Giant cerebral cavernoma

Case report with literature review

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ABSTRACT

يعد الورم الكهفي الدماغي الضخم من التشوهات النادرة والآفات الوعائية الخفية التي تصيب الدماغ. نستعرض في هذا المقال حالة نادرة بهذا الورم حيث شُخصت تشخيصاً خاطئاً في البداية. لقد دخلت المريضة البالغة من العمر 40 عاماً إلى المستشفى بعد إصابتها بفالج أيمن مع فقدان للوعي قبل 3 أيام من ظهور الفالج. أظهرت الأشعة المقطعية تجمعاً دموياً شديداً في الجزء الأيسر، وعلى أثر ذلك أُجريت لها عملية جراحية طارئة مباشرةً، غير أن حدوث نزيف دموي شديد أدى إلى إيقاف العملية حيث توقع الأطباء وجود آفة في الأوعية الدموية. وأظهرت صور الرنين المغناطيسي وجود آفة كهفية ضخمة، وبعد ذلك تم استئصال هذه الآفة بالكامل. لقد كانت فترة ما بعد العملية الجراحية هادئة وخالية من المضاعفات، وقد أكد اختبار الأنسجة تشخيص هذه الحالة بالورم الوعائي الكهفي. وهكذا نستنتج من هذه المقالة بأنه يجب أخذ الورم الوعائي الكهفي الضخم بعين الاعتبار عند تشخيص الأنواع المختلفة للورم الدموي الشديد داخل الدماغ.

Giant cerebral cavernoma is a rare malformation classified as a brain occult vascular lesion. We report a case of initially misdiagnosed giant cavernous angioma revealed by a spontaneous intracerebral hemorrhage. A 40-year-old woman was admitted with right hemiplegia and altered consciousness occurring 3 days prior to presentation. A non-contrast CT scan showed a left parietal gross hematoma, and she was immediately taken to the operating room for emergency surgery. However, the procedure was interrupted by massive bleeding, and therefore a vascular lesion was suspected. Magnetic resonance images suggested a giant cavernous malformation. Afterward, she underwent total removal of this lesion. The postoperative period was uneventful, and histopathological examination confirmed the diagnosis of cavernous angioma. Thus, the differential diagnosis of gross spontaneous intracerebral hematoma should include giant cavernous angioma.

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Cavernoma also known as cavernous malformation or cavernous angioma is a benign vascular lesion that may occur in the CNS as well as in other organs such as the liver or skin.[1,2] The CNS cavernoma accounts for 5-13% of all intracranial vascular anomalies, and they vary in size from a few millimeters to a few centimeters in diameter.[2-4] However, giant cavernomas defined by Kan et al[3] as a cavernoma with a diameter greater than 4 centimeter (cm) on preoperative MRI are very rare. We describe a case of spontaneous intracerebral hemorrhage due to a giant cavernoma operated on with satisfactory outcomes. The objective in presenting this particular case is to highlight an important differential diagnosis of spontaneous intracerebral hematoma.

Case Report. A previously healthy 40-year-old woman was admitted to our hospital with a Glasgow coma score (GCS) of 13 after a sudden onset of right hemiplegia and altered consciousness occurring 3 days earlier. A non-contrast CT scan revealed a spherical mixed hyperdense intraaxial lesion at the left parietal lobe measuring 5.5x4.5x5 cm surrounded by a narrow edema mimicking a spontaneous hematoma (**Figure 1**). She was taken to the emergency operating room to remove the hematoma. During surgery, a vascular lesion was suspected because of profuse bleeding and the operation was aborted. An MRI revealed a single large lesion occupying the left parietal lobe measuring 5x4.5x5 cm and showed mixed intensity on T1 and T2-weighted images (WI) with poor enhancement. A peripheral hypointense rim seen on T2-WI was highly

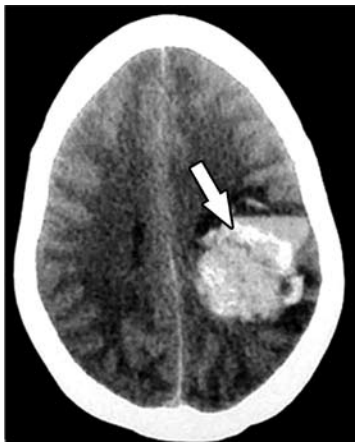

Figure 1 - Preoperative axial non contrast CT scan showing a left parietal hematoma with mixed appearance (admission CT scan).

