

CADASIL; a rare cause of a common presentation

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INTRODUCTION

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), is a single-gene disorder of the cerebral small blood vessels caused by mutations on chromosome 19p13.12 involving the *NOTCH3* gene resulting in recurrent stroke, migraine, psychiatric symptoms, and progressive cognitive impairment. The infrequency with which it occurs makes it a formidable diagnostic challenge.

Due to recurrent ischemic infarcts despite daily aspirin therapy, he was switched to daily clopidogrel and was initiated on atorvastatin 80 mg daily. A MRA brain, carotid artery Dopplers and an ECHO with bubble study were obtained for further work-up and were all found to be unremarkable. Given recurrent ischemic cerebrovascular accidents without an identifiable underlying risk factor, he was evaluated for a possible underlying prothrombotic state, however, this was also unremarkable.

Additional history revealed a history of recurrent ischemic cerebral infarcts in the patient's mother and maternal grandfather occurring in their 30s to 40s with the patient's mother having a positive *NOTCH3* gene mutation, consistent with CADASIL, after extensive work-up. The patient was noted to have some interval improvement in right-sided weakness during his hospital stay and was discharged to acute rehab for ongoing PT. Outpatient neurology follow-up with genetic testing confirmed a diagnosis of CADASIL.

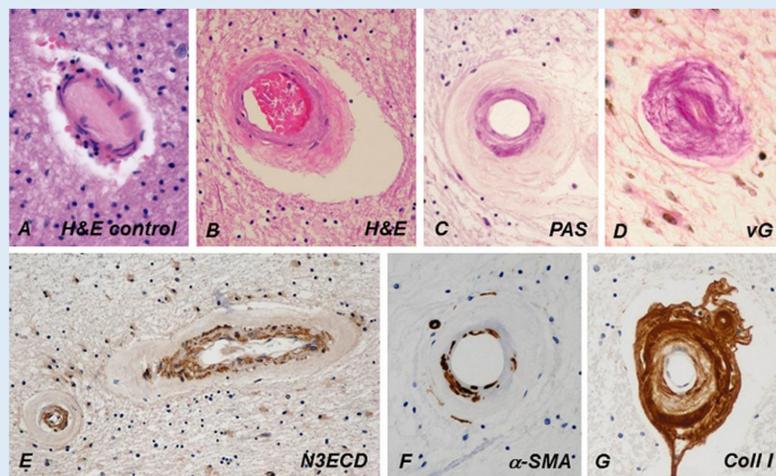


Figure 1. CADASIL results in small vessel and arteriole stenosis secondary to fibrotic thickening of the basement membrane of the vessels (image B and C) when compared to normal cerebral vessels (A); the pathological hallmark is the deposition of granular osmiophilic material in close relation to the vascular smooth muscle cells¹.

CASE

A 43-year-old male with a past medical history of a cerebrovascular accident at age 33, on daily aspirin, presented with a 2-day history of progressively worsening right-sided arm and leg weakness. CT brain on presentation showed multiple lacunar infarcts throughout the frontal lobes, thalami and basal ganglia with MRI brain showing an acute ischemic infarction of the left basal ganglia-internal capsule-corona radiata.

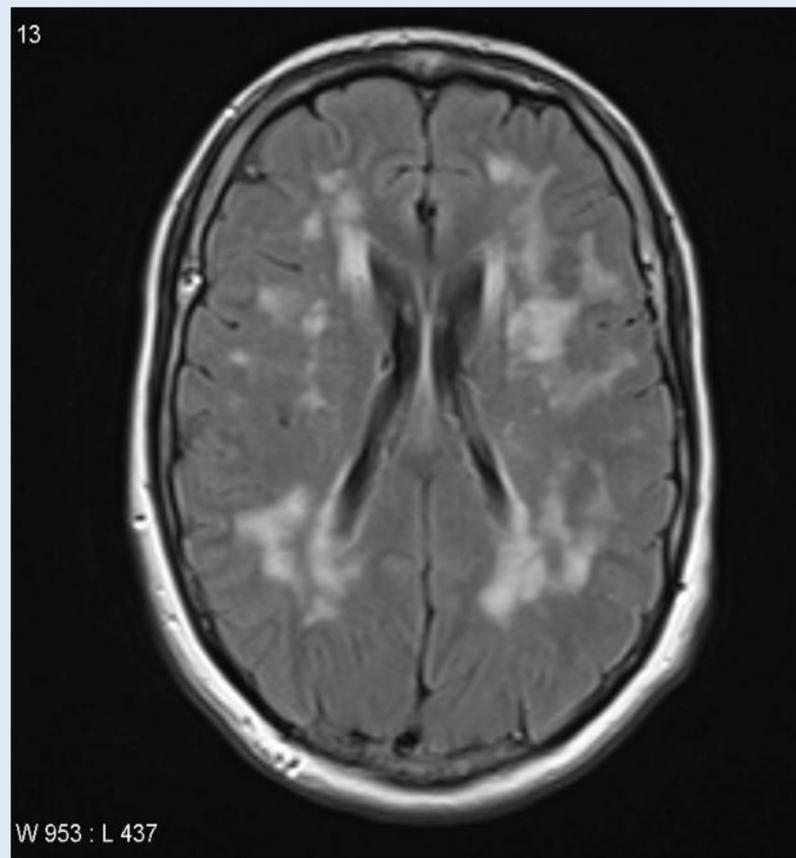


Figure 2. MRI is the investigation of choice in CADASIL, often demonstrating widespread confluent white matter hyperintensities. More circumscribed hyperintense lesions are also seen in the basal ganglia, thalamus and pons² (consistent with our patient's MRI findings).

DISCUSSION

- This case aims to highlight CADASIL as an etiology of recurrent, early onset cerebrovascular disease and the importance of thorough history taking.
- Though rare, it is the most common inheritable cause of stroke and vascular dementia in adults.
- There is thus far no specific treatment for CADASIL and management entails minimization of vascular risk factors such as smoking cessation.
- CADASIL should be considered in young patients presenting with recurrent cerebrovascular accidents, without any obvious risk factors for cerebrovascular disease and a family history of early-onset cerebrovascular disease or dementia³ in order to facilitate early recognition and genetic counselling for families given its progressive course.

REFERENCES

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