**Letter to the Editor**


# Respiratory insufficiency in Leigh syndrome is multifactorial and requires further investigation in addition to polysomnography

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**Introduction**

We read with interest the article by Wang *et al*. about a retrospective study of six patients with Leigh syndrome who underwent polysomnography revealing increased wake after sleep onset [1]. Additionally, Leigh syndrome patients had greater values of heart rate, 3% oxygen desaturation-index, and lower values of sleep efficiency, respiratory arousal-index, and total sleep time [1]. The study is appealing but raises concerns.

According to table-1 patient-3 and patient-6 had electro-encephalography (EEG) abnormalities [1]. Because Leigh syndrome is commonly associated epilepsy [2], we should know what EEG abnormalities were recorded in these two patients, if they were on a long-term treatment with anti-seizure drugs (ASDs), and if their history was positive for epilepsy. Surprisingly, in none of the six patients was the history positive for epilepsy.

A limitation of the study is that the included patients were not investigated for cardiac disease. Leigh syndrome can be complicated by cardiac involvement, which includes hypertrophic cardiomyopathy, dilated cardiomyopathy, noncompaction, ventricular arrhythmias, or sudden cardiac death [3, 4].

Leigh syndrome can be complicated also by a number of orthopaedic abnormalities, which may decrease cardiac and pulmonary functions. These include scoliosis, thorax deformities, hyperlordosis, hyperkyphosis, and hyperlaxity of joints. These abnormalities can reduce lung function significantly and can lead to respiratory dysfunction.

Because Leigh syndrome is commonly complicated by lactic acidosis and because lactic acidosis can lead to breathing abnormalities [5], it is crucial to know the results of blood gas analysis (BGA) and how many of the six patients with Leigh had lactic acidosis or acidemia due to other causes.

Because cerebral magnetic resonance imaging (MRI) showed a brainstem lesion only in patient four and therefore does not explain breathing abnormalities in the other patients, it cannot be ruled out that patients without brainstem affection had

involvement of the respiratory muscles. Myopathy can be a phenotypic feature of patients with Leigh syndrome, and respiratory muscles can be affected in these patients. Patient-4 and patient-2 had myopathy but how was myopathy ruled in the other four patients?

Overall, the interesting study has limitations that challenge the results and their interpretation. Clarifying these weaknesses would strengthen the conclusions and could improve the study. Diagnosing mitochondrial encephalopathy, lactic acidosis and stroke-like episode (MELAS) syndrome requires not only the presence of an appropriate phenotype but also documentation of a causal genetic defect. Because breathing abnormalities in patients with Leigh syndrome are multi-causal, it is crucial to evaluate respiratory insufficiency not only by polysomnography but also by cerebral MRI, BGA, needle electromyography (EMG), and EEG.

**Declarations**

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Consent for publication: was obtained from the patient
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