operative brain computed tomography and magnetic resonance imaging. A: Non-contrast computed tomography shows cystic-solid mass (white arrows) with internal calcifications (black arrows) in body of left lateral ventricle and intraventricular hemorrhage (arrowheads) resulting in hydrocephalus; B: Axial T1 weighted image; C: Axial T2 weighted image; D: Sagittal T2 weighted image; E: Axial T2* weighted mage; F: Axial T1 weighted post gadolinium administration image show a solid-cystic intraventricular mass (arrows) at the left trigone and body of left lateral ventricle with internal calcification, perilesional brain edema and various stages of hemorrhage; bubbles of blood appearance. Another small slightly enhanced nodule (arrowhead) at the subependymal region of the posterior body of the left lateral ventricle is seen.

Treatment: He underwent right frontal ventriculostomy with shunt placement and a left frontoparietal craniotomy with partial tumor removal. A hypervascular intraventricular tumor with lobulated shape was found in the left lateral ventricle with signs of an old hemorrhage.

Final diagnosis: The pathological diagnosis was compatible with "cavernous hemangioma with hemorrhage" (Figure 2).

Outcome and follow-up: An MRI study 2 years later after the patient had developed chorea showed a larger size CM and. He was scheduled for a second surgical tumor removal.

Case 2

Chief complaints: A 21-mo-old boy was referred to our institute due to left hemiparesis.

History of present illness: The left hemiparesis has been progressed for 5 mo.

History of past illness: The patient had no previous medical history and no relevant family history.

Physical examination: The patient had left hemiparesis grade 4. The other general conditions of the patients were normal.

Laboratory examinations: The patient's routine laboratory investigations were within normal limits.

Imaging examinations: A brain MRI study showed multifocal multilobulated cystic masses with variously staged hemorrhages at the right periventricular region, right foramen of Monro, right ventricular trigone and occipital horn of the right lateral ventricle with perilesional brain edema. The largest mass involved the right basal ganglia and right thalamus. Old intraventricular hemorrhage and superficial hemosiderosis were evident. A mass effect caused subfalcine, mild right uncal

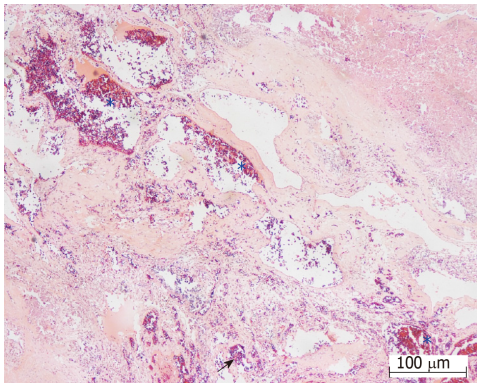

Figure 2 Histopathology of the post-operative removed mass. Histological findings revealed multiple medium-sized vessels (asterisk) lined by endothelial cells with an area of hemorrhage (arrow). Hematoxylin and eosin stain, original magnification × 100).

herniation and moderate hydrocephalus. There was no associated venous angioma (Figure 3).

Treatment: The patient underwent a keyhole right parieto-temporal craniotomy with partially tumor removal. The operative findings were a mulberry-liked solid-cystic mass and old blood clot and mild cerebral edema with hemosiderin straining along the arachnoid plane.

Final diagnosis: The pathological diagnosis was fibrous tissue, calcification, and hemorrhage (Figure 4) and compatible with cavernous hemangioma.

Outcome and follow-up: After the operation, his motor power was partially improved.

DISCUSSION

Relevant articles were searched for using the keywords GCM, pediatric, intraventricular, paraventricular and intraventricular hemorrhage. Seven articles were found, including 13 cases of intraventricular and paraventricular GCM[8,12-17]. The details are shown in Table 1. The GCM is rare and can occur along the neural axis as a CM with the most common location at supratentorial region[8,12]. Intraventricular and paraventricular GCMs are uncommon locations and 44% of them are located in the third ventricle, 27% in the lateral ventricle, 20% in the trigone, and 9% in the fourth ventricle[5].

The pathogenesis of CMs is still unclear. Various studies have proposed that integrin-binding protein ICAP-1 and Krev interaction trapped protein 1 may play important roles in the pathogenesis of the cerebral CM (CCM) and GCM[18]. The increase in size of GCMs is thought to involve a process of cavernous proliferation from repetitive hemorrhages, pseudo-capsule formation, and expansion. The osmotic effect of the breakdown of blood products in cysts causes characteristic multicystic lesions with blood in various stages and surrounded by hemosiderin rings or bubbles of blood appearance on MRI[17]. One of our cases had a larger-than-normal size, and an intralesional hemorrhage was one possible reason for the growth of CM.

