CCM3 mutations are associated with a high risk of early-onset cerebral hemorrhage and with the presence of multiple meningiomas [1)].

A CCM3 mutation was identified in 54 probands.

Thirteen had a deletion encompassing one or several coding exons, including 8 whole gene deletions. Forty-one probands had a point mutation leading to a premature stop codon.

Thirty-one different point mutations were identified including 6 recurrent ones (3 found twice, 2 found 3 times, and 1 found 4 times). Point mutations leading to an abnormal splicing accounted for 42% (13/31); nonsense mutation and small insertions or deletions leading to a frameshift and premature stop codon accounted each for 29% (9/31). Two deletions involved only noncoding exons. One was a deletion of exons 1-3 that happened de novo in a 5-year-old boy (C270) with typical multiple cerebral cavernomas.

The second one was a deletion of exons 1 and 2 that cosegregated with the affected phenotype within family C085. They were both considered as probably deleterious. The de novo appearance of mutations was established in 4 probands (C052, C146, C107, and C270) and was deduced from familial haplotype analysis for the father of proband C044.

1)
Riant F, Bergametti F, Fournier HD, Chapon F, Michalak-Provost S, Cecillon M, Lejeune P, Hosseini H, Choe C, Orth M, Bernreuther C, Boulday G, Denier C, Labauge P, Tournier-Lasserve E. CCM3 Mutations Are Associated with Early-Onset Cerebral Hemorrhage and Multiple Meningiomas. Mol Syndromol. 2013 Apr;4(4):165-72. doi: 10.1159/000350042. Epub 2013 Apr 3. PubMed PMID: 23801932; PubMed Central PMCID: PMC3666455.