Cavernomas of the central nervous system: clinical and neuroimaging manifestations in 47 patients

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Abstract

Forty seven cases of central nervous system cavernous angioma (21 males and 26 females) are described. The main clinical signs were epilepsy and brainstem syndromes. Digital subtraction intra-arterial angiography, when used, failed to reveal cavernoma. CT detected many of the lesions, but the most successful supplementary diagnostic procedure was MRI which produces highly characteristic images of cavernous angioma. The diagnosis of cavernous angioma was confirmed in the 18 cases in which the tumour was removed surgically.

The four categories of vascular malformations of the CNS are, in descending order of incidence, arteriovenous malformation, cavernous angioma, venous angioma and telangiectasis.¹ Since cavernous angiomas (cavernomas) are slow-flow vascular lesions, their angiographic appearance is avascular, and they are accordingly classed together with venous angioma, telangiectasis and thrombosed arteriovenous angioma as "cryptic" or "angiographically occult" CNS vascular malformations.²⁻⁷ Cavernomas consist of sinusoid vascular spaces with a single layer of endothelial cells separated from each other by connective tissue without intervening neural components. They have no connective capsule, but are usually well delimited by peripheral gliosis. Intrinsic thrombosis and haemorrhage frequently occur, as does calcification, which is probably secondary to the former events. Cholesterol and haemosiderin deposits may also be found.⁸⁻¹¹

The incidence of cavernomas is not known precisely, different studies have reported them as accounting for 2-17% of CNS vascular malformations.¹²⁻¹⁵ In 1976 Voigt and Yasargil¹⁶ reviewed 164 published cases, 100 of them based on necropsies. There are multiple and familial cavernomas.¹⁶⁻²⁰ Cavernomas are often asymptomatic, and when symptoms are present they depend on the location and the size of the lesion. Cavernomas are usually located in the supratentorial compartment, preferably in the white matter, but have also been reported in intraventricular, pineal and dural locations and in the cavernous sinus, in Meckel's cave and the ponto-cerebellar angle.²¹⁻²⁵ Clinical manifestations, the most important of which are epilepsy and focal neurological deficits,¹⁵ are due to compression, but cavernomas never give rise to ischaemic symptoms such as occur with high-flow vascular malformations.⁸ Except in the rare case

of hypervascular cavernomas,²⁶ cavernomas do not show up on angiograms, or at most give rise to nonspecific angiographic abnormalities.²⁻⁷ CT and MRI, however, have both proved to be valuable diagnostic aids, the latter especially^{27,28} (the number of cavernomas diagnosed may be expected to increase rapidly in the near future). CT shows cavernomas as hyperdense or heterogeneous lesions (more rarely as hypodense ones), and a variable degree of enhancement after intravenous contrast injection is quite common, as is calcification.²⁷⁻³⁰ Triple-dose injection with delayed detection has been used to improve sensitivity.^{31,32}

In this article we describe and discuss the clinical, angiographic, CT and MRI signs of 47 patients with CNS cavernomas.

Patients and methods

We studied retrospectively 47 patients in a three year period (December 1986-November 1989) with various neurological manifestations, referred to our centre from all areas of our country. In all cases clinical histories were recorded and neurological examination performed by a neurologist. Digital subtraction intra-arterial angiography was carried out in 24 cases (double contrast dose injection and repeated radiology was not used). Cranial CT was performed in 45 patients before and after intravenous contrast injection; in no cases was a triple dose with delayed detection used. MRI was performed in all 47 patients using a Philips 0.5 T Gyroscan; 6-8 mm sagittal, axial and coronal sections were taken using spin-echo sequences with T1 (TR 500 ms, TE 50 ms) and T2 (TR 1500-2200 ms, TE1 50 ms, TE2 100 ms) weighted and without paramagnetic contrast; the number, location, size (maximum diameter) and signal characteristics of lesions was recorded in each case. Neuroimaging studies were carried out and evaluated by a neuroradiologist.

Results

Of the 47 patients studied, 26 (55.3%) were females and 21 (44.7%) males. Age at diagnosis was 39 years (range 5-79 years) in the whole patients group, 44.5 years in the female group (range 15-69 years) and 32.2 years in the male group (range 5-79 years). Clinical signs are listed in table 1 together with the number and percentage of cases in which each was observed.

