



Case Report: Cerebral Autosomal Dominant Arteriopathy with Sub-Cortical Infarcts and Leukoencephalopathy (CADASIL) with Ataxia

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Article History

Received: 03.11.2023

Accepted: 08.12.2023

Published: 12.12.2023

Abstract: Mood disorders, cognitive decline, headaches, and stroke are among the key symptoms of cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy, or CADASIL [1]. Rarely, ataxia has been noted as a presenting ailment in this case [2]. A man 48 years of age showed signs of developing ataxia. Magnetic resonance imaging (MRI) of the brain showed focal tiny infarct in left internal capsule, subacute intraparenchymal hemorrhage involving left temporal lobe, few old lacunar infarct in bilateral ganglio capsular region, right thalamus and bilateral fronto-parietal periventricular white matter. A mutation in the NOTCH3 gene was verified through genetic testing. It found a variant c.268C>T (p.Arg90Cys). We also address the potential etiology of cerebellar ataxia linked to CADASIL and other factors that could lead to a different differential diagnosis. CADASIL is an uncommon cause of progressive ataxia.

Keywords: Cadasil, Notch 3, Cerebellar hemorrhage, small-vessel disease, Ataxia.

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INTRODUCTION

A hereditary small artery disease that causes dementia and impairment is called cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy, or CADASIL [1]. Hereditary multi-infarct dementia is another name for it. Aura-producing migraines, psychiatric disorders, recurrent strokes, and cognitive impairment are some of the hallmark signs of CADASIL [3, 4]. Small blood arteries, particularly those in the brain, are damaged and cause these symptoms. CADASIL is classified as a rare disease in European definition, meaning that the prevalence of mutation carriers is expected to be between 0.8 and 5 per 100,000 individuals than 1 person in 2,000), an illness that is uncommon (Razvi *et al.*, 2005; Narayan *et al.*, (2012), Moreton *et al.*, (2014), and Chabriet *et al.*, (2009). Recent information, however, points to a greater frequency of NOTCH3. Unhealthy variations in the global populace, with the highest incidence

among people of Asian descent, indicating that milder clinical forms of CADASIL may appear. Continue to be undetected at this time (Rutten *et al.*, 2016; Rutten *et al.*, (2019) [2-5]. A mutation in the NOTCH3 gene results in CADASIL. The NOTCH3 gene codes for a transmembrane receptor protein, the exact function of which is unknown. On the surface of smooth muscle cells that encircle arteries is the NOTCH3 receptor. The extracellular portion of the NOTCH3 receptor's epidermal growth factor-like repeat domains are where mutations are usually found. In small and medium-sized cerebral arteries, accumulation of the pathogenic NOTCH3 receptor protein is the cause of the etiology and phenotypic manifestation of CADASIL. Fibrosis and thickening of the walls of tiny and medium-sized arteries cause cerebral infarctions. Based on symptoms, family history, and brain MRI lesions that are compatible with the disease, CADASIL is a possibility [6]. Although CADASIL patients' brains can be identified

Citation: Shreya N. Jani & Mayank Prajapati (2023). Case Report: Cerebral Autosomal Dominant Arteriopathy with Sub-Cortical Infarcts and Leukoencephalopathy (CADASIL) with Ataxia, Glob Acad J Pharm Drug Res; Vol-5, Iss-6 pp- 61-63.

by MRI, these changes are not exclusive to CADASIL and can also occur with other disorders. Thusly, the CADASIL determination must be affirmed by DNA testing of blood tests for trademark changes in the NOTCH3 quality or by distinguishing granular osmiophilic material considerations on a skin biopsy [7]. At the present, there is no treatment that can fix the sickness or forestall its beginning. Patients ought to be treated for factors that can additionally harm veins, like hypertension, and ought to be urged to keep away from smoking. The viability of tPA for treatment of intense strokes in CADASIL patients is dubious; albeit no contraindication to tPA has been laid out for this particular populace, cautious assessment of earlier microbleeds is proposed. Headaches can be treated with customary analgesics like acetaminophen or NSAIDs. Different medications regularly used to treat intense headache assault like vasoconstrictors: particularly triptans or ergot derivates, are not suggested for patients with CADASIL. Medication, for example, hostile to hypertensive, against convulsants, and antidepressants might be utilized for avoidance of headaches in CADASIL patients. Drug treatment for despondency or other mental anomalies are in some cases required. Mental help is in many cases fundamental, and hereditary guiding is suggested for impacted people and their families [4, 5].

CASE REPORT

A 48-year-old male patient was admitted to the neurology department OPD complaining of left lower and upper limb paralysis, speech difficulties and trouble swallowing for the past three days. He was also spitting out enormous amounts of aggravated saliva. For six months, he had been a recognised case of DM. And he did not take his usual dose of DM medication. He also suffered a stroke six months ago. Additionally, he had a 15-year smoking and chronic alcoholism history. First, lateral medullary syndrome's prognosis was determined. And CADASIL was confirmed as a diagnosis following the confirmation of signs and symptoms and lab tests. His urea levels were quite high in the lab test, at 66 mg/dl. Every other laboratory parameter was normal. The notch 3 mutation test was also carried out; it revealed a positive result for the notch 3 gene and was suggestive of CADASIL. A brain MRI was also performed, and it revealed a small focal acute infarct that included the left internal capsule as well as a partially defined subacute intraparenchymal haemorrhage that affected the left temporal lobe but had no obvious mass effect. It further suggests CADASIL. The abdomen's USG suggested grade 2 fatty liver. The results of the echocardiogram also point to a modest LVH. The patient was initially admitted to the medical ICU before being transferred to the ward. Neurological examination also revealed that patient had ataxia in initial phase. He was given injection

glycopyrrolate to inhibit excessive salivation. He was given metformin for diabetes He was advised for physiotherapy and other symptomatic treatments were given.

DISCUSSION

Any patient who has experienced a transient ischemic attack or stroke, significant mood disorders, an aura-producing migraine episode, dementia, or both, and whose MRI shows widespread signal abnormalities in the subcortical white matter and basal ganglia, should be evaluated for CADASIL. An investigation into the family's genealogy, encompassing all first- and second-degree relatives, need to be prompted by this correlation. To validate the disease's genetic basis, clinical or neuroimaging data—or both—obtained from these sources are essential [7]. Genetic testing can confirm the diagnosis with or without a skin biopsy. Among other conditions, cerebral bleeding can occur in people with cerebral amyloid angiopathy, CADASIL, and hypertensive arteriopathy. Cerebral microbleeds are significant markers of the structural integrity of small blood vessels [2]. Brain hemorrhage mainly occur in the following areas: brainstem, cerebellum, thalamus, basal ganglia, subcortical white matter, and grey-white matter junction [2, 3].

CONCLUSION

In conclusion, our presentation of a CADASIL case aims to increase public awareness of this uncommon but fatal illness. We show that such rare illnesses can induce acute ischemic stroke in patients with typical vascular risk factors. Therefore, we need to adopt a broader perspective, particularly when dealing with patients who have unexpected clinical presentations or diagnostic exam results, like this patient's ataxia and large number of intraparenchymal microbleeds [2].

Acknowledgement

The authors are sincerely thankful to all the members of Department of Pharmacy, Sumandeep Vidyapeeth Deemed to be University (SVDU) for their support.

Conflict of Interest:

The authors declare no conflict of interest.

Abbreviations

CADASIL (Cerebral Autosomal Dominant Arteriopathy with Sub-cortical Infarcts and Leukoencephalopathy), NSAIDs (Nonsteroidal anti-inflammatory drugs) tPA (Tissue plasminogen activator)

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