The papers also found that in children with CM, about 10% of cases were familial and about 17% had multiple lesions[1,19]. Most of the multiple-lesion cases were familial, up to 84%, and the rest were sporadic (30%)[17]. Only one case of intraventricular and paraventricular GCMs, which presented at 18 mo, had multiple lesions detected on T2* sequence (Table 1)[17]. One of our cases was first reported as multiple paraventricular GCMs at 6 mo of age. The studies also suggest that multiple CMs had a greater risk of de novo cavernoma-genesis than solitary CMs (7.1% and 0.6% per lesion per year)[19]. Both of our cases had multiple lesions, unfortunately genetic studies were not performed.

Initial CT imaging of our cases revealed solid-cystic masses with internal calcifications and small multifocal subependymal lesions that mislead us to suspect intra-/paraventricular tumors and subependymal seedings. MRI helped characterize the lesions by revealing bubbles of blood appearances and multi-stage hemorrhages mimicking solid components on CT. The MR imaging findings of our cases were characteristic imaging features of CMs, showing multicystic lesions with various

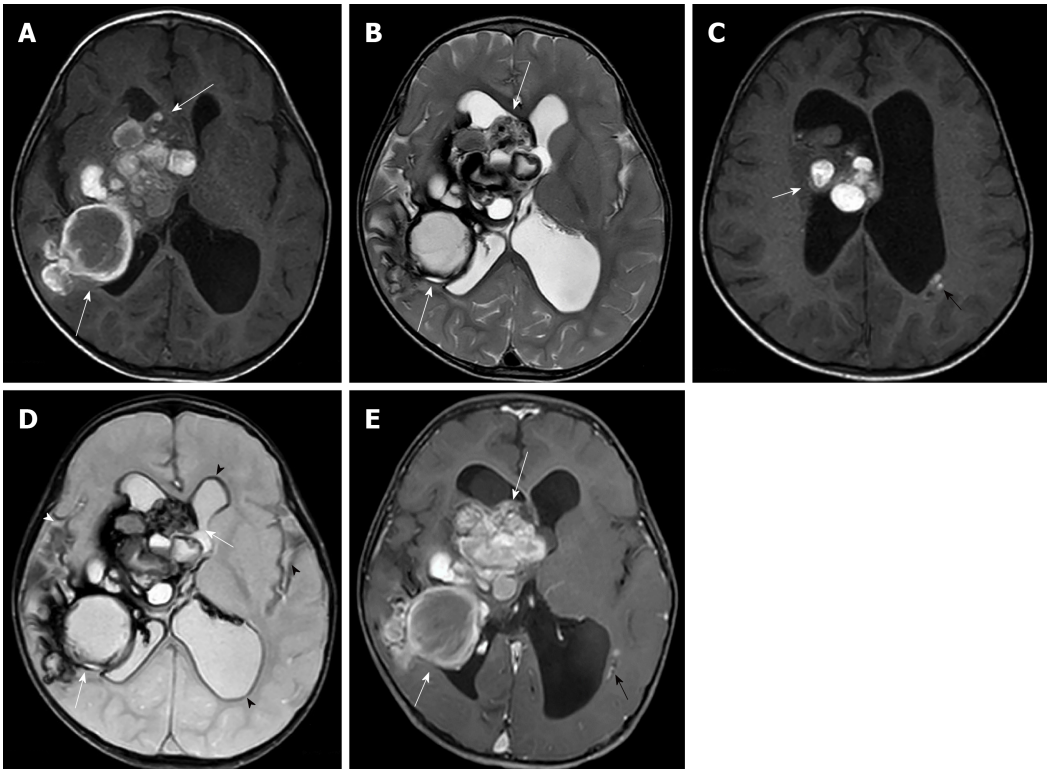

Figure 3 Pre-operative magnetic resonance imaging. A: Axial T1 weighted image; B: Axial T2 weighted image; C: Axial FLAIR image; D: Axial T2* weighted image; E: Axial T1 weighted post-contrast image show multifocal multilobulated cystic masses with various stages of hemorrhage or bubbles of blood appearance, at the right periventricular region, right foramen of Monro, right trigone, occipital horn of the right lateral ventricle (white arrows) and body of left lateral ventricle (black arrow) with moderate hydrocephalus. Old intraventricular hemorrhage and superficial siderosis (arrowheads) at both fronto-temporal sulci and all subependymal lining are in axial T2* weighted image.

stages of hemorrhages and hemosiderin rims. Minimally enhanced lesion in one of our cases could be from heterogeneity of CCMs relative to blood–brain barrier behavior[20].

Pediatric CMs are classified by imaging according to the Mottolese *et al*[2]'s study. The findings in our cases seem to fall-between Mottolese classification type IIIA (non-enhancing macroscopic cysts of mixed signal intensities surrounded by lower signal of hemosiderin rim on T2 weighted image) and IIIC (large solid mass with heterogeneous inner signal on T1 and T2 and peripheral low signal on T2* weighted image) that can mimic neoplasm. None of the paraventricular GCM in all of the previous reports had intraventricular hemorrhage as in both of our cases. CCMs in pediatric patients have about a 0.5% per lesion per year risk for hemorrhage[19]. The history of previous hemorrhage increases the annual hemorrhagic risk to 11.3%[19].