None of the 24 angiograms showed the presence of a cavernoma. The abnormalities that did show up in angiograms were avas-

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Table 1 Clinical manifestations in 47 patients with cavernomas of CNS

	Number	%
Epilepsy	16	34
Brainstem syndromes	14	30
Focal hemispheric deficits	5	10.6
Subarachnoid haemorrhage	1	2.1
Cerebellar syndromes	2	4.3
Intracranial hypertension	1	2.1
Spastic paraparesis	1	2.1
Epilepsy and subarachnoid haemorrhage	1	2.1
Epilepsy and cerebellar syndromes	1	2.1
Incidental findings	5	10.6

cular masses associated with vascular displacement (in four patients), early venous drainage (two patients) and an abnormal surface venous system arrangement (in one patient).

CT allowed detection of lesions in 40 of the 45 patients with whom it was used. The images were hyperdense or heterogeneous in 35 cases and hypodense in 5. Nine lesions were calcified. One patient exhibited tri-ventricular hydrocephalus with suspected intrinsic aqueductal stenosis, and another a parasagittal meningioma. Intravenous contrast injection achieved variable enhancement of lesions that were visible under CT without contrast.

MRI showed 56 cavernomas in the 47 patients studied, six of the patients proved to have multiple lesions. The T2-weighted images of the cavernomas showed well-defined lesions with a low peripheral signal due to haemosiderin and a heterogeneous central signal due to haemosiderin, calcium and blood in various states (flow, thrombosis, haemorrhage), while recently growing cavernomas (because of intralesional haemorrhage or thrombosis) occasionally produced images with a high-signal outer ring due to gliosis and/or oedema. The T1-weighted images

Table 2 MRI signal characteristics of cavernoma components

Component	T1 signal	T2 signal
Blood:		
Flow	↓	↓
Fresh haemorrhage (haemoglobin)	=	↓
Haemorrhage > 48 h (metaHb)	↑	↑
Old haemorrhage (haemosiderin)	↓	↓
Calcium	↓	↓
Gliosis	=	↑
Oedema	=/↓	↑

↑: High signal; ↓: Low signal; =: Isosignal.

showed the haemosiderin peripheral low signal with a heterogeneous central signal, whilst peripheral oedema and gliosis were undetected (isosignal) (fig 1 and table 2). Of the 56 cavernomas, 33 (59%) were supratentorial, 22 (39%) infratentorial and one (2%) spinal (table 3). Their maximum diameters in the MRI images ranged from 1 to 4 cm.

The six patients with multiple cavernomas (fig 2) comprised three females with three lesions each, two females with two lesions each and one male with two lesions. A woman with multiple cavernomas showed aqueductal stenosis due to a lesion in the anterior

Table 3 Locations of 56 CNS cavernomas in 47 patients

Location	Number	%
Supratentorial:	33	59
Frontal	4	7.25
Temporal	13	23
Parietal	8	14.5
Occipital	2	3.5
Thalamus	4	7.25
Infratentorial:	22	39
Cerebral peduncles	4	7.25
Pons	10	18
Medulla	2	3.5
Cerebellum and connections	6	10.25
Spinal cord (D4):	1	2

Figure 1 A) Sagittal MR image (T2, TE1) of a medullar cavernoma: peripheral low signal ring (haemosiderin) and central heterogeneous signal. B) Axial MRI (T2, TE2) of a pontine cavernoma with two haemorrhagic nodules within the lesion (arrow) and one outside (arrowhead). Note the parenchymal high signal because of oedema (*).

Figure 2 Coronal MRI (T2, TE1) of a patient with multiple cavernomas: left cerebellar lesion with homogeneous high signal because of recent haemorrhage and a second right temporal one (a third right parietal lesion not included in this image).

Figure 3 A) Axial CT image showing triventricular hydrocephalus without evidence of parenchymatous lesion. B) Coronal MRI (T2, TE1) of the same woman reveals a superior vermian cavernoma causing aqueductal stenosis and a right cerebellar cavernoma.

Figure 4 Incidental finding of a small left occipital cavernoma in axial MR image (T2, TE2) of a patient with Parkinson's disease.

cerebellar vermis and triventricular hydrocephalus (fig 3). A case of cavernoma of the corpus callosum also showed parasagittal meningioma. Two patients had associated cavernous-venous malformations, and the male with two cavernomas showed abnormal surface venous drainage due to partial agenesis of the superior longitudinal sinus. In five patients cavernoma was an incidental finding (fig 4).

Discussion

A striking feature of these findings is the age difference between the male and female groups. Eleven of the 21 males (52.4%) were diagnosed as cavernoma cases before the age of 30 years, compared with only three of 26 females (11.5%). It seems possible that as yet unknown hormonal factors may play some role in the biology of cavernomas.

