Case Report

Stroke-Like Episodes and Epilepsy in a Patient with COQ8A-Related Coenzyme Q10 Deficiency

Rithvik Ramesh[1,2], Sundar Hariharan[3], Latha Sundar[4]

[1]Department of Neurology, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai, Tamil Nadu, [2]Consultant Neurologist, Hariharan Diabetes and Heart Care Hospitals, Chennai, Tamil Nadu, Departments of [3]Cardiology and [4]Anasthesiology, Hariharan Diabetes and Heart Care Hospitals, Chennai, Tamil Nadu, India

Abstract

Coenzyme q10 (CoQ10) deficiency is an extremely uncommon disease that has very rarely been reported in adulthood. This case describes an elderly male with ataxia since adolescence, and visual disturbance since 40, presenting with recurrent episodes of seizures. Imaging revealed stroke-like episodes, with other immune and infective evaluations being negative. He was eventually diagnosed to have Primary CoQ10 deficiency secondary to *CoQ8A* mutation. This account highlights the challenges in diagnosing and managing primary Coenzyme Q10 deficiency, especially when it presents later in life with atypical features such as stroke-like episodes.

Keywords: Mitochondrial diseases, primary CoQ deficiency, stroke like episode

Introduction

Coenzyme Q10 (CoQ10) is a naturally occurring compound found primarily within the mitochondria, which facilitates ATP synthesis in the electron transport chain and also acts as a potent antioxidant. Primary CoQ10 deficiency manifests predominantly in early childhood with five major phenotypes: encephalomyopathy, nephropathy, cerebellar ataxia, infantile multisystemic disease, and isolated myopathy.[1] Presentations similar to POLG-like encephalopathy with stroke-like episodes have been rarely reported, manifesting earlier in age.[2] To the best of our knowledge, this case represents the first reported instance of Coenzyme Q10 (CoQ10) deficiency in India and the first known case diagnosed after the age of 60. We report an elderly male with recurrent stroke-like episodes, eventually diagnosed with primary CoQ10 deficiency.

Case Vignette

A 62-year man presented with recurrent episodes of left focal-onset seizures with impaired awareness. He had normal birth and developmental milestones, but suboptimal academic performance, with no family history of neurological illness. He had a seizure) at the age of 15 years. Since then, he had mild tremulousness in his left hand and mild unsteadiness in walking. He had a gradual decline in vision in the fourth decade; ophthalmological evaluation showed macular degeneration. At the age of 57 years, he was hospitalized for acute-onset right homonymous hemianopia and altered sensorium. During the hospital stay, he had focal myoclonus involving the left upper limb. MRI brain showed gyri-form diffusion restriction in the left parietooccipital region [Figure 1a] and left posterior parietal subcortical white matter with corresponding FLAIR hyperintensities, and diffuse cerebral and cerebellar atrophy. He had been initiated on antiplatelets, and antihypertensives and a workup for stroke revealed normal cardiac and carotid evaluation. In follow-up, levodopa and amantadine were tried for apparent parkinsonism, but there was no benefit. At the age of 61, the patient had sudden non-specific visual complaints associated with altered sensorium. MRI brain revealed diffusion restriction in the left thalamus and gyri-form diffusion restriction in the left temporoparietal region [Figure 1b]. With the cerebrospinal fluid analysis and workup for immune-mediated encephalitis and infective etiology being normal, empirical treatment with antiviral and pulse steroids was initiated. The patient's sensorium recovered over the next week, with increased residual myoclonus and visual loss.

During this admission for focal seizures, examination revealed left-sided limb and facial myoclonus, left upper limb dystonia, and mirror movements. MRI showed gyri-form diffusion restriction in the right frontal and parietal region without gliosis or residual changes of previous episodes [Figure 1c]. EEG indicated epileptiform activity in the right frontal region [Figure 2]. CSF analysis and blood routines were normal except for elevated C-reactive protein. Breakthrough seizures progressed to focal status epilepticus despite levetiracetam

Address for correspondence: Dr. Rithvik Ramesh, No. 1, Voltas Colony Main Road, Nanganallur, Chennai, Tamil Nadu - 600 061, India.
E-mail: rithvy@gmail.com

Submitted: 09-Jun-2023 **Revised:** 13-Aug-2023 **Accepted:** 14-Aug-2023
Published: 25-Sep-2023

DOI: 10.4103/aian.aian_511_23

and clobazam. Considering a possible mitochondrial disorder, valproate and sodium-channel blockers were avoided, and perampanel was added. High-dose steroids, antivirals, and mitochondrial supplements were administered, and genetic analysis was sent. Gadolinium-enhanced MRI showed increased gyri-form diffusion restriction in the frontal and temporal lobes with no contrast enhancement. Immune and infective workup was normal, and empirical treatment halted the seizures. After stabilization and supportive care, the patient was discharged with severe persistent myoclonus.

Whole exome sequencing detected a homozygous missense variant (p.Arg299Trp) in the COQ8A gene; the variant is classified as likely pathogenic as per the American College of Medical Genetics recommendations and has been reported previously.[3] His Coenzyme Q10 supplement was increased from 30 mg to 300 mg per day, along with L-carnitine (500 mg), riboflavin (20 mg), pyridoxine (40 mg), ascorbic acid (100 mg) and vitamin E (100 mg) and his statin dose was reduced. After a month of follow-up, the patient reported no further seizures, with almost complete cessation of his myoclonus, though he continued to be bed bound, with grade 4 weakness of his left upper limbs.

