Hereditary cerebral small vessel disease

This category includes SVDs caused by specific genetic mutations. The most well-known genetic forms of SVD include:

CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy): Caused by mutations in the NOTCH3 gene. It is characterized by recurrent strokes, migraine with aura, and progressive cognitive decline.

CARASIL (Cerebral Autosomal Recessive Arteriopathy with Subcortical Infarcts and Leukoencephalopathy): Caused by mutations in the HTRA1 gene. It presents with early-onset ischemic strokes, alopecia, spondylosis, and cognitive decline. Fabry Disease: Caused by mutations in the GLA gene. It is a lysosomal storage disorder that affects the small vessels of the brain, heart, and kidneys, and can lead to strokes and white matter lesions. COL4A1/A2-Related Disorders: Caused by mutations in the COL4A1 or COL4A2 genes. These are collagen-related disorders that can cause cerebral microangiopathy, hemorrhagic stroke, and porencephaly. Hereditary Cerebral Hemorrhage with Amyloidosis (HCHWA): Caused by mutations in the APP gene (amyloid precursor protein), resulting in amyloid deposits in the small blood vessels of the brain. 3. Other Hereditary Syndromes Associated with SVD: There are other less common genetic disorders that can present with cerebral SVD, such as:

MELAS (Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-like episodes): A mitochondrial disorder often presenting with stroke-like episodes and white matter changes. RVCL (Retinal Vasculopathy with Cerebral Leukodystrophy): A rare autosomal dominant condition affecting the small vessels of the retina and brain. Sickle Cell Disease: Though primarily a hematologic disorder, it can lead to cerebrovascular disease affecting small vessels, especially in children. Summary: Cerebral small vessel disease is classified based on its cause—either sporadic (typically due to aging and vascular risk factors) or hereditary (due to specific genetic mutations). Understanding the classification helps in diagnosis, management, and treatment strategies for affected individuals.

White matter hyperintensity (WMHs) on brain magnetic resonance imagings are characteristic of hereditary cerebral small vessel disease (CSVD), including high-temperature requirement serine peptidase A1 (HTRA1)-related CSVD. Although HTRA1-related CSVD is increasingly recognized, the diagnosis is still challenging. Kitahara et al. encountered two patients with HTRA1-related CSVD who were misdiagnosed with other diseases, including multiple sclerosis and idiopathic normal pressure hydrocephalus. Both patients had extended WMHs in addition to multiple lacunes and microbleeds on brain MR images, which are characteristic of CSVD. If lacunes or microbleeds are found in patients with severe WMHs, genetic tests for hereditary CSVD should be considered [1)].

1)
Kitahara S, Tsuboguchi S, Uemura M, Nozaki H, Kanazawa M, Onodera O. Patients with heterozygous HTRA1-related cerebral small vessel disease misdiagnosed with other diseases: Two case reports. Clin Neurol Neurosurg. 2022 Dec;223:107502. doi: 10.1016/j.clineuro.2022.107502. Epub 2022 Oct 31. PMID: 36334553.