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Cerebral cavernous malformations: Spectrum of neuroradiological findings☆

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Abstract Cavernous malformations (cavernomas) are hamartomatous lesions formed by sinusoidal vascular spaces, with no cerebral parenchyma between them. Seizures are the most usual clinical presentation. They are dynamic lesions, producing changes throughout their evolution. The majority are located in the supratentorial region, but up to 20% of cases they are found in the posterior fossa. In computed tomography (CT) and in magnetic resonance (MR) their typical presentation is as a well defined round or oval lesion, with or without a minimal mass effect or oedema, with little or no contrast enhancement. Their appearance in magnetic resonance imaging (MRI) will depend on the stage of the haemorrhage, a T2 echo gradient being the most sensitive sequence. Angiography do not usually detect cavernomas. However, it may demonstrate a venous developmental anomaly. Cavernomas may present with atypical characteristics, as regards their size, appearance, location and number.

PALABRAS CLAVE
Cavernoma;
Angioma cavernoso;
Hemangioma cavernoso;
Cavernomatosis múltiple;
Tomografía computarizada;

Malformaciones cavernosas intracraneales: espectro de manifestaciones neurorradiológicas

Resumen Las malformaciones cavernosas (cavernomas) son lesiones hamartomatosas formadas por espacios vasculares sinusoidales sin parénquima cerebral entre ellos. Las crisis son su presentación clínica más habitual. Son lesiones dinámicas en las cuales se producen cambios a lo largo del tiempo. La mayoría son de localización supratentorial, pero hasta un 20% de los casos se presentan en la fosa posterior. Tanto en la tomografía computarizada como en la resonancia magnética (RM) su presentación típica es como una lesión redondeada u ovoidea, bien definida, sin o con un mínimo efecto masa o edema, y con poco o ningún realce. Su apariencia

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Resonancia magnética; Arteriografía

en la RM dependerá del estadio de la hemorragia, siendo la secuencia más sensible el eco de gradiente T2. El cavernoma no es visible en la arteriografía. No obstante, ésta puede demostrar una anomalía del desarrollo venoso asociada. Los cavernomas pueden presentar características atípicas en cuanto a su tamaño, apariencia, localización y número.

Introduction and epidemiology

Cavernomas are non-encapsulated, well-defined, vascular hamartomatous lesions formed by sinusoidal vascular spaces with no cerebral parenchyma between them. They are one of the four major types of vascular malformations of the central nervous system, together with developmental venous anomalies, arteriovenous malformations, and capillary telangiectasias.[1] The literature offers a wide range of synonyms of *cavernoma*, such as *cavernous angioma*, *cavernous malformations*, and *angiographically occult vascular malformation*. Although cavernomas were first classified as a rare condition, they are now becoming a more and more common finding in neuroimaging studies, particularly after the advent of magnetic resonance imaging (MRI).

Since they are normally asymptomatic, their actual incidence is not well known. According to series of autopsies, carvernomas occur in about 0.4% of subjects, accounting for 5–13% of all cerebral vascular malformations, and are only second to venous developmental anomalies in incidence.[2] Cavernomas occur equally in males and females and usually appear between the second and fifth decade of life.[3]

All cavernomas were initially thought to have a congenital cause. However, it has been shown that they are dynamic lesions that undergo changes overtime (*de novo* appearance, growth, size reduction).[4] On some occasions, carcinomas disappear after a hemorrhage.[5] Several factors associated with *de novo* formation of carcinoma have been reported[6]: previous cranial irradiation, infection of specific viruses, influence of hormones, genetic causes, seeding along the needle track during biopsy, and venous developmental anomalies.[7] The association of cavernoma and developmental venous anomaly should be considered since both disorders co-occur in about 30% of cases according to the medical literature.[8] In this respect, it would be very useful to complete the radiological studies with the injection of intravenous contrast material because, unlike cavernoma, developmental venous anomaly shows intense enhancement (Fig. 1). There are also studies reporting the rare association between cavernoma, developmental venous anomaly, and capillary telangiectasia as spectrum of one same disorder. Capillary telangiectasia is best detected following intravenous contrast administration.[9] Based on a number of histological and immunohistochemical studies, a theory has been suggested for cavernoma formation in case of previous developmental venous anomaly[10,11] (Fig. 2).

Recent genetic studies have provided evidence of dysfunction of specific genes involved in angiogenesis in patients with inherited forms of cerebral cavernomas. These genes encode proteins that interact at the junction of endothelial cells. These patients would present with increased vascular permeability caused by the absence or dysfunction of the junctions between the endothelial cells. Three genes associated with familial forms of cerebral cavernoma have been identified to date. These genes have been named after the abbreviation *CCM* (cerebral cavernous malformations): CCM1 (KRIT1), CCM2 (MGC4607), and CCM3 (PDCD10). Of all three, gen CCM3 is associated with a higher risk of hemorrhage, and thus, with appearance of the disease at an earlier age.[12]

Histological features

On histological examination, cavernomas are composed of dilated vascular channels variable in size lined by a thin and

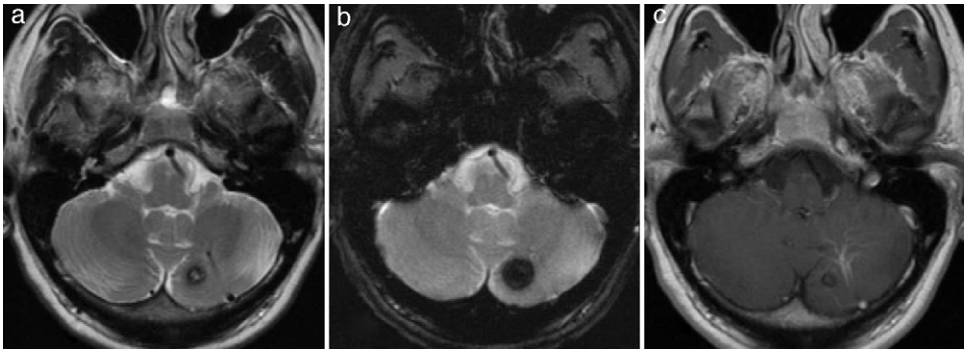

Figure 1 Cavernoma in the left cerebellar hemisphere with associated developmental venous anomaly whose collecting vein drains into the left transverse sinus. (a) and b) T2-weighted cranial MR image and T2 gradient-echo cranial MR image in the axial plane. Cavernoma in the left cerebellar hemisphere. An associated developmental venous anomaly can be guessed in (a). (c) Axial T1-weighted sequence clearly shows enhancement of the developmental venous anomaly and absence of enhancement of the cavernoma after administration of intravenous gadolinium.