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Case Report

LYRM7-associated mitochondrial complex III deficiency presenting as infantile hemiparesis with chronic cerebral infarction: a case report

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ABSTRACT

Mitochondrial oxidative phosphorylation (OXPHOS) disorders are rare genetic diseases that primarily affect organs with high energy demands, especially the brain. Although stroke-like episodes are recognised manifestations, presentation as chronic cerebral infarction in infancy is uncommon. Variants in the LYRM7 gene causing mitochondrial complex III deficiency are extremely rare. We report an infant who presented with an acute-onset right-sided hemiparesis following a febrile illness and was found to have a chronic left middle cerebral artery territory cerebral infarction on neuroimaging. The child had delayed developmental milestones, elevated serum lactate, and magnetic resonance spectroscopy findings suggestive of mitochondrial dysfunction. Whole-exome sequencing identified a pathogenic homozygous variant in the LYRM7 gene, confirming mitochondrial complex III deficiency. Supportive management and multidisciplinary rehabilitation resulted in gradual improvement in motor function and developmental progress in follow-up. This case broadens the phenotypic spectrum of LYRM7-associated mitochondrial disease by presenting an unusual case. Recognition of mitochondrial disorders in infants presenting with stroke-like neurological deficits is essential for timely genetic diagnosis, appropriate management, family counselling, and long-term follow-up.

Keywords: Mitochondrial oxidative phosphorylation, LYRM7, Gene

INTRODUCTION

Mitochondrial diseases are a heterogeneous group of inherited metabolic disorders caused by defects in oxidative phosphorylation (OXPHOS), the primary pathway responsible for cellular energy production.[1] Neurological features are common and include developmental delay, seizures, encephalopathy, movement disorders and stroke-like episodes.[2] Mitochondrial complex III deficiency is a rare form of OXPHOS disorder caused by pathogenic variants in several nuclear and mitochondrial genes. Among these, the LYRM7 gene is exceptionally rare and has been reported only in a limited number of cases.[3,4] The clinical phenotype is variable, ranging from developmental delay and hypotonia to progressive neurological deterioration and lactic acidosis.[4,5] However, focal neurological deficits presenting as chronic cerebral infarction in infancy have rarely been described.[5]

The diagnosis of mitochondrial disorders is often challenging because of their diverse clinical presentation and the absence of specific laboratory findings. Advances in molecular genetic testing have significantly improved the identification of rare mitochondrial diseases, enabling early diagnosis, appropriate management, and genetic counselling for affected families.[3]

Here, we report a 10-month-old infant with right-sided hemiparesis and magnetic resonance imaging findings suggestive of chronic left frontoparietal cerebral infarction, who was subsequently diagnosed with

LYRM7-associated mitochondrial complex III deficiency through genetic analysis. This case expands the phenotypic spectrum of LYRM7-related disease and highlights the importance of considering mitochondrial disorders in infants presenting with unexplained focal neurological deficits or stroke-like lesions.

CASE REPORT

A 10-month-old male infant, part of a preterm twin gestation, presented with reduced spontaneous use of the right upper limb, as reported by parents over the past few months. The child had a birth weight appropriate for gestational age and did not require prolonged neonatal intensive care. There was no history of perinatal asphyxia, neonatal seizures, trauma, or central nervous system infection. Developmental concerns centred mainly on asymmetry of limb use, while social interaction and feeding behaviour were appropriate for age. The co-twin, a female, showed normal growth and met neurodevelopmental milestones.

On examination, the child weighed 8.5 kg. Neurological assessment showed decreased active movements of the right upper limb, with increased tone and brisk deep tendon reflexes compared with the left side, consistent with an upper motor neuron pattern of weakness. No cranial nerve deficits were found. The rest of the systemic examination was unremarkable.