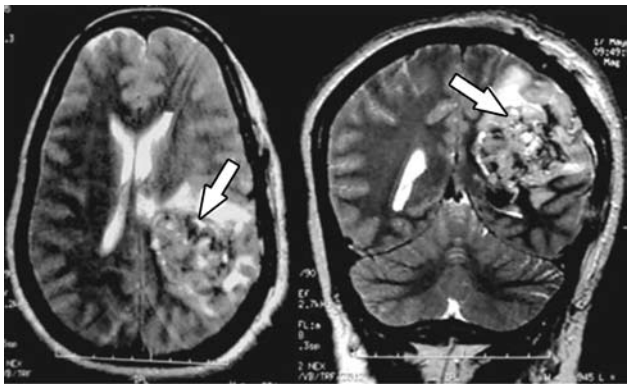

Figure 2 - Patient MRI showing **a**) T2 weighted axial, and **b**) coronal images after the first surgery showing a left parietal round-shape mixed intensity image surrounded by a hypointense rim.

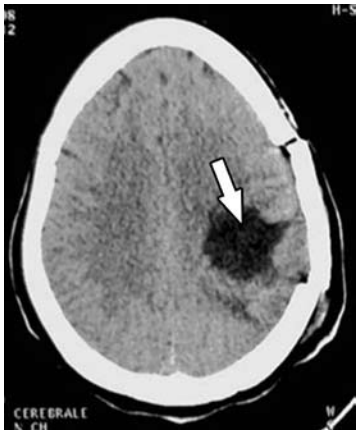

Figure 3 - Postoperative axial non contrast CT scan showing total removal of the lesion (after the second surgery).

suggestive of cavernous angioma (**Figure 2**). Angiography MRI was normal. No other locations (liver, retina, skin, and so forth) were found. She underwent a second stage surgery under surgical microscope, which showed a multilobulated lesion with tortuous and disorganized vascular channel. The lesion was totally excised, and a follow-up CT-scan confirmed the total removal (**Figure 3**). The histopathologic examination revealed a multiple dilated vascular space lined by endothelium resulting in cavernous angioma. After surgery, she was conscious with a GCS of 15, without any new neurological deficit. The postoperative follow-up was uneventful with an important improvement of her right hemiplegia after one year.

Discussion. Cerebral giant cavernous angiomas are very rare with only 65 cases in literature over these last 62 years and since the first case of Penfield et al in 1948.[5] At least half of them have been reported from 2008 to date (**Appendix 1**). Their clinical and radiological variability remain misleading. The incidence of cavernous angioma accounts for around 0.4-0.9% in studies based on autopsy and MRI series.[2,3] The gender ratio seems to be the same in most cavernous angiomas, as in our literature review. Some authors advocated that a quarter of cavernous angiomas are seen in the pediatric population.[6] This literature review revealed that the average age of patients was around 16.5 years, with 59.4% of giant cavernomas occurring in the pediatric population (less than 15 years old). Lew[1] reported that familial cerebral cavernomatosis accounts for 10-20% of cases and is prone to be more symptomatic, likely due to the higher incidence of multiple lesions in these patients and the propensity for the novo cerebral cavernous malformation formation. In our patient, there was a single lesion with a negative familial cerebral cavernomatosis history. On literature review, only the 2 cases of giant cerebral angioma reported by Lew presented with multiple lesions and a familial cerebral cavernomatosis history.[1] Moreover in one of these cases, the patient's brother, mother, and maternal grandfather were subsequently found to be carriers for the CCM1 gene mutation associated with familial cerebral cavernomatosis.

