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Letter to the Editor

Late onset Leigh syndrome mimicking central nervous system vasculitis

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Dear Sir,

Leigh syndrome is typically a disorder of infancy and early childhood. Only a few patients with late onset Leigh syndrome have been reported [1]. The disorder is most likely underdiagnosed in adolescents and adults. In the past, many adults with Leigh syndrome were misdiagnosed with multiple sclerosis [2,3].Here, we describe a 17 year old girl with Leigh syndrome mimicking as central nervous system vasculitis. This patient with history of learning disability developed blurring of vision and dysphagia followed by tiredness, fever, chest pain, shortness of breath, and intermittent double vision. On examination, she had tachycardia, hypertension, and anisocoria. MRI of the brain showed lesions in the right brainstem and the left basal ganglia concerning for stroke. CT angiography showed diffuse, subtle irregularities of intracranial arteries suggesting vasculitis. A detailed work for vasculitis was unremarkable except a high ESR at 33. She was treated with intravenous pulse methylprednisone followed by oral steroids. Her symptoms improved and steroids were tapered. However, she developed irregular breathing and poor respiratory effort during the taper. She developed restricted lateral gaze bilaterally and mild vertical nystagmus in upward gaze. A repeat MRI of the brain showed small foci of T2 hyperintensities bilaterally within the basal ganglia, midbrain, posterior pons, and medulla (Fig. 1). This worsening in symptoms was considered secondary to a flare up of vasculitis due to steroid tapering. Aggressive immunosuppressive therapies were instituted but the patient had no improvement. Bilateral carotid and left vertebral artery angiogram was normal. Based upon repeat MRI findings, a mitochondrial etiology was suspected. Respiratory chain enzyme analysis on skeletal muscle biopsy showed decreased activity of all complexes except complex II. A next generation sequencing panel for mitochondrial DNA and nuclear genes implicated in mitochondrial disorders, performed on skeletal muscle detected c.626 C > T (p.R181Sfs*5) mutations in homozygous state in *MTFMT* gene. In a recent study, pathogenic mutations in *MTFMT* gene were found in 11 patients with Leigh syndrome [4]. The age at onset of symptoms in the cohort ranged from birth to 17 years. The most common pathogenic mutation in *MTFMT*, c.626 C > T, was

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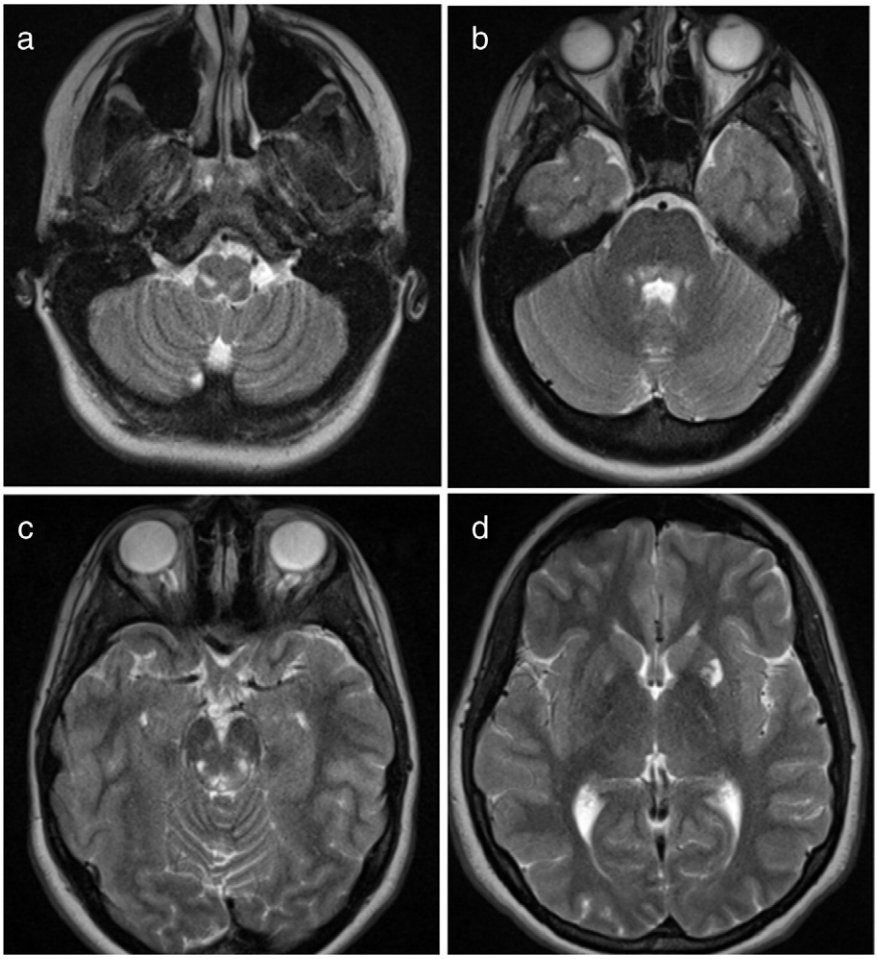

Fig. 1. MRI of the brain of the patient showing small foci of hyperintensities in the medulla (a), posterior pons (b), midbrain (c), and basal ganglia (d) bilaterally in T_2-weighted axial scans.

detected in this patient and is estimated to have allele frequency of 0.1% in the European population. This case underscores the importance of considering Leigh syndrome in differential diagnosis of acute or sub-acute neurological symptoms in adolescents and adults. Symptoms related to the basal ganglia or brain stem, history of developmental delays or learning disability, high plasma or CSF lactate, characteristic radiological findings, multisystem involvement, and absence of a unifying diagnosis should alert the clinician to the possibility of a mitochondrial disorder.

Author contribution

Dr. Pankaj Prasun was involved in patient care, laboratory interpretation, initial drafting of the manuscript, and revisions of each draft.

Dr. Loren Del Mar Pena supervised the case report, was involved in patient care, laboratory interpretation, and revising the manuscript critically for important intellectual content.

All authors have approved the article as it is written. This work was carried out at the Duke University Medical Center.

Declaration of conflicting interests

Dr Pankaj Prasun has no potential conflicting or competing interests that could in any way affect the conduct of the study, interpretation of results, or preparation of the manuscript.

Dr Loren Del Mar Pena has no potential conflicting or competing interests that could in any way affect the conduct of the study, interpretation of results, or preparation of the manuscript.

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