The incidence of cavernoma has been reported to be greater among males than females,³³ greater among females than males,³⁴ and the same for both sexes.¹⁶ In this study there were more female than male patients (26 against 21) and more females had multiple lesions than males (19.2% versus 4.8%).

As in other studies^{8 16 18} the incidence of familial cavernomas in this series was low, the two patients who were sisters, making up just 4.3% of the group, but we did not systematically investigate the families of the patients. Family screening increases the number of diagnoses of familial cavernoma;³⁵ Rigamonti *et al*²² found that 54% of their patients were familial cases, and that multiple cavernoma was much commoner in this group.

The location of the cavernomas (table 3) correlated well with clinical manifestations. Eighteen of the 33 patients with supratentorial lesions had epilepsy, while 14 of 22 infratentorial lesions had ictal, progressive or fluctuating brainstem syndromes. Tentative clinical

cal diagnoses in some infratentorial cases included multiple system atrophy, multiple sclerosis and Miller-Fisher syndrome. There was a high incidence of asymptomatic lesions, 21.4% (12 lesions) if the clinically unobtrusive lesions of the multiple cavernoma cases are included. The commonest site of supratentorial cavernomas was temporal lobe (13 lesions), and that of infratentorial cavernomas the pons (10 lesions).

In all the 24 cases in which it was performed, angiography failed to reveal cavernoma. The observed angiographic alterations (vascular displacement, early drainage) are not specific for cavernomas, since they may also be observed in cases of telangiectasis, venous angioma, thrombosed arteriovenous malformations, ischaemic lesions, glioma and inflammatory states.³⁶⁻⁴⁰ In no case did we observe peripheral capillary blush, but then this shows up better after a second injection series⁴¹ that was not performed in this study. Nor did we detect any case of so-called hypervascular dural cavernoma of the middle cranial fossa.^{23 24 26 41} The abnormal surface drainage vein of the man with two cavernomas is attributed to the partial lack of the superior sagittal sinus.

CT detected 40 cavernomas in the 45 patients with whom it was performed. The radiological characteristics of these lesions were similar to those described previously.^{28 29 30 42 43 35} (87.5%) had high or heterogeneous density, were poorly delineated and were only slightly enhanced by intravenous contrast injection, while five (12.5%) were hypodense. Nine (22.5%) exhibited calcification. No totally calcified cavernoma, or "cerebral stone"^{44 45} was observed. Triple-dose contrast injection was not used because MRI was available; reports³¹ that it improves cavernoma detection by CT have not been confirmed by other authors.³²

In the 45 patients on whom both CT and MRI were employed, MRI detected 54 cavernomas, including 14 that CT had failed to detect (most of them small lesions located deep in the temporal fossa or in the infratentorial compartment). No cavernoma detected by CT went undetected by MRI. CT is more specific for detecting calcium, which in MRI images may be confused with blood flow, haemosiderin or other alterations, but calcified areas were not invisible in MRI images as has been reported.⁶ Since the shape and location of the lesions and the signal characteristics listed in table 2 made the MRI of the cavernomas much more distinctive than their CT images, we consider MRI to be both more sensitive and more specific than CT for cavernoma diagnosis. MRI is also useful for monitoring the evolution, since signals vary according to the stage after a haemorrhage and with the variations in oedema around the lesion. Mass effect, diffuse high signals and other possible features of cavernomas or their images may hinder differential diagnosis of entities such as metastases and haematomas; in such cases diagnosis should be based on clinical and neuroimaging features.^{27 28 46}

The spinal (D4) cavernoma, which like the

other 17 surgically removed tumours was confirmed histopathologically, was not detected by computer-assisted myelography.

In two radiated brainstem cavernomas, MRI showed transient high peripheral T2 signals due to oedema, which disappeared in two weeks, so that the pre- and post-radiated images were similar. Some authors^{8 47} consider surgical treatment to be mandatory in cases—including brainstem cases⁸—which exhibit recent haemorrhage or mass effect, since their removal is facilitated by the circumscribing peripheral gliosis.

We conclude that cavernomas with clinical consequences seem to occur at an earlier age in males than in females. Multiple lesions are more common among females. The main clinical manifestations are epilepsy and brainstem syndromes, though many lesions are asymptomatic. Angiography fails to detect this kind of CNS vascular malformation, and a significant number go undetected by CT. The most sensitive and specific technique for detection, characterisation and monitoring of CNS cavernomas is MRI.

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