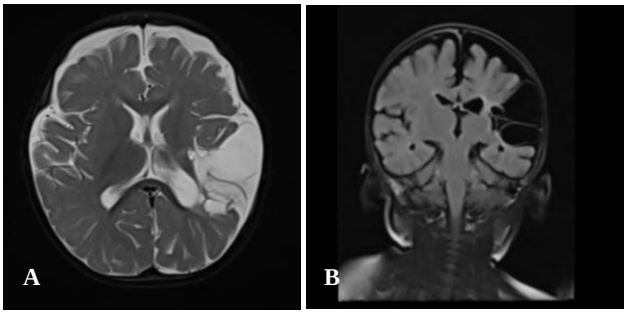

Figure 1: (A) Axial T2-weighted image showing a large cystic encephalomalacic cavity involving the left frontoparietal region with surrounding gliosis, diffuse left cerebral hemispheric volume loss, and ex vacuo dilatation of the left ventricle, consistent with chronic cerebral infarction and (B) coronal FLAIR image demonstrating extensive left frontoparietal cortico-subcortical encephalomalacia with associated left cerebral hemispheric atrophy, corresponding to chronic cerebral infarction.

Magnetic resonance imaging (MRI) of the brain showed extensive cortico-subcortical gliosis and encephalomalacia involving the left frontoparietal junction, extending into the insular cortex, frontal operculum, and the ipsilateral temporal lobe, consistent with chronic cerebral infarction. Mild T2 FLAIR (T2 weighted fluid-attenuated inversion recovery) hyperintensities were seen in the basalis pontis and the bilateral middle cerebellar peduncles, with mild diffusion restriction in the latter. Associated findings included diffuse asymmetric atrophy of the left cerebral hemisphere with white-matter volume loss, ex vacuo prominence of the left lateral ventricle, and mild ipsilateral striatal atrophy. Mild diffuse thinning of the corpus callosum was also noted. No imaging features indicative of acute ischaemia were identified.

Given the early onset of focal neurological deficits without a clear vascular or perinatal cause, metabolic and genetic causes were suspected. Genetic analysis identified a pathogenic autosomal recessive mutation in the LYRM7 gene, confirming a mitochondrial OXPHOS disorder due to mitochondrial complex III deficiency (nuclear type 8). The diagnosis was based on clinical, radiological, and molecular genetic findings.

The child was started on supportive management, including structured physiotherapy aimed at improving motor function and preventing contractures. Parents were counselled about the genetic nature of the disorder and prognosis. At follow-up, the child showed gradual improvement in limb use with ongoing rehabilitative therapy, while developmental surveillance continued. The unaffected co-twin remained developmentally normal.

DISCUSSION

OXPHOS disorder results from defects in the mitochondrial respiratory chain, leading to impaired ATP (adenosine triphosphate) production and cellular energy failure. Organs with high metabolic demand, especially the central nervous system, are most vulnerable to mitochondrial dysfunction, causing various neurological symptoms like developmental delay, stroke-like episodes, seizures, and encephalopathy.[4]

Previous reports have described patients with LYRM7-associated complex III deficiency commonly presenting with developmental delay, cavitating leukoencephalopathy, lactic acidosis and progressive neurological deterioration.[5] In contrast, our patient presented predominantly with infantile hemiparesis and unilateral chronic cerebral infarction, thereby expanding the phenotypic spectrum of this rare disorder.

The LYRM7 gene encodes a mitochondrial protein crucial for the assembly and stabilisation of respiratory chain complex III (cytochrome bc1 complex).[6] Pathogenic variants in LYRM7 disrupt electron transport and oxidative phosphorylation, leading to reduced ATP production and increased oxidative stress.[7] Complex III deficiency is a rare mitochondrial disorder, with only a limited number of phenotypes reported in the literature, most often involving progressive neurological impairment and multisystem disease.[8] This case broadens the clinical spectrum by showing a mainly focal neurological presentation associated with unilateral cerebral injury.

