Natural history of intracranial cavernous malformation

The incidence of symptomatic hemorrhage or rehemorrhage is higher in brainstem lesions. First symptomatic hemorrhage increases the chance of symptomatic rehemorrhage, which decreases after 2 years [1)]

Cavernous malformations may be familial or nonfamilial. A systematic review of Taslimi et al., compares the natural history of cavernous malformations in familial compared to non-familial cases.

They searched MEDLINE, Web of Science, and EMBASE for the natural history studies on cavernous malformations until Sept 2018. They included studies that followed at least 20 untreated patients. Primary outcomes were hemorrhage, seizures and neuroimaging changes in familial and nonfamilial cases. Incidence rate per person-year (PY) or lesion year (LY) of follow-up were used to pool the data using fixed or random effects models. They used the incidence rate ratio for comparison.

They could not compare hemorrhage rates between familial and nonfamilial cases mainly due to mixtures of subgroups of patients. The seizure rate was similar in familial and non-familial cases with pooled incidence rate of 1.5%/PY (1.1%-2.2%). The re-seizure rate was higher than the seizure rate ($P<0.001$). New lesion development was higher in familial cases (32.1% versus 0.7% /PY, $P<0.001$). Signal change on neuroimaging ranged from 0.2% to 2.4% per LY in familial cases. In familial cases incidence rate of size change was 8% (5.2%-12.2%) and 1.1%(0.6%-1.6%) per PY and LY respectively.

Familial cavernous malformations show higher dynamic changes than non-familial cases. However, the presence of actual dynamic changes needs further assessment in non-familial cases. Cavernous malformations demonstrate a low incidence of seizure. First-time seizure increases the chance of recurrence seizure. Seizure rate based on the location and type of the lesion should be investigated further [2)].

Literature reports on the natural history of cerebral cavernous malformations (CMs) are numerous, with considerable variability in lesion epidemiology, hemorrhage rates, and risk factors for hemorrhage.

Gross et al., performed a meta-analysis of 11 natural history studies. The overall male-to-female ratio was 1:1, and the mean age at presentation was 30.6 years. Overall, 37% of patients presented with seizures, 36% with hemorrhage, 23% with headaches, 22% with focal neurological deficits, and 10% were asymptomatic. Some patients had more than one symptom. Seizure presentation was most prevalent among supratentorial CMs, while focal neurological deficits were common in patients with infratentorial CMs. By location, CMs were in the cerebral hemispheres (66%), brainstem (18%), basal ganglia or thalamus (8%), cerebellum (6%), and other (2.5% [combined supra- and infratentorial, callosal or insular]). Overall, 19% of patients harbored multiple intracranial CMs, and 9% had radiographically apparent associated developmental venous anomalies. An overall annual hemorrhage rate of 2.4% per patient-year (range 1.6%-3.1%) was identified across 3 studies. Prior hemorrhage and female sex were risk factors for bleeding, while CM size and multiplicity did not affect hemorrhage rates. Although not impacting the hemorrhage rate itself, deep location was a risk factor for increased clinical aggressiveness [3)].

Aiba et al., reviewed the clinical records of 110 patients with intracranial cavernous malformations diagnosed by histological examination and/or magnetic resonance imaging over a mean follow-up period of 4.71 years. These cases were divided, based on their presentation, into a hemorrhage group, a seizure group, and an incidentally diagnosed group. The rate of subsequent symptomatic bleeding was investigated in relation to age at onset, sex, and location of the initial lesion. A high rate of subsequent symptomatic bleeding episodes was found in the hemorrhage group, especially among younger females. The nonhemorrhagic-onset cases had a very low incidence of bleeding. The outcome was generally good, except in patients with lesions in the basal ganglia and brainstem. These findings will be helpful in planning a rational therapeutic strategy for intracranial cavernous malformations [4].

In 1998, Thirteen papers on different aspects of cerebral cavernomas were reviewed; interest in this condition has increased since magnetic resonance imaging (MRI) became widely available. The prevalence of cavernomas is uncertain, but they are the most common of the angiographically occult vascular malformations. Some are isolated occurrences, and some are familial, with a dominant inheritance. Screening with MRI of first-degree relatives is justified. The reported annual risk of haemorrhage varies widely and is probably between 1 and 3%, with a possible increase in risk after a first haemorrhage; the risk may also be higher in deep or brain stem cavernomas. Opinions on when surgery should be offered vary, with prophylactic surgery not usually recommended. After symptomatic haemorrhages, surgery may be more justified for easily accessible lesions. For those that are more difficult to approach safely, especially in the brain stem, operation is not usually recommended unless there has been at least one clinically significant haemorrhage. Epilepsy owing to hemisphere cavernomas can often be successfully managed medically, with surgery reserved for intractable seizures. In children with epilepsy, there is a stronger argument for surgery. Radiosurgery has been used for symptomatic cavernomas that are surgically inaccessible. Strong arguments have been advanced both for and against this treatment, and the risks probably outweigh the benefits. Suggestions for a randomised trial have been made [5].

1)
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