Many authors agree that cerebral cavernoma is a dynamic lesion and the growth can be explained by repeated intralesional micro hemorrhages followed by organization of the clot, pseudocapsule formation, and secondary enlargement.[2,3,7] The large size of the cavernoma in our case may be explained on this hypothesis. There is also a possibility of accelerated growth due to hormonal changes during puberty and pregnancy.[1,2]

The clinical presentation of giant cavernoma seems to have no differences than the other CNS cavernomas. The most common presentation is seizure (ranging from

30-70% of cases),[3] followed by neurological deficit, hemorrhage, and headache.[2,7] This literature review revealed seizures in 52% of cases, but hemorrhage (32%) was more frequent than neurological deficit (20%). The risk of hemorrhage has been estimated at 0.7-1.1% per lesion per year.[1,8] Fatal outcomes due to hemorrhage from cavernoma angioma are rare.[4] Most of the time, this extralesional hemorrhage is not immediately devastating,[3] but there is a high risk of rebleeding with intervals ranging from weeks to years and may lead to catastrophe.[2,9] In our case, despite the important size of the lesion (more than 5 cm in diameter), the patient was just confused; and the neurological deficit was related to the localization of the hematoma.

On MRI, the classical appearance of "bubbles of blood" with a hypointense rim of hemosiderin on T2 weighted images is nearly pathognomonic.[3,7,8] However, MRI variability is frequent.[2,3,7,8] In our case, the initial appearance on MRI has been changed by the previous surgery, but a hypointense rim of hemosiderin on T2 WI was present. Moreover, gradient echo MRI is useful to exclude other small cavernous angiomas that may be occult on T1 and T2-WI. On CT scan, giant cavernomas often present punctate or large calcification, and the mass effect is usually less than expected for the size of the lesion.[2,3,8] In our literature review, calcifications were shown in 57.9% of cases (11/19 cases) in giant cavernous angiomas. According to their location, giant cavernomas were involved in the posterior cranial fossa in 16.6% (6/36 cases) with the propensity to be early symptomatic in childhood (mean age of 5.2 years). This was certainly due to the narrowness of this space; and the average diameter was 5 cm against 6 cm supratentorially. The differential diagnosis of this vascular malformation includes not only low-grade or malignant cystic glioma, primitive neuroectodermal tumor, oligodendroglioma, thrombosed arteriovenous malformation, but also spontaneous intracerebral hematoma as in our case.[2,7,8] In many instances, the final diagnosis of cavernous angiomas is based on histopathological examination that shows abnormal dilated blood vessels lined by a single endothelium layer. These vessels are in contact with each other without any intervening neural tissue and with no direct communication of the arterial with the venous system.[2] The vessels are separated by fibrotic tissue containing foci of calcification with hemosiderin deposition.[2,3,10]

Surgical excision is the treatment of choice for symptomatic lesions located in accessible, non eloquent, cerebral or cerebellar regions.[2,11] The management of less accessible, deep cerebral, and brainstem lesions increasingly require stereotactic radiosurgery.[2,8] Thus, the surgical approach was justified in our case. According to many authors, small cavernous angiomas located in eloquent area or in asymptomatic patients require observation;[2,3] however, there is no clear guideline for giant cavernous angiomas in these cases in so far as all the 65 cases were symptomatic. Because these are benign lesions, a total excision of the cavernoma results in cure from the disease.[2,3,10]

In conclusion, giant cavernous angiomas remain rare lesions that should always be included in the differential diagnosis of spontaneous intracerebral hemorrhages. The diagnosis is often suggested on preoperative MRI, but its confirmation requires histopathological examination. A balance must be made between the risk of surgery and the natural course of the cavernoma above all in asymptomatic patients. Surgery is indicated as far as possible for symptomatic cavernomas located in accessible areas.

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Appendix 1 - Summary of the most reported cases of giant cerebral cavernomas in the literature from 2008 to date (2011).