Stroke-like lesions in mitochondrial disease differ from classical vascular infarctions in that they arise primarily from metabolic failure rather than arterial occlusion.[9] Neuronal energy deficiency may lead to selective cortical vulnerability, impaired ion homeostasis, and ultimately tissue loss and gliosis.[9] The extensive cortical-subcortical encephalomalacia and hemispheric atrophy noted in this patient likely represent chronic consequences of mitochondrial energy failure during early brain development.[10] The absence of acute diffusion restriction on neuroimaging further supports a chronic metabolic process rather than an acute thromboembolic event.[10]

A key aspect of this case is the discordant phenotype observed between twins, with the co-twin exhibiting normal neurodevelopment. This finding strengthens the argument for a genetic basis of disease expression and emphasises phenotypic variability even when prenatal environments are shared. Recognising such variability is crucial, as mitochondrial disorders can be mistaken for static perinatal brain injury or cerebral palsy when presenting with early hemiparesis.

The diagnostic pathway in this patient highlights the importance of considering metabolic and genetic causes in infants presenting with unexplained focal neurological deficits. Early neuroimaging suggested a non-vascular cause due to asymmetric cerebral atrophy and chronic changes without a clear perinatal insult. Subsequent genetic testing enabled a definitive diagnosis, emphasising the growing role of genomic evaluation in paediatric neurology.

Management of mitochondrial complex III deficiency primarily involves supportive care, including rehabilitation, symptomatic treatment, and genetic counselling. Early physiotherapy can enhance functional outcomes by encouraging neuroplasticity and preventing secondary musculoskeletal issues.

Limitations

This report is limited by its single-case design and the absence of longitudinal follow-up data. Functional enzymatic studies were not accessible. Nevertheless, the clinical, radiological, and genetic findings collectively support the diagnosis.

CONCLUSION

LYRM7-associated mitochondrial complex III deficiency can present with focal neurological deficits that resemble infantile stroke. Early recognition of mitochondrial disease and prompt genetic testing are crucial for accurate diagnosis, multidisciplinary management and genetic counselling.

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REFERENCES

1. Lax NZ, Gorman GS, Turnbull DM. Review: Central nervous system involvement in mitochondrial disease. Neuropathol Appl Neurobiol. 2017;43:102-18.
2. Fernandez-Vizarra E, Zeviani M. Mitochondrial disorders of the OXPHOS system. FEBS Lett. 2021;595:1062-106.
3. Invernizzi F, Tigano M, Dallabona C, Donnini C, Ferrero I, Cremonte M, et al. A homozygous mutation in LYRM7/MZM1L associated with early onset encephalopathy, lactic acidosis, and severe reduction of mitochondrial complex III activity. Hum Mutat. 2013;34:1619-22.
4. Luke ND, Vijayakrishnan Nair A, Sivadasan A, Muthusamy K, Thomas MM, Yoganathan S, et al. A novel presentation and variable phenotypic spectrum of homozygous start-loss variant in LYRM7-associated mitochondrial complex III deficiency. Am J Med Genet A. 2025;197:e64105.
5. Khan GS, Bayat S, Azizimalamiri R, Nikoohemmat M, Mashayekhi N, Nabilou S, et al. Expanding the clinical spectrum of LYRM7-associated mitochondrial complex III deficiency: insights from new cases and literature review. J Mol Neurosci. 2026;76:72.
6. Kirby DM, Thorburn DR. Approaches to finding the molecular basis of mitochondrial oxidative phosphorylation disorders. Twin Res Hum Genet. 2008;11:395-411.
7. Alfattal R, Alfarhan M, Algaith AM, Albash B, Elshafie RM, Alshammari A, et al. LYRM7-associated mitochondrial complex III deficiency with non-cavitating leukoencephalopathy and stroke-like episodes. Am J Med Genet A. 2023;191:1401-11.
8. Hempel M, Kremer LS, Tsiakas K, Alhaddad B, Haack TB, Löbel U, et al. LYRM7-associated complex III deficiency: A clinical, molecular genetic, MR tomographic, and biochemical study. Mitochondrion. 2017;37:55-61.
9. Tabarki B, Hakami W, Alkhuraish N, Graies-Tlili K, Nashabat M, Alfadhel M. Inherited metabolic causes of stroke in children: mechanisms, types, and management. Front Neurol. 2021;12:633119.
10. Finsterer J, Zarrouk-Mahjoub S. Cerebral imaging in paediatric mitochondrial disorders. Neuroradiol J. 2018;31:596-608.

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