Adult-Onset Leukoencephalopathy with Brain Stem and Spinal Cord Involvement and Lactate Elevation Letter to the Editor

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Dear Editor,

In their recent paper entitled 'Leukoencephalopathy with Brain Stem and Spinal Cord Involvement and Lactate Elevation First Case Report in Thai Patient', Aungsumart et al. present an interesting case of a 37-year-old female patient manifesting as ataxic dysarthria and gait ataxia for 10 months[1]. The patient was diagnosed with leukoencephalopathy with brain stem and spinal cord involvement and lactate elevation (LBSL) based on typical MRI and MRS findings without genetic confirmation of a *DARS2* mutation. As the authors claimed that this is the first case report in Thailand, there are some additional points that should be highlighted.

First, most often LBSL is a childhood- or juvenile-onset disorder, it rarely occurs as an adult-onset form as presented in the authors' report[2]. However, adult-onset (18 years and older) LBSL has been reported in the Han Chinese and European populations[3,4]. The phenotypic differences between childhood-onset and adult-onset LBSL have not been well characterized; however, clinical information collected from the Amsterdam study indicates that the clinical severity varies from a rapidly fatal disease of infantile onset to a slow and mild disease of adult onset[4]. In addition, early-onset cases usually have severe clinical disease, including intelligence and cognition decline[3]. In the authors' case report, the patient's onset of neurological deficits was at approximately 36-37 years of age, which might be considered a rather late-onset compared to previously published adult-onset case reports[3,4].

Second, LBSL is typically characterized by slowly progressive pyramidal, cerebellar and dorsal column dysfunction[2]. In the authors' case, the patient's clinical symptoms progressed from gait

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ataxia to abnormal coordination of upper limbs, and finally to ataxic dysarthria during a 10-month period prior to diagnosis. The progression of cerebellar symptoms was rather prominent with a slight degree of pyramidal tract signs and normal proprioception. Feng et al. reported an adult-onset case with the age of onset of pyramidal and cerebellar symptoms at 20 years of age, in which it took 18 years to develop dependent ambulation[3]. Knaap et al. reported in their cross-sectional observational study that 50% of adult-onset cases required support for walking and 13% were fully wheelchair dependent[4]. It would be interesting to monitor the authors' late-onset case in order to observe the length of time it takes for the patient to develop dependent ambulation, and if this occurs, whether it relates to the deterioration of the pyramidal or proprioceptive dysfunction.

Third, axonal neuropathy is a major feature and can be found in approximately 60% of LBSL patients[5]. Reduced motor conduction velocities and decreased motor amplitudes in lower limbs can be observed in nerve conduction studies (NCS). Electromyography (EMG) can reveal chronic axonal injury, showing spontaneous activity in distal leg muscles, and reduction in the number of motor units[5]. EMG usually reveals axonal, distal more often than proximal, and motor more often than sensory neuropathy[6]. Axonal degeneration in peripheral nerves has also been observed in pathological studies[7]. However, all of the reports of axonal injury have been investigated in early-onset LBSL patients. It might be worthwhile to conduct NCS and EMG on the authors' patient for evidence of peripheral axonal neuropathy in this late-onset case.

Overall, the first case report of adult-onset LBSL in a Thai patient as presented by the authors strongly demonstrates that the clinical course of LBSL is not uniform and that the clinical severity varies from early onset to adult onset. Long-term monitoring of the patient will provide additional longitudinal data on this spectrum of the disease. Currently, research on the natural history of LBSL is being conducted[8]. Further studies of the molecular background, involving either common or novel mutations of the *DARS2* gene, of Thai patients with typical LBSL findings from MRI and spectroscopy should be carried out.

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