Case No.	Authors and dates	Gender and age	Symptoms	MRI
1		M/11m	Macrocrania (>98%), 3 week history of change in vision and mental status, seizure, and hemiparesis	Hyperintense on T1, multicystic with multiple hemosiderin rings on T2, hyperintense on FLAIR, hypointense on GRE
2		M/23y	NA	Hyperintense on T1, multicystic with multiple hemosiderin rings on T2, hyperintense on FLAIR, hypointense on GRE
3		M/9y	Progressive left hemiparesis, seizures, failure-to-thrive	Isointense, salt-and-pepper appearance on T1, hyperintense, salt-and-pepper appearance with flow voids on T2 + a dark rim of hemosiderin
4		M/43y	NA	Isointense on T1, multicystic with multiple hemosiderin rings on T2, hyperintense on FLAIR, hypointense on GRE
5		M/30y	Seizure, right sided weakness	Heterogeneous, hyperintense on T1, multicystic with multiple hemosiderin rings on T2, hypointense on GRE
6		M/1day	Macrocephalic, tense fontanelle, flaccid x4, and intubated for apneic episodes; care withdrawn (autopsy proven cavernoma)	Heterogeneous, hyperintense on T1, multicystic with multiple hemosiderin rings on T2
7	Kan et al 2008[3]	F/2 y	Headache, nausea/vomiting, hydrocephalus	Heterogeneous, hyperintense on T1, multicystic on T2, hypointense on GRE
8		F/44y	Sudden onset of headache, then obtunded, hydrocephalus	Heterogeneous, hyperintense on T1, multicystic on T2, hypointense on GRE
9		M/2.5m	NA	Heterogeneous, hyperintense on T1, multicystic with multiple hemosiderin rings on T2
10		M/66y	NA	Heterogeneous, isointense on T1, multicystic with multiple hemosiderin rings on T2, heterogeneous hyperintense on FLAIR, hypointense on GRE
11		F/25y	NA	Hypointense on T1/T2
12		M/1.2m	Irritability, bulging fontanelle (hydrocephalus)	Hyperintense on T1, multicystic with multiple hemosiderin rings on T2, hyperintense on FLAIR
13		F/16y	NA	Hyperintense on T1, multicystic with multiple hemosiderin rings on T2
14		M/19y	NA	Hyperintense on T1, heterogeneous on T2
15		NA	NA	Heterogeneous on T1, multicystic with multiple hemosiderin rings on T2
16		NA	NA	Heterogeneous on T1, multicystic with multiple hemosiderin rings on T2
17		NA	NA	Heterogeneous on T1, multicystic with multiple hemosiderin rings on T2
18		NA	NA	Heterogeneous on T1, multicystic with multiple hemosiderin rings on T2
19	Son et al 2008[4]	F/20 Y	Two episodes of generalized convulsion	Heterogeneous on T1, multicystic with a surrounding ring of hemosiderin on T2
20	Gezen et al 2008[8]	M/10 m	Right focal seizure for 3 days	Mixed intensity on T1 and T2. Hypointense ring of hemosiderin on T2
21	Newton et al 2008[9]	F/43 y	Headache and seizure	Mixed intensity on T1 and T2, hypointense ring of hemosiderin on T2 associated with left middle cerebral aneurysm
22	Lew 2010[1]	M/4 m	Increased intracranial pressure symptoms for 2 weeks followed by numbness with opisthotonos, family history of cerebral cavernomatosis	Heterogenous hyperintense on T1
23		F/7 m	Lethargy with tense fontanelle, family history of cerebral cavernomatosis	Not done
24		F/2 y	Seizure	Bubbles of blood with hypointense rim on T2
25		M/4 y	Seizure	Bubbles of blood with hypointense rim on T2
26		F/8 m	Seizure	Bubbles of blood with hypointense rim on T2
27	Ozgen et al 2010[6]	M/18 m	Seizure	Bubbles of blood with large hematoma and hypointense rim on T2
28		F/1 y	Vomiting and altered consciousness	Bubbles of blood with large hematoma and hypointense rim on T2
29		M/3 y	Seizure	Heterogenous reticular core with large hematoma and hypointense rim on T2
30		M/3 y	Seizure	Bubbles of blood with hypointense rim on T2
31		F/9 y	Seizure	Heterogenous reticular core with hypointense rim on T2
32		M/8 y	Headaches	Heterogenous reticular core with hypointense rim on T2
33	Kasliwal et al 2010[7]	F/13 y	Headache	Heterogenous with an hypointense rim on T2
34	Thakar et al 2010[11]	M/3 y	Right hemiparesis with symptoms of raised intracranial pressure	Heterogenous hyperintense with hypointense rim on T2
35	Amenta et al 2011[2]	F/52 Y	Left homonymous hemianopsia	Large cystic mass with an enhancing mural nodule
36	Present case	F/40 y	Sudden onset of right hemiplegia and altered consciousness (GCS: 13 on admission)	Heterogeneous on T1 and T2, surrounded by hypointense ring of hemosiderin on T2

Appendix 1 continued - Summary of the most reported cases of giant cerebral cavernomas in the literature from 2008 to date (2011).

