A 63-year-old man was referred to the memory clinic of Queen Mary Hospital in December 2021 for early-onset dementia. He had stepwise deterioration in cognitive function over the previous 6 months, especially in short-term memory, poor judgement, and spatial and temporal disorientation. His home environment was poor with rotten food. Physical examination revealed symmetrical parkinsonism. Montreal Cognitive Assessment Hong Kong version score was 10/30 (<2nd percentile). Vitamin B₁₂, folate and thyroid function tests were normal. A review of his medical history revealed three episodes of stroke since the age of 50 years. These episodes presented as left lower limb monoplegia, left-sided hemiplegia and slurring of speech 12 years, 8 years, and 1 year ago, respectively. Extensive workup including 24-hour Holter monitoring and transthoracic echocardiogram was unremarkable. He had hypertension and hyperlipidaemia and was prescribed amlodipine 5 mg and rosuvastatin 20 mg daily. His blood pressure was under control and the latest low-density lipoprotein was 1.7 mmol/L. A review of his computed tomography of the brain over the last 11 years showed a progressive increase in periventricular hypodensities (Fig 1). Brain magnetic resonance imaging (1 year previously) showed extensive periventricular hyperintensities and an old ischaemic insult over bilateral external capsules (Fig 2). Family history was notable for multiple first-degree relatives with young-onset stroke in their fifties and a suspected autosomal dominant inheritance pattern (Fig 3). Genetic testing of the neurogenic locus notch homolog protein 3 (NOTCH3) gene revealed a heterozygous mutation with a pathogenic variant (c.1630C>T; p.Arg544Cys), confirming the diagnosis of cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). The family was referred for genetic counselling.

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy is caused by cysteine-altering pathogenic variants in the NOTCH3 gene, with consequent vasculopathic changes, predominantly involving small penetrating arteries, arterioles, and brain capillaries.¹ ² The mutation leads to an odd number of cysteine...
residues with deposition of osmiophilic material and progressive degeneration of vascular smooth muscle cells.\textsuperscript{1,2} The key to diagnosis includes a strong family history of young-onset stroke, an absence of strong vascular risk factors, and salient findings on brain magnetic resonance imaging, especially extensive white matter abnormalities and subcortical infarcts involving external capsules. Genetic testing for the NOTCH3 gene can be arranged after consultation with chemical pathologists in major
public hospitals.3,4 The principle of management for symptomatic patients is similar to that of other patients with stroke, ie, antiplatelet therapy, lipid-lowering agents, and blood pressure control. There is no disease-modifying therapy currently available. Family members of affected individuals should be referred for genetic counselling with referral to tertiary centres for potential pre-implantation genetic testing to avoid transferring the mutation to offspring.5 There have been four other reported families with CADASIL in Hong Kong with different mutations. The mean age of symptom onset for index patients of these families was 51 years.3,4 The mutation in our patient has been commonly found in Fujian province and Taiwan, accounting for up to 14.5% to 70% of CADASIL cases.1

In summary, clinicians should obtain a detailed history and be alert to suspicious magnetic resonance imaging findings. Referral to chemical pathologists for genetic testing is key to the diagnosis of CADASIL.

Author contributions
All authors contributed to the concept or design of the study, acquisition of the data, analysis or interpretation of the data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest
The authors have no conflicts of interest to disclose.

Funding/support
This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics approval
The patient was treated in accordance with the Declaration of Helsinki. Patient consent was obtained for all investigations.

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