MR imaging cavernous angioma: normal variants and atypical locations.

Poster No.: C-1637
Congress: ECR 2011
Type: Educational Exhibit
Authors: J. Sánchez Hernández¹, M. Vacas Rodríguez¹, P. Hernández Palomino¹, P. Carreño Morán¹, E. Gálvez González¹, J. C. Paniagua Escudero¹, J. F. Asensio Calle¹, J. M. Villanueva Rincón¹, A. Ortiz de Mendivil Arrate²; ¹Salamanca/ES, ²Madrid/ES

Keywords: Neuroradiology brain, MR
DOI: 10.1594/ecr2011/C-1637

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Learning objectives

1. To give a histological overview of cavernomas and their imaging characteristics.
2. To summarise the key imaging features that allow a precise diagnosis.
3. To present some atypical locations that result in a series of differential clinical and radiological characteristics
Background

Cavernous angioma, also known as cerebral cavernous malformation (CCM), cavernous hemangioma, and cavernoma, is a vascular disorder of the central nervous system that may appear either sporadically or exhibit autosomal dominant inheritance. Cavernous angiomas are the most common vascular malformation. They can affect up to 0.5% of the population.

Types of vascular malformations are differentiated from one another on the basis of their gross and histopathologic characteristics. Traditionally, intracranial vascular malformations are grouped into the following four groups by Newton and Troost:

1. Arteriovenous malformations are by far the most common, and are easily recognized on angiography as a tortuous mass of vessels. Usually both enlarged feeding arteries and draining veins can be identified.

2. Capillary telangiectases consist of abnormally dilated capillaries without muscle or elastic fiber within their walls. These lesions are distinguished from cavernous angiomas by the presence of normal neural tissue between the telangiectatic capillaries. They are relatively common but are usually asymptomatic.

3. Venous malformations closely resemble arteriovenous malformations, except that arterial structures are absent. The lesion wall shows smooth muscle or connective tissue thickening but no elastic tissue.

4. Cerebral cavernous malformations are congenital vascular hamartomas composed of dilated blood vessels with a single layer of endothelium and an absence of neuronal tissue within the lesions. These thinly-walled vessels resemble sinusoidal cavities filled with stagnant blood surrounded by hemosiderin deposits and gliosis, which may or may not be thrombosed. Blood vessels in patients with cavernous angioma can range from a few millimeters to several centimeters in diameter, (usually, <3 cm). Re-endothelialization of the hemorrhagic cavities, growth of new blood vessels, and the proliferation of granulation tissue may account for the apparent growth of some cavernous angiomas. They are multiple or single, are often encapsulated and multilobar, and are occasionally calcified. Since they are lobulated and dark red to blue in color, the lesions grossly resemble small mulberries.

Cerebral cavernous malformations appear as single, solitary, sporadic lesions or as multiple familial lesions. A mutated form of KRIT1/CCM1 is thought to be responsible for the induction of cerebral cavernous malformation in 40% of familial cases, with CCM2 and CCM3 accounting for the remaining 60%.

These mutations are not simple missense mutations. Rather, they all appear to cause splicing errors that result in the production of truncated protein.
Cavernous malformations can be found throughout the central nervous system including every region of the brain and the brainstem in a volume distribution, and also the spinal cord, the cranial nerves, and the ventricles.

Cavernous angiomas can be found in any part of the brain because they can occur at any location along the vascular bed. A deep location in the basal ganglia, hypothalamus or ventricular system is infrequent. Cerebral cavernomas are dynamic lesions that are prone to vary in number and size over time. Cavernous malformations are a shockingly dynamic set of lesions, growing tremendously at times or shrinking considerably but rarely remaining quiescent. The mechanism of growth has been hypothesized to be a result of repeated microhemorrhage at the site of the lesion and/or recanalization after intraluminal thrombosis. Although once thought of as a developmental disorder, the de novo appearance of Cavernous angioma has been firmly established, most notably after radiation.

The clinical presentation of these lesions is highly variable, ranging from incidental finding at neuroimaging to discovery in autopsy after fatal hemorrhage. The most common symptom of cavernous malformation is seizure followed by focal neurological deficits, acute hemorrhage, and headache. However, in most cases they are asymptomatic and are only discovered incidentally. The onset of symptoms occurs most commonly in the third and fifth decade of life but can occur at any point in life, from children to the very elderly.

The most widely cited risk factor for clinically significant hemorrhage, apart from family history, is prior history of hemorrhage.

