# Imaging in Sequential Stroke-like Episodes in Adult MELAS

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Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS) is a mitochondrial disorder with diverse clinical manifestations including diabetes, short stature, sensorineural hearing loss, and clinical or subclinical myopathy related to energy failure from highly metabolically active tissues resulting in lactic acidosis.[1,2] Seizures or stroke-like episodes occur with cortical imaging abnormalities which do not follow single vascular territories due to metabolic insufficiency and smooth muscle dysfunction within vessel walls as opposed to thrombosis.[1,3] Repeated episodes can lead to cumulative neurologic deficit and laminar necrosis.[3] Patients are treated with arginine acutely and as maintenance therapy with coenzyme Q10.[4] The most common mutation is in mitochondrial m.3243 A > G, and while the majority present before age 40,[1,2] older onset is reported[5] making the diagnosis more difficult when presenting in later life, mimicking ischemic stroke. Magnetic resonance imaging (MRI) can differentiate stroke-like episodes in MELAS from traditional ischemic strokes.

A 53-year-old woman with diabetes mellitus presented to a peripheral hospital with aphasia and right hemiparesis. Ischemic stroke was suspected; however, computed tomography (CT) and CT angiography showed no cerebrovascular abnormality. She was treated empirically for viral encephalitis, cerebrospinal fluid (CSF) was bland with negative viral studies, and MRI demonstrated left posterior hemispheric cortical ribboning with cytotoxic edema (Figure 1). Due to concern for neoplasm or prion disease, she was referred to our tertiary center for brain biopsy which showed non-specific inflammatory infiltrates without vasculitis or evidence of prion disease or infectious cause.

She was transferred to our service and it became apparent she had sensorineural hearing loss and short stature. The possibility of MELAS was raised and arginine and coenzyme Q10 were started with stabilization of symptoms. Serum and CSF lactate were significantly elevated at 12.2 mmol/L (reference: 0.5–2.2) and 4.5 mmol/L (reference: 2.0–4.0), respectively. Weakness resolved and there was no electromyographic evidence of subclinical myopathy; however, biopsy of the right deltoid revealed ragged-red fibers suggestive of mitochondrial myopathy and ultimately blood leukocytes tested positive for heteroplasmic m.3243A > G mutation. She had a second stroke-like episode 1 year later, with MRI changes in the right hemisphere (Figure 2) which stabilized again, but with persistent partial fluent aphasia without weakness at last follow up.

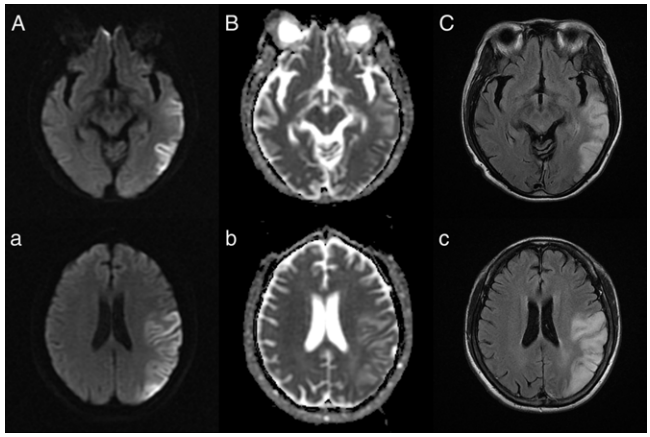


***Figure 1:*** *Axial brain magnetic resonance imaging during stroke-like episode. Diffusion-weighted imaging (A,a) shows cortical hyperintensity in the left temporal, parietal, and occipital lobes with cortical restricted diffusion on apparent diffusion coefficient map (B,b). T2-Fluid attenuated inversion recovery sequences (C,c) show cortical hyperintensity with edema and sulcal effacement in the same areas.*

This case highlights sequential hemispheric cortical ribboning and subsequent laminar necrosis from stroke-like episodes in MELAS, with typical posterior predominance.[6,7] Cortical predilection reflects higher relative metabolic demand and while also seen in status epilepticus, hypoxic-ischemic injury, encephalitis, toxic-metabolic encephalopathy such as hyperammonemia, and prion disease, in those situations is usually bilateral.[3,8] Magnetic resonance spectroscopy may show a characteristic lactate doublet peak[7,9] and can be useful to monitor treatment response;[9] however, it has limitations as lactate levels fluctuate and may be below the level of detection with CSF lactate < 4.0 mmol/L.[7]

