



Correspondence

The “Toenail Sign” in MELAS May Be the End Stage of a Stroke-like Lesion



To the Editor:

I read with interest the article by Kuwabara et al. about an 11-year-old boy with mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) due to the variant m.3243A>G who presented with gyral necrosis and cerebral atrophy on cerebral magnetic resonance imaging (MRI) compared with images three years earlier.¹

Partial gyral signal suppression on T2/fluid-attenuated inversion recovery sequences resembles black toenails, hence the term “black toenail sign” was coined by Whitehead et al. in 2017.² The underlying pathologic mechanism is unknown, but it has been speculated that the toenail sign may result from hypoxia, ischemia, impaired supply of substrates, impaired removal of reactive oxygen species or toxins, or neuronal overactivity with consecutive energy depletion.¹

Pathogenic mechanisms not considered by the authors include gyral bleeding and stroke-like episodes. Gyral bleeding should be considered because cortical laminar necrosis, a typical stage of a stroke-like lesion, the morphological equivalent on imaging of a stroke-like episode in the subacute stage, may be the result of intracortical gyral hemorrhage or petechial gyral microhemorrhages.³ Stroke-like lesions should be considered because they may be restricted to the cortex and associated with epileptiform discharges on electroencephalography and cortical hyperperfusion on single-photon emission computed tomography in the acute stage.³ Stroke-like lesions typically present on multimodal MRI as vasogenic edema (diffusion-weighted imaging hyperintense, apparent diffusion coefficient hyperintense).

It would be interesting to know whether the index patient had a history of stroke-like episodes before the MRI investigation. Such episodes can manifest clinically with headache, seizures, psychiatric abnormalities (confusion, hallucinations, psychosis), hemiparesis, hemianopia, apraxia, alexia, or speech disturbance.⁴ Stroke-like episodes are characteristic of MELAS syndrome but may occasionally occur in mitochondrial disorders other than MELAS.⁵

Overall, the “black toenail sign” may also be the end stage of a stroke-like lesion or of gyral microbleeds. Identification of a stroke-like episode/lesion is crucial as treatment with nitrous oxide precursors may prevent their recurrence.

References

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