Another important risk factor is found in young women wishing to become pregnant. The hormonal state of pregnant women is such that endothelial cell proliferation may increase the risk for hemorrhage substantially.

Other controversial risk factors include age and location.

All seizure types, including simple seizures, complex partial, and generalized seizures, have been known to present in patients with supratentorial cavernous angioma. The pathogenesis of seizure is related to the presence of iron products after red blood cell breakdown secondary to multiple microhemorrhages. Most patients with seizure present with lesions in the frontal and temporal lobe. The estimated risk of developing seizure is 1% to 2% per person-year exposure and median age at time of first seizure is 42 years.

Although virtually all cavernous malformations show signs of repeated microhemorrhaging, clinically significant hemorrhage is a far rarer phenomenon with a risk per annum at 0.25% to 6%. However, this level of risk is not insignificant, especially when considered over a lifetime in younger patients and in few cases in which massive fatal hemorrhage has occurred.
The results of surgical extirpation of accessible symptomatic cavernomas are excellent with improved control of intractable epileptic seizures, restoration of neurological function, and decreased risk of future hemorrhage.

The well circumscribed nature of these lesions, the low flow arterial supply, and the free communication with venous drainage make resection of accessible cavernous angiomas relatively easy. In removing the cavernoma, the neurosurgeon must take care not to remove associated venous angioma, which provides anatomically disordered but physiologically essential drainage, because of the possibility of inducing venous infarction. Magnetic resonance imaging and magnetic resonance angiography are of enormous help in elucidating the venous angioma from the cavernoma.
Radiographically, high resolution MR imaging is the diagnostic tool of choice for detecting and identifying cavernous malformations (CMs).

Cerebral cavernous malformations are characterized by small, nonsymptomatic hemorrhages typically confined to the location of the lesion, only occasionally resulting in clinically significant haemorrhaging. Hemoglobin degradation products such as methemoglobin, hemosiderin, and ferritin present at the site of the lesion alter the local magnetic environment allowing for magnetic resonance imaging (MRI) detection. The appearance of cavernous angima on MRI allows grouping into 4 broad categories.

High-field MRI is the diagnostic tool of choice owing to its high sensitivity and specificity for these small angiographically cryptic lesions. Diagnosis is most commonly made accidentally by routine magnetic resonance imaging (MRI).

Since CM are low flow lesions (they are hooked into the venous side of the circulatory system), they will be angiographically occult (invisible). If a lesion is discernible via angiogram in the same location as in the MRI, then an arteriovenous malformation becomes the primary concern.

In up to 30% there is a coincidence of CM with a venous angioma, also known as a developmental venous anomaly (DVA). These lesions appear either as enhancing linear blood vessels or caput medusae (radial orientation of small vessels that resemble the hair of Medusa). These lesions are thought to represent developmental anomalies of normal venous drainage. These lesions should not be removed, as venous infarcts have been reported. When found in association with a CM that needs resection, great care should be taken not to disrupt the angioma.

CT

Unless large these lesions are difficult to see on CT. CM frequently appear as focal areas of increased density within the brain often without mass effect. The increased density either represents calcium, blood, or a combination of the two. The margins of the lesion are usually indistinct and the increased density may have a stippled appearance. They do not enhance. If large then a region of hyperdensity can be seen. If there has been a recent bleed then it is more conspicuous and may be surrounded by a mantle of edema. CT scanning has only a limited role in the diagnosis of cavernous angiomas, largely because of its relative lack of specificity. The differential diagnosis on CT scan includes low-grade gliomas, hematomas, granulomas, and inflammatory conditions such as tuberculomas and sarcoidomas. When calcified and located near the dura, cavernous angiomas can even resemble meningiomas. CT images also cause
small lesions to be missed altogether, and cavernomas, when they present as acute intracerebral hematomas, may not be detected by using nonenhanced CT scanning.

CT scan is a relatively sensitive test to detect cavernous malformations, but it is not specific. On CT the presence of thrombosis and hemorrhage in various stages of evolution cannot be accurately characterized.

MRI

MR imaging is required to make a more definitive diagnosis. The sensitivity of magnetic resonance imaging (MRI) to flowing blood and blood products of varying ages, as well as the greater contrast resolution of MRIs, greatly increases the specificity of MRI compared with that of CT scanning. Combining multiple MRI sequences has largely eliminated misdiagnosis of cavernous angiomas, because they have relatively specific signal characteristics. Additionally, gradient-echo imaging, with its increased sensitivity to susceptibility artifact, is useful in the detection of smaller and concomitant lesions, which may not be detected with traditional sequences.