Non-contrast CT scan	Location and size	Treatment	Follow up and outcome
Hyperdense, heterogeneous, calcification	Left fronto-parietal, intraventricular, crosses midline, 9x6 cm	Surgery	NA
Hyperdense, heterogeneous	Left frontal 4x3 cm	Surgery	NA
Hyperdense, heterogeneous, calcification	Right fronto-temporo-parietal, 11x5 cm	Surgery	NA
Hyperdense, heterogeneous, punctate calcification	Right parietal, 4x3 cm	Surgery	NA
NA	Left deep parietal, extending down to the left thalamus, 3x3 cm to 6x5.5 cm in 41 days	Surgery	NA
Hyperdense, heterogeneous	Bifronto-temporo-parietal, 11x9 cm	No treatment, care withdrawn	Deceased (autopsy proven cavernoma)
NA	Left cerebellum, paramedian, 4x3x3 cm	Surgery	NA
Hyperdense, heterogeneous	Hypothalamic/third Ventricular, 4x3 cm	Surgery	NA
NA	Cerebellum, paramedian, 4x3 cm	Surgery	NA
NA	Right lateral ventricle, 4x3 cm	Surgery	NA
NA	Right frontal extra/intracranial, 5x4 cm	Surgery	NA
Hyperdense, heterogeneous, calcification	Cerebellum, 6x6 cm	Surgery	NA
NA	Left thalamic, extending down to the left midbrain, 4x4 cm	Surgery	NA
Hyperdense, consistent with hemorrhage	Left frontal, 4x4 cm	Surgery	NA
NA	Left cerebellar, extending into the left pons, 5x4 cm	Surgery	NA
Hyperdense with punctate calcification	Right atrium, 4x4 cm	Surgery	NA
Hyperdense with punctate calcification	Right caudate, thalamic, bilateral lateral ventricles, 4x4 cm	Surgery	NA
Hyperdense with punctate calcification	Right-sided, deep mesial frontal, 4x4 cm	Surgery	NA
Mixed density with multifocal calcifications, on contrast enhanced CT scan: heterogeneous enhancement and traversing vascular structure on the postero medial portion	Left frontal and basal ganglia region, 7x5x5 cm	Surgery (the venous angioma in the posteromedial portion was left untouched)	Uneventful
Heterogenous hyperintense with patchy calcification	Left parietal, 6x4x4.5 cm	Surgery	Uneventful and the patient was seizure-free after surgery
Heterogenous hyperintense with calcification	Left temporo-parietal, 5 cm	NA for the GCA, clipping of ruptured aneurysm	Moderate neurological deficit
Hemorrhagic lesion (hyperdense)	Cerebellum and fourth ventricle, 4 cm	Surgery in 2 stages: external ventricular drain on admission, gross total resection of the lesion 3 days later	Uneventful with normal psychomotor development
Hemorrhagic lesion	Brainstem and cerebellum	Surgery after external ventricular drain (subtotal resection)	Asymptomatic after surgery
NA	Left parietal, >4 cm	Surgery	Uneventful
NA	Medial temporal, >4 cm	Surgery	Uneventful
NA	Left parietal, >4 cm	Surgery	Uneventful
NA	Left parietal, >4 cm	Surgery	Uneventful
NA	Left parietal, >4 cm	Surgery	Uneventful
NA	Left frontal, >4 cm	Surgery	Uneventful
NA	Left frontal, >4 cm	Surgery	Uneventful
NA	Left parietal, >4 cm	Surgery	Uneventful
NA	Intraventricular, >4 cm	Surgery	Uneventful
Heterogeneous hyperdense with calcification and hemorrhage	Right temporal, >5 cm	Surgery	NA
Hyperdense with hemorrhage	Left trigonal, >6 cm	Surgery	Recovery of hemiparesis
NA	Right occipital, >6 cm	Surgery	Uneventful with normal visual fields at one month follow up
Hyperdense mimicking non traumatic intracerebral hematoma	Left parietal, 5x4.5x5 cm	Surgery	Uneventful with an important improvement of her right hemiplegia after one year

NA - not available, FLAIR - fluid-attenuated inversion recovery, GRE - gradient echo imaging, GCA - giant cavernous angioma, F - female, M - male, y - years, m - month, cm - centimeter, CGS - Glasgow coma score