The differential diagnosis of a hemorrhagic intraventricular mass in small children includes choroid plexus tumor, teratoma and subependymal giant astrocytoma. All neoplasms reveal significant enhancement in post-contrast enhancement. Minimal enhancement, bubbles of blood and absence of associated findings of tuberous sclerosis such as cortical tubers may help to differentiate a GCM from intraventricular tumors.

The standard treatment of CCM is conservative or surgical removal[10]. Conservative treatment is preserved for asymptomatic patients. Most GCMs are symptomatic or occasionally indistinguishable from brain tumors, so the surgical removal is the treatment of choice. In our cases, the GCMs were partially removed because the tumors were located in eloquent areas and leading to limited choice of surgical technique[11].

CONCLUSION

In conclusion, we present two rare cases of multifocal intraventricular/paraventricular GCM in small children. CT findings in GCMs can show a mixed solid-cystic mass with internal calcified solid components. The characteristic MRI findings of multicystic lesions and hemosiderin ring or bubbles of blood appearance can help

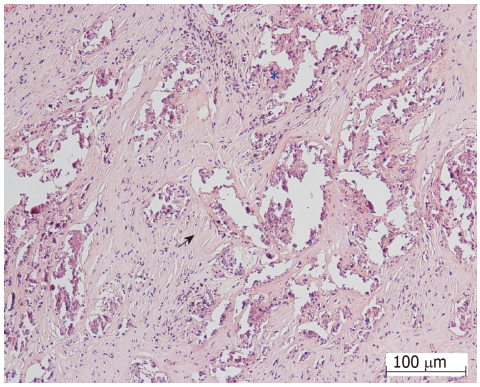

Figure 4 Histopathology of the post-operative removed mass. Histological findings revealed fibrous tissue (arrow) with calcification and hemorrhage (asterisk) (Hematoxylin and eosin stain, original magnification × 100).

to differentiate GCMs from other intraventricular tumors.

Table 1 Intraventricular and paraventricular giant cavernous malformations in pediatric patients reported in the literature

No.	Ref.	Age, sex	Size (cm)	Location	Lesion number	Symptoms	Computed tomography scan	Magnetic resonance imaging	Post-operative status
1	Kawagishi *et al*[11], 1993	11 mo, boy	10	Right paraventricle	Single	Left hemiparesis	Multilobular high density enhanced rim/septum	Heterogeneous signal intensity on T1w/T2w with hemosiderin rim	Improved
2	Van Lindert *et al*[10], 2007	3 mo, girl	6-7	Left paraventricle	Single	Generalized seizure	Left fronto-temporal multicystic	-	Improved
3	Gezen *et al*[12], 2008	10 mo, boy	6 × 4 × 4.5	Left paraventricular parietal lobe	Single	Focal seizure	-	Lobulated, hemorrhages	Hemi-paresis
4	Nieto *et al*[13], 2003	11 yr, girl	5	Left trigone	Single	Seizure	-	Rounded and well-delineated	Improved
5	Kumar *et al*[14], 2006	8 yr, boy	5	Right trigone	Single	Mass effect	Hyperdense enhanced, calcifications	-	Improved
6	Kan *et al*[8], 2008	0.9 yr, boy	9 × 6	Left fronto-parietal, intraventricle	Single	Seizure, right hemiparesis	Hyperdense, heterogeneous calcifications	Multicystic with multiple hemosiderin rings	NA
7	Ozgen *et al*[15], 2011, 7 reported cases	2 yr, girl	> 4	Left parietal	Single	Seizure	-	Macroscopic cysts and huge calcification	NA
8		4 yr, boy	> 4	Medial temporal	Single	Seizure	-	Multicystic hemosiderin ring	NA
9		8 mo, girl	> 4	Left parietal	Single	Seizure	-	Multicystic cysts with subacute hematoma	NA
10		18 mo, boy	> 4	Peri-atrial of left parietal region	Multiple	Seizure	-	Multicystic with fluid level	NA
11		1 yr, girl	> 4	Left parietal	Single	Vomiting, altered consciousness	-	Macroscopic cysts, huge calcification	NA
12		9 yr, girl	> 4	Left parietal	Single	Seizure	-	Solid, well-defined	NA
13		8 yr, boy	> 4	Intraventricle	Single	Headache	-	Solid, well-defined	NA
14	Two present cases	6 mo, boy	9.4	Left intraventricle	Multiple	Increased head circumference	Solid-cystic	Heterogeneous enhancing solid cyst	Hemi-paresis
15		21 mo, boy	8.2	Right paraventricle	Multiple	Left hemiparesis	Multilobulate rim enhancement	Multicystic hemorrhage	

NA: Not available.

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