The characteristic MR imaging appearance is a well-defined, lobulated lesion with a reticulated core of heterogeneous signal intensity on both T1 and T2 weighted sequences resulting from thrombosis, fibrosis, calcification, and hemorrhage. Extracellular and intracellular methemoglobin and thrombosis are responsible for the high intensity signal within the lesion, while calcifications, fibrosis, and acute and subacute blood are responsible for the low signal areas. On T2 weighted or gradient echo images, there is a peripheral ring of hypointensity that corresponds to the deposition of hemosiderin and iron in the surrounding brain parenchyma. (Fig 1, 2, 3).

The hemosiderin ring may not be evident in intraventricular cavernous malformations. Intraventricular CMs can exhibit rapid growth and be quite voluminous, leading to a diagnosis of a tumor instead of a vascular malformation.

MRI may cause small lesions to be missed if T2-weighted pulse sequences, such as T2-weighted fast spin-echo sequences, are used because these can be less sensitive to chronic hemorrhage. Additionally, even standard T1- and T2-weighted images can fail to depict minute concomitant lesions. Therefore, T2-weighted gradient-echo sequences, with their increased magnetic susceptibility effects, are able to delineate these lesions better than T1 or T2 weighted images. In patients with familial or multiple cavernous angiomas GRE T2* sequences are very important in identifying the number of lesions missed by conventional Spin echo sequences.

Zabramski et al classified CMs into four types (I- IV) based on the MR imaging appearance. Type I is a subacute bleed dominated by methemoglobin and therefore homogeneously hyperintense on T1 weighted images. Type II lesions have the classic
"popcorn" appearance, heterogeneous on both TI and T2 weighted sequences. Type III lesions are isointense to hypointense on both TI and T2 weighted images because of the predominance of chronic blood products. Type IV lesions are tiny, punctate, foci hypointense on both TI and T2 weighted sequences. These type IV lesions are often multiple and best seen on gradient echo sequences. In contrast with telangiectasias, type IV lesions rarely enhance. Gradient echo sequences best identify these lesions because of the susceptibility artifact from microscopic deposits of hemosiderin. Several authors have noted that patients with type I and type II lesions were more commonly symptomatic compared with the other types.

In cases where a CM is suspected but the radiologic image is not pathognomonic, serial imaging is of value if immediate surgical intervention is not warranted.

Differential diagnoses is that of other causes of cerebral microhaemorrhages, including: Cerebral amyloid angiopathy (usually numerous small foci), chronic hypertensive encephalopathy( more common in the basal ganglia), diffuse axonal injury (DAI), cerebral vasculitis, radiation vasculopathy, haemorrhagic metastases and Parry-Romberg syndrome.

CT scanning and MRI can be used in the follow-up monitoring of patients with known cavernous angiomas, particularly when hemorrhagic events are suspected. Although the MRI appearance of cavernous angiomas is not helpful in predicting future bleeds, MRI is the method of choice for the long-term follow-up of patients with cavernous angiomas and for the assessment of family members in whom similar lesions are suspected. In addition, MRI is extremely helpful in presurgical planning to assess the extent of the lesion, define borders, and plan the surgical approach and exposure.

There are pitfalls in the interpretation of post-operative MR imaging of CM. The postoperative MR imaging often appears similar to the preoperative image. This occurs despite the impression at surgery that there was a complete resection. The most plausible explanation for this is that the excision cavity is filled with organizing blood products. The natural history of such postoperative findings is unknown, so ongoing serial imaging and clinical follow-up is prudent.

Functional magnetic resonance imaging has emerged as an enormously beneficial modality in assisting with case selection, designing surgical approaches using frameless stereotaxy to avoid cortical eloquent tissue, and preventing the neurosurgeon from undermining eloquent tissue by interrupting pertinent penetrating fibers in white matter. In combination with diffusion-weighted MRI and frameless stereotactic navigation, functional MRI may offer the best prospect of guiding future neurosurgical interventions for cavernomas.

ANGIOGRAPHY
Cavernous malformations are angiographically occult lesions. They are by far the most common type of angiographically occult vascular malformation. Earlier reports on angiography in CMs described venous pooling or a capillary blush in some lesions.

**ATYPICAL RADIOGRAPHIC FEATURES.**

Atypical features of cavernomas results in a series of differential clinical and radiological characteristics that can make the diagnosis of these lesions extremely difficult and lead to procedures that endanger the patient like biopsy. We consider necessary to known the different presentations that can lead to missing the correct diagnosis.