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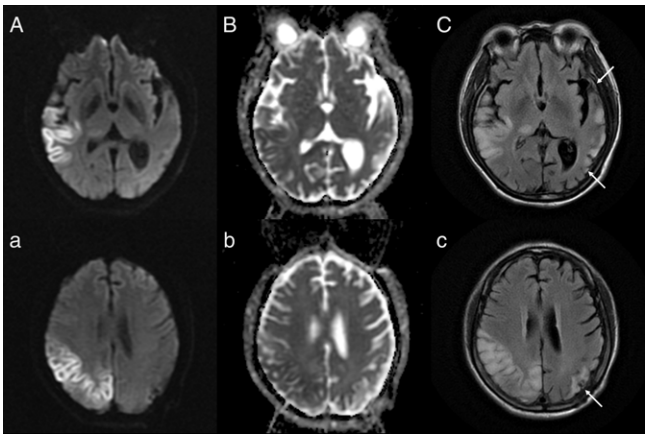


***Figure 2:*** *Axial brain magnetic resonance imaging during second stroke-like episode. Diffusion-weighted imaging (A,a) shows cortical hyperintensity now involving the right temporal, parietal, and occipital lobes with cortical restricted diffusion on apparent diffusion coefficient map (B,b). T2-Fluid attenuated inversion recovery sequences (C,c) shows cortical hyperintensity in those areas, with atrophy and residual hyperintensity in the left temporal and occipital cortex (arrows).*

Instead, the diagnosis in this case was confirmed on muscle biopsy and genetic testing with compatible clinical features of mitochondrial cytopathy. Perivascular inflammatory infiltrates on brain biopsy have been reported but are non-specific.[10] Although rare, MELAS can mimic stroke in older patients, but is distinguished on MRI and with appropriate clinical suspicion, unnecessary biopsy may be avoided.

## Disclosures

The authors report no disclosures or conflicts of interest.

## Statement of Authorship

TC provided conception and study design, acquisition of data, analysis and interpretation of data, and drafting the manuscript. LW provided analysis and interpretation of data and critical revision of the manuscript for intellectual content.

## References

1. DiMauro S, Schon EA, Carelli V, Hirano M. The clinical maze of mitochondrial neurology. Nat Rev Neurol. 2013;9(8):429–44.
2. Johns DR. Mitochondrial DNA and disease. N Engl J Med. 1995;333(10):638.
3. Valanne L, Paetau A, Suomalainen A, Ketonen L, Pihko H. Laminar cortical necrosis in MELAS syndrome: MR and neuropathological observations. Neuropediatrics. 1996;27(3):154–60.
4. Pfeffer G, Majamaa K, Turnbull DM, Thorburn D, Chinnery PF. Treatment for mitochondrial disorders. Cochrane Database Syst Rev. 2012;2012(4):CD004426.
5. Sinnecker T, Andelova M, Mayr M, et al. Diagnosis of adult-onset MELAS syndrome in a 63-year-old patient with suspected recurrent strokes - a case report. BMC Neurol. 2019;19(1):91.
6. Sproule DM, Kaufmann P. Mitochondrial encephalopathy, lactic acidosis, and strokelike episodes: basic concepts, clinical phenotype, and therapeutic management of MELAS syndrome [published correction appears in Ann N Y. Ann N Y Acad Sci. 2008 2009;1142(1):133–58.
7. Lin DD, Crawford TO, Barker PB. Proton MR spectroscopy in the diagnostic evaluation of suspected mitochondrial disease. AJNR Am J Neuroradiol. 2003;24(1):33–41.
8. Sheerin F, Pretorius PM, Briley D, Meagher T. Differential diagnosis of restricted diffusion confined to the cerebral cortex. Clin Radiol. 2008;63(11):1245–53.
9. Möller HE, Kurlemann G, Pützler M, Wiedermann D, Hilbich T, Fiedler B. Magnetic resonance spectroscopy in patients with MELAS. J Neurol Sci. 2005;229:131–9.
10. Testai FD, Gorelick PB. Inherited metabolic disorders and stroke part 1: fabry disease and mitochondrial myopathy, encephalopathy, lactic acidosis, and strokelike episodes. Arch Neurol. 2010;67(1):19–24.



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