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Letter to the Editor

Before a Diagnosis of Primary Pulmonary Hypertension is Made in the Context of MELAS, All Secondary Causes Must be Carefully Ruled Out

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Letter to the Editor

The article by Kanai *et al.* ^[1] is interesting, but several points warrant discussion.

First, the diagnosis of MELAS is questionable ^[1]. MELAS is typically a multisystem disorder diagnosed using the Hirano criteria or the Japanese criteria ^[2, 3]. According to the Japanese criteria, MELAS is diagnosed when there are signs of encephalopathy associated with dementia or epilepsy, stroke-like episodes (SLEs) at a young age, lactic acidosis, and the presence of ragged-red fibers (RRF) in a muscle biopsy ^[3]. According to the Hirano criteria, MELAS is diagnosed when SLEs occur before the age of 40, accompanied by seizures or dementia, lactic acidosis, or RRF, and there is a history of normal early development alongside recurrent headaches or recurrent vomiting ^[2]. Applying these criteria, the patient did not have MELAS, but rather a non-syndromic mitochondrial disorder.

Second, various secondary causes of pulmonary hypertension (PH) were not adequately ruled out ^[1]. There is no mention of whether thiamine levels were normal or low ^[1]. Since thiamine deficiency is associated with PH, it is essential to determine whether levels of this vitamin were normal. Likewise, a normal pulmonary CT-angiography does not necessarily rule out tiny subsegmental thrombi, given the limited resolution of the scan. Was the D-dimer level elevated? Furthermore, connective tissue disease, HIV infection, obstructive sleep apnea, chronic high-altitude exposure, sarcoidosis, and chronic hemolytic anemia were not ruled out ^[4]. What was the cause of the index patient's anemia? It is also conceivable that the preceding pneumonia caused the PH.

Thirdly, the diagnosis of an SLE remains questionable ^[1]. No MRI scans were presented, and the progression of the cerebral lesion was not described. SLEs manifest on imaging as stroke-like lesions exhibiting a characteristic pattern on multimodal MRI and FDG-PET ^[5]. These lesions are hyperintense on T2/FLAIR, DWI, and PWI and hypointense on OEF. They show hypermetabolism on FDG-PET, are not confined to a vascular territory, and initially enlarge to a maximum size before decreasing in size and intensity, ultimately persisting as a cyst, white matter lesion, "toenail sign," laminar cortical necrosis, or atrophy ^[5]. MRS reveals a lactate-peak within the stroke-like lesion. Was such a pattern observed in the patient in question? Did the patient exhibit typical features of an SLE, such as seizures, hemiparesis, hemianopsia, headaches, or aphasia?

Finally, the patient's long-term clinical course was not reported. Did the PH and cerebral lesions resolve completely by the one-year follow-up? Did the patient develop further phenotypic features of MELAS syndrome in addition to PH, SLE, anemia, or elevated amylase levels?

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