Cavernomas may have atypical radiographic features in:

1. **Size.** (Fig 4-5)

Blood vessels in patients with cavernous angioma can range from a few millimeters to several centimeters in diameter, (usually, <3 cm). Cerebral cavernomas are dynamic lesions that are prone to vary in number and size over time. Re-endothelialization of the hemorrhagic cavities, growth of new blood vessels, and the proliferation of granulation tissue may account for the apparent growth of some cavernous angiomas.

There may be large lesions (>3cm), these are known as giant cavernomas.

2. **Number (multiple cavernous.** (Fig 6,7,8)

Approximately 15-20% going to find more than one injury. In such cases there will be a family history of cavernomas in more than 80% of patients and there will be increased tendency to bleed, so they tend to debut a a younger age.

In patients with familial or multiple cavernous angiomas GRE T2* sequences are very important in identifying the number of lesions missed by conventional Spin echo sequences. In T2 gradient echo sequences results in the image of "black multiple injuries."

3. **Location.** (Figs 7-17)

Cavernous angiomas can be found in any part of the brain because they can occur at any location along the vascular bed. 80% of all cavernous angiomas are supratentorial, and they appear more often on the deep white matter and the cortico-subcortical joint of
the frontal and temporal lobes. When they are located on the posterior fossa (20%) they are more common on the pons and the cerebellar hemispheres. When they are located elsewhere can give other unusual symptoms.

A deep location in the basal ganglia, hypothalamus or ventricular system is infrequent.

There cavernomas described in all locations including:
- Intraventricular.
- Spinal Cord (3%).
- Cranial nerves.
- Pineal.
- Subarachnoid space.
- Subdural.
- Even extradural.

4. Appearance. (Figs 16-36)

If there is a recent bleed or thrombosis in a CM, which usually coincides with clinical events, the typical features of a CM are not evident. The hemosiderin ring may be obscured by a recent bleed and therefore follow-up MR imaging is important to establish CM as the cause for the bleed. Peri-lesional and extralesional hemorrhage may be evident outside the hemosiderin ring. Repeat MR imaging is also needed in patients who report a worsening of symptoms or when new deficits are detected by the clinician.

The presence of edema and mass effect on MR imaging may correlate with new signs and symptoms that the patient has developed. Hemorrhage outside the hemosiderin ring may be evident in patients with new clinical findings or worsening of an existing deficit. A fluid/fluid level may be evident in some active CMs. On serial MR imaging, a change in the signal intensity within the lesion may or may not correspond with recent clinical events. Clinical deterioration can, however, also occur without any significant change in the MR imaging. On MR imaging, there may be changes in the size of the CM or the signal intensity within the lesion without a corresponding clinical event in the patient. In summary, the atypical features respect the appearances are:

- Edema
- Mass Effect
- Loss of hemosiderin ring
- Level liquid-liquid
- The presence of perilesional hemorrhage.
When the lesions occur in combination with other vascular malformations, as they do in as many as 30% of patients with venous malformations as the developmental venous anomaly, MRI characteristics become more complicated, less specific and may demonstrate a feeding artery or draining vein. In these patients, angiography can be helpful in further defining the lesions. (Fig 15-17)

In addition, cavernomas may appear associated with other injuries such as hypertrophic olivary degeneration (DHO) if there is involvement of the dento-rubro-olivary pathway. (Fig 18)
Fig. 0: Axial T2 weighted MRI. Typical appearance and location of cavernous angioma. It’s located on the cortico-subcortical joint of the right temporal lobe.

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
**Fig. 0:** Axial T2* weighted MRI. Gradient echo sequence with their increased magnetic susceptibility effects is able to delineate this lesion better than T1 or T2 weighted images. Image of the previous cavernous angioma.

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
**Fig. 0:** Axial T2* weighted MR image shows another typical location of cavernous angioma: cortico-subcortical joint of the left parietal lobe.

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
Fig. 0: Axial T2 weighted MR image. Atypical cavernoma for its large size and by eroding the adjacent bone

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
Fig. 0: Sagittal T1 weighted MR image. Atypical cavernoma for its large size and by eroding the adjacent bone.

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
**Fig. 0:** Axial T2 weighted MRI shows two cavernous angiomas on the cortico-subcortical joint of the occipital and parietal left lobes in a patient with multiple cavernous.

© Ana Ortiz, Hospital Sanchinarro.Madrid
**Fig. 0:** Coronal Flair MR image in a patient with multiple cavernous angiomas shows one of them parasagittal with mass effect on left horn ventricle, the other is located on left deep basal ganglia.

