Familial multiple cavernous malformation syndrome

Familial multiple cavernous malformation syndrome is uncommon, accounting for only a minority of cavernous malformations.

Epidemiology

It has been more frequently reported in patients of Hispanic descent [1)]

Clinical features

The presentation is most commonly with seizures (38-55%) [2)] and focal neurological deficits while recurrent large hemorrhages and headaches are less frequently encountered.

Pathology

In sporadic cases up to a third of cavernous malformations are multiple. When familial the number of cavernomas is higher, typically five or more [3)] and may be as high as dozens and dozens.

Familial cases usually have an autosomal dominant pattern of inheritance with incomplete penetrance [4)] [5)]

The definition of familial multiple cavernous malformation syndrome is when there is one or more of the following [6)] [7)]

multiple cerebral cavernous malformations

five or more cavernomas, or...

one cavernoma and at least one other family member with one or more cavernomas

mutations in one of the three genes, KRIT1, CCM2 or PDCD10, which are associated with this disease

See: Zabramski classification of cerebral cavernomas.

Radiographic features

The radiographic appearance of each cavernous malformation depends on size although in many instances individuals have innumerable lesions randomly distributed throughout the brain.

For a discussion of the radiographic appearances see: cavernous malformations. Differential diagnosis

The differential is that of other causes of cerebral microhemorrhages, including [8]

cerebral amyloid angiopathy: usually numerous small foci

chronic hypertensive encephalopathy: more common in the basal ganglia

diffuse axonal injury (DAI)

cerebral vasculitis

radiation vasculopathy

hemorrhagic metastases

Parry-Romberg syndrome [9]

MRI appearance may be mimicked by:

artificial heart valve metallic emboli (very rare)

pneumocephalus (very rare) [10]

[1], [2], [3], [4]
Brunereau L, Labauge P, Tournier-lasserve E et-al. Familial form of intracranial cavernous angioma: MR imaging findings in 51 families. French Society of Neurosurgery. Radiology. 2000;214 (1): 209-16.
[5], [8], [9]
Jain R, Robertson PL, Gandhi D et-al. Radiation-induced cavernomas of the brain. AJNR Am J Neuroradiol. 2005;26 (5): 1158-62. AJNR Am J Neuroradiol
[6]
Rosário Marques I, Antunes F, Ferreira N, Grunho M. Familial cerebral cavernous malformation: Report of a novel KRIT1 mutation in a Portuguese family. (2017) Seizure. 53: 72-74. doi:10.1016/j.seizure.2017.10.020
[7]
Mespreuve M, Vanhoenacker F, Lemmerling M. Familial Multiple Cavernous Malformation Syndrome: MR Features in This Uncommon but Silent Threat. (2016) Journal of the Belgian Society of Radiology. 100 (1): 51. doi:10.5334/jbr-btr.938
[10]
Palma JA, Zubieta JL, Dominguez PD et-al. Pneumocephalus mimicking cerebral cavernous malformations in MR susceptibility-weighted imaging. AJNR Am J Neuroradiol. 2009;30 (6): e83. doi:10.3174/ajnr.A1549