A case of cerebral cavernous malformations in a young patient with a rare CCM2 gene mutation (c.658_660 del, p. Val 220 del)

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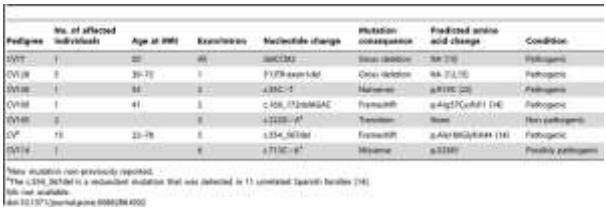
Objectives: We describe a case of a CCM2 gene mutation in a young patient. Cerebral cavernous malformations (CCMs) are congenital vascular malformations of the central nervous system, with a 0.16 to 0.5% prevalence in the general population. To date, several mutations have been identified within the CCM2 gene, summarized in *Figure 1*. Lesions are often clinically silent in young patients, whereas focal neurological signs, seizures, or recurrent headache are the most frequent clinical presentations [1,2,3].

Methods: On 12th November, 2024, a 31 year-old man, with negative history, accessed our Emergency Department presenting with left facial nerve peripheral paralysis, and mild paresis of left arm and leg, with acute onset 45 minutes before hospital arrival.
Suspecting an acute ischemic stroke, the patient underwent urgent brain computed tomography (CT) scan, CT angiography of cerebral arteries, and perfusion cerebral study (according to the RAPID protocol), resulting negative for acute ischemic lesions and blood vessels occlusions.
Cerebral perfusion maps were also normal. Anyhow, two mild-hyperdense small areas in the left thalamus were identified: for this reason, the patient did not receive intravenous thrombolysis, but he was admitted to our neurology ward.
He underwent a magnetic resonance imaging (MRI) study, showing multiple cerebral angiomas in left temporal and parietal lobes, basal ganglia, left cerebellar hemisphere, pons and medulla oblongata *(Figure 2*).

Results: Genetic testing for hereditary CCMs confirmed the diagnosis of cerebral cavernous malformation due to the **CCM2 gene heterozygous variant NM_031443:4:c.658_660 del, p. Val 220 del**, a new mutation non-previously reported.



Pedigree	No. of affected individuals	Age at MRI	Exon/intron	Nucleotide change	Mutation consequence	Predicted amino acid change	Condition
[illegible]	1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	3	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	15	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

Figure 1. Most frequently reported mutations within the CCM2 gene.

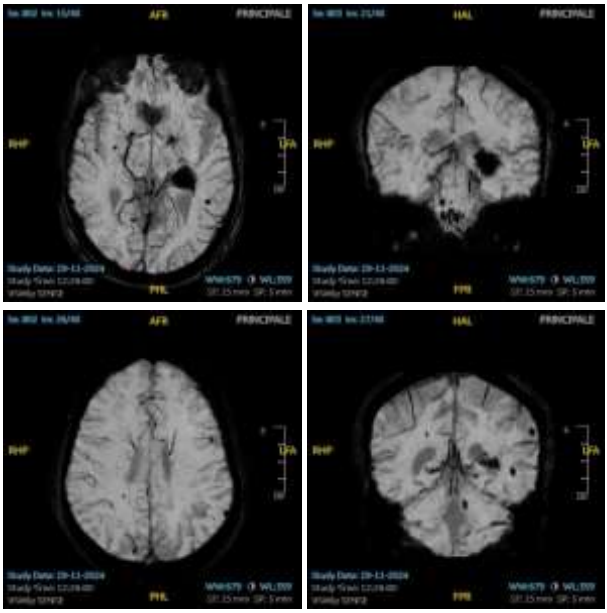


Figure 2. MRI imaging study (SWI sequences) showing multiple cerebral angiomas in left temporal and parietal lobes, basal ganglia, left cerebellar hemisphere, and brainstem in our patient.

References

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Conclusions: Differential diagnosis of CCMs from acute ischemic stroke may be challenging, especially in young patients, as these lesions, unless large-sized, may be undetected on CT scan. Despite their rarity, CCMs should been considered as a possible cause of acute-onset focal neurological signs when approaching patients in Emergency settings.