© Esther de Luis, Hospital Sanchinarro, Madrid.
Fig. 0: Coronal Flair MR image in a patient with multiple cavernous angiomas shows one of them parasagittal with mass effect on left horn ventricle, the other is located on left deep basal ganglia.

© Esther de Luis, Hospital Sanchinarro, Madrid.
Fig. 0: Axial T2 MRI shows subtle hyperintense lesion in right dorsolateral pons corresponding to cavernous angioma.

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
Fig. 0: Gradient-echo sequence, with their increased magnetic susceptibility effects, is able to delineate the previous lesion better than T2 weighted image.

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
**Fig. 0:** Axial T2 weighted image shows cavernous angioma in the left cerebellar peduncle.

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
Fig. 0: Axial T2 weighted MR image shows a cavernous angioma located in the posterior right thalamus.

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
**Fig. 0:** Sagittal T1 weighted MR image shows cavernous angioma located in the posterior right thalamus

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
**Fig. 0:** Axial T2* weighted MR image of the previous patient.

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
Fig. 0: Axial T2 weighted MR image shows a cavernoma in the left dorsolateral part of the pons

© Ana Ortiz, Hospital Sanchinarro, Madrid.
**Fig. 0:** Axial contrast-enhanced T1 weighted shows the previous cavernoma in association with venous angioma, note the draining vein.

© Ana Ortiz, Hospital Sanchinarro, Madrid.
**Fig. 0:** Axial contrast enhanced T1 MR imaging at a lower level of the previous shows the associated venous angioma. These lesions appear either as enhancing linear blood vessels or caput medusae.

© Ana Ortiz, Hospital Sanchinarro, Madrid.
**Fig. 0:** Hipertrophic olivary degeneración associated with previous cavernoma by damage of the dento-rubro-olivary pathway.

© Ana Ortiz, Hospital Sanchinarro, Madrid.
**Fig. 0:** Sagittal T1 weighted MR image shows a cavernous angioma has recently bleeding.

© Esther de Luis, Hospital Sanchinarro, Madrid.
**Fig. 0:** Axial T1 weighted MR image shows a cavernous angioma has recently bleeding.

Fig. 0: Axial T2 weighted MR image of the previous patient shows edema, enlargement and mass effect on left ventricle occipital horn.

**Fig. 0:** Axial T2 weighted MR image of the previous patient.

**Fig. 0:** Coronal flair MR image of the previous patient.

Fig. 0: Axial T2 MR image of the previous patient three months later. Noting the significant decrease in size and the disappearance of surrounding edema.

Fig. 0: Axial T2* weighted MR image three months later.

**Fig. 0:** Axial T2* weighted MR image six months later shows further decrease the size of cavernous angioma.

Fig. 0: Coronal T2* weighted MR image six months later shows actual size of the cavernous angioma.

Fig. 0: Large cavernous angioma with peri-lesional edema located in the left temporal lobe. Axial T2 weighted MR image.

**Fig. 0:** Large cavernous angioma with peri-lesional edema located in the left temporal lobe. Coronal flair MR image.

Fig. 0: Large cavernous angioma with peri-lesional edema located in the left temporal lobe. Axial T2* weighted MR image.

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
**Fig. 0:** Axial T1 weighted MR image shows large hemorrhage outside the hemosiderin ring that may be evident in patients with new clinical findings or worsening of an existing deficit.

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
Fig. 0: Peri-lesional and extralesional hemorrhage may be evident outside the hemosiderin ring. Axial T2 weighted MR image.

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
**Fig. 0:** Axial T2 weighted MR image previous patient. Noting the edema and the important mass effect.

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
Fig. 0: Axial T2 weighted MR image of the previous patient. Noting the edema and the significant mass effect.

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
Fig. 0: Coronal flair MR image of the previous patient.

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
**Fig. 0:** Axial T2* weighted MR image of the previous patient.

© Radiology, Hospital Universitario de Salamanca - Salamanca/ES
Conclusion

MR imaging is the diagnostic tool of choice for detecting and identifying cavernous malformations owing to its high sensitivity and specificity for these small angiographically cryptic lesions.

MRI is the method of choice for the long-term follow-up of patients with cavernous angiomas and for the assessment of family members in whom similar lesions are suspected.

The small lesions are depicted more clearly and are more numerous on gradient-echo images because of the increased susceptibility effects of the sequences.

Atypical features of cavernomas results in a series of differential clinical and radiological characteristics that can make the diagnosis of these lesions extremely difficult and lead to procedures that endanger the patient like biopsy.
References