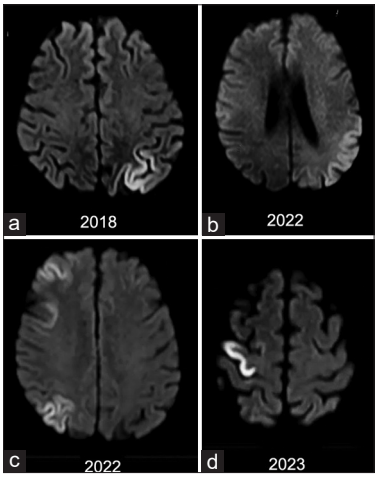

Figure 1: MRI brain diffusion-weighted sequence, axial sections showing (a) left parieto-occipital gyri-from diffusion restriction during his first stroke-like episode in 2018, (b) left parietal gyri-form diffusion restriction in 2022 (c) right frontal and parietal gyri-from diffusion restriction again at the end of 2022 (d) right high frontal gyri-from diffusion restriction in 2023

A month later, the patient's myoclonus worsened, followed by focal seizures with impaired awareness possibly triggered by a urinary tract infection. The seizures evolved into super refractory status myoclonus, persisting despite maximum doses of midazolam and propofol. MRI showed a right frontal gyri-form diffusion restriction similar to the previous episodes [Figure 1d]. Treatment included oral arginine, injectable methylprednisolone, and multiple antiepileptics. Ketamine and anesthetic agents were attempted, followed by the ketogenic diet and intravenous immunoglobulin. The myoclonus subsided temporarily, but the patient eventually succumbed to sepsis during hospitalization.

Discussion

Primary CoQ10 deficiency can be caused by biallelic pathogenic variants in the COQ8A gene.[4,5] Case reports of *CoQ8A* mutations causing POLG-like encephalopathy with stroke-like episodes, status epilepticus, and movement disorders have been described, albeit extremely rare and manifesting at a much earlier age[2] and the literature review shows <10 cases with a similar presentation. This is the first case with a diagnosis of CoQ10 deficiency above the age of 60 years and the first such case from India.[2]

Though it is unclear what caused the destabilization of functionality in this patient, it can occur due to drugs like statins.[6] An interesting investigatory abnormality, in this case, was the elevated CRP levels which are usually associated with inflammatory or infection conditions. Poor mitochondrial health has been associated with systemic inflammation, which

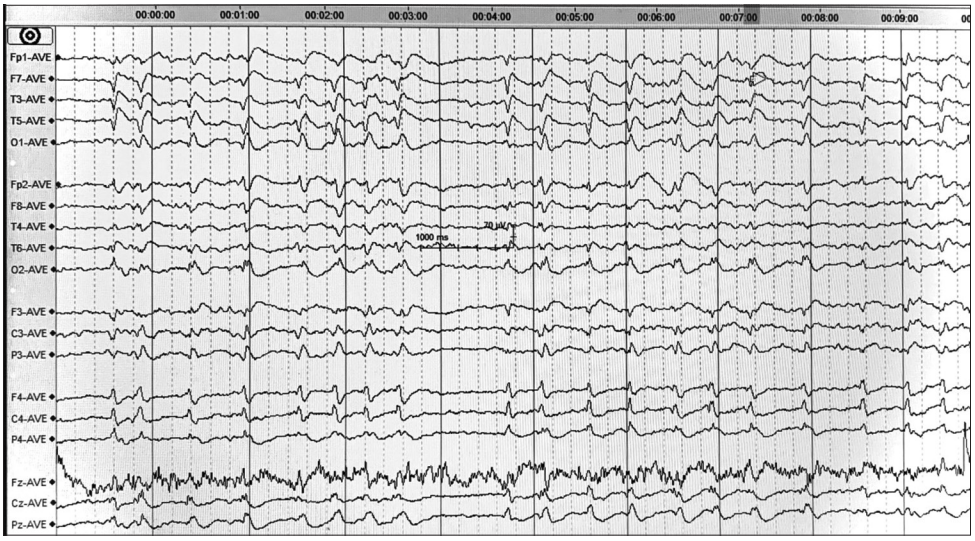

Figure 2: Ictal EEG recording showed periodic lateralized epileptiform discharges

could explain the high levels seen in our case.[7] Response to CoQ10 supplementation is not uniform, with presentations like ataxia and movement disorders showing a better response, with starting doses of 5 mg/kg to a maximum of 15 mg/kg maintained for at least 6 months.[8] Considering the lipophilic nature of the molecule, administration with fats or oils is recommended.[9]

Stroke-like episodes represent vasogenic edema, secondary to both mitochondrial cytopathy and mitochondrial arteriopathy.[10] Nitrous oxide, which is important for endothelium-dependent vascular relaxation, is depleted, secondary to the overactivity of cytochrome c oxidase to which it gets bound.[11] So, the theoretical role of arginine, which is a precursor for NO synthesis, in patients with stroke-like episodes has been considered, with reports for[10] and against it.[12] Intravenous arginine was unavailable locally, so oral sachets were administered to our patient.

In conclusion, an elderly male presented with recurrent stroke-like episodes due to coenzyme Q10 deficiency. Considering mitochondrial disorders in patients above 60 with stroke-like episodes is crucial.

Ethical approval

The authors confirm that the approval of an institutional review board was not required for this work.

Informed consent

Obtained.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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