International Journal of Scientific Research in Dental and Medical Sciences

www.ijsrdms.com

Leukoencephalopathy with Brain Stem and Spinal Cord Involvement and Lactate Elevation (LBSL) Based on Typical MRI and MRS Findings: A Case Report

Mohammad Ali Sahraian*, Abootorab Shahmohammadi, Sareh Shahmohammadi, Rozita Doosti

Sina MS Research Center, Department of Neurology, Sina Hospital, Tehran University of Medical Sciences, Hassan Abad square, Tehran, Iran

ARTICLE INFO

Article history:
Received 05 December 2021
Received in revised form 23 January 2022
Accepted 06 February 2022
Available online 15 February 2022

Keywords:
Brain stem
Leukodystrophy
Leukoencephalopathies
Spinal cord
White matter

ABSTRACT

Leukoencephalopathy with brain stem and spinal cord involvement and lactate elevation (LBSL) is a rare autosomal recessive disorder that has been known in recent years. Clinically, patients usually present slowly progressive symptoms of pyramidal, cerebellar and dorsal column dysfunction. In 2012 magnetic resonance imaging (MRI) criteria were proposed for diagnosing these patients based on characteristic MRI abnormalities in selective areas of the brain and spinal cord. These imaging features help clinicians to distinguish it from other white matter diseases. Here we report a case diagnosed based on characteristic MRI abnormalities in selective areas and high lactate in the magnetic resonance spectroscopy (MRS).

1. Introduction

Leukoencephalopathies are generally recognized as a disease associated with white matter changes of the brain, and in many of them, the underlying causes are still unknown. In some of these cases, involvement of specific areas of the brain can provide diagnostic keys to find the cause of the disease.[1, 2] Leukoencephalopathy with brain stem and spinal cord involvement and lactate elevation (LBSL) is a rare autosomal recessive disorder. In the adult-onset type, cord involvement and its symptoms may sometimes be misdiagnosed as an autoimmune disease of the nervous system, such as demyelinating diseases. Here we report a case with MRI criteria of LBSL.[1]

2. Case presentation

A 36-year-old woman who has developed symptoms of dizziness, imbalance, hand tremor and weakness with a predominance of lower extremity involvement about two years before her last visit. She was diagnosed with a possible metabolic or genetic disease during two years, and conservative treatment was recommended. The patient can fully perform daily activities up to one years before her referral. Last year, she noticed an exacerbation of the disease and weakness in the lower extremities (right more than left), which was re-evaluated, and corticosteroids were administered that time with the possibility of superimposed inflammatory disease. The patient's symptoms show a relative improvement, and her progression of the disease stopped for a few months after the corticosteroid pulse. The recent patient's complaint was an exacerbation of tremor in her upper limbs and imbalance while walking, which she felt like walking on a cotton surface. On neurological examination, her force was 4/5 in the lower extremity and normal in the upper limbs with hyperreflexia and positive Babinski. The patient had asymmetric intention tremor, and the position and Romberg test both were impaired, and she could not perform the tandem gait.

Routine lab tests including complete blood count (CBC), liver function test (LFT), Thyroid Stimulating Hormone (TSH), lactate, pyruvate, serum B12 level, antinuclear antibody (ANA), Human T-Lymphotropic Virus type 1.2 (HTLV1.2) antibody, and human immunodeficiency virus (HIV) antibody were negative. Because of relative steroid response, a cerebrospinal fluid (CSF) study was performed, and IgG index and oligoclonal band (OCB) were negative. The cranial magnetic resonance imaging (MRI) showed multifocal signal abnormalities as hyperintense lesion on T2-weighted and flair in the cerebral white matter, splenium of the corpus callosum in the supra-tentorial location (Fig. 1).and cerebellar white matter, a pyramidal tract of the medulla

* *Corresponding author. Sareh Shahmohammadi*
E-mail address: drsarehsh@gmail.com
Sina MS Research Center, Department of Neurology, Sina Hospital, Tehran University of Medical Sciences, Hassan Abad square, Tehran, Iran
http://doi.org/10.30485/IJSRDMS.2022.325233.1241

oblongata, superior cerebellar peduncle, intra-parenchymal trajectories of the trigeminal nerves and medial lemniscus in the infra-tentorial location, and the dorsal columns and the lateral corticospinal tracts of cervical and thoracic part of the spinal cord without any abnormal enhancement (Fig. 2).

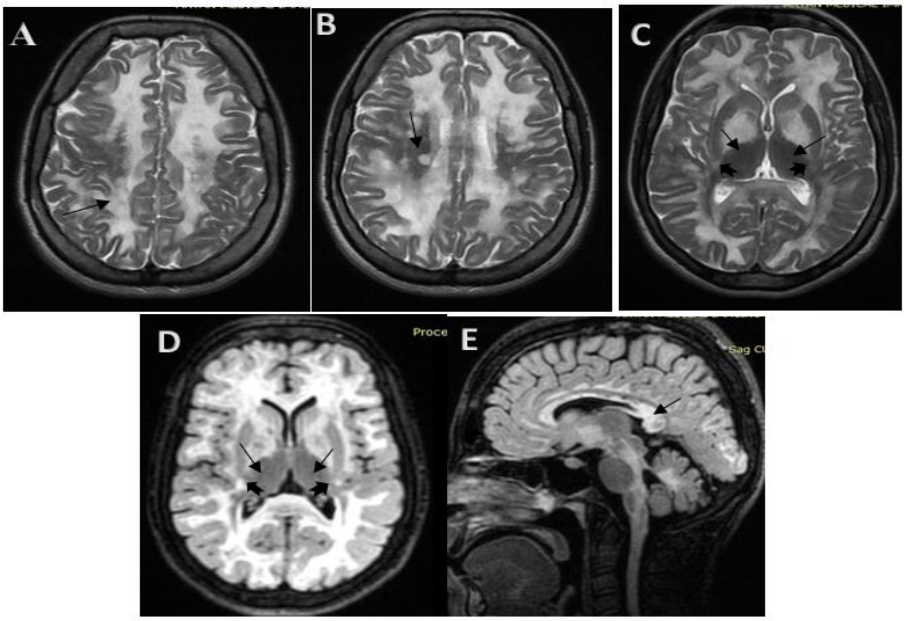

Fig. 1. Flair: (A) Hyper-intense confluent and (B) Spotty lesions in the cerebral white matter. (C, D) Sparing of the thalamus (thin arrows); Posterior limb of the internal capsule involvement (thick arrows). (E) Splenium of the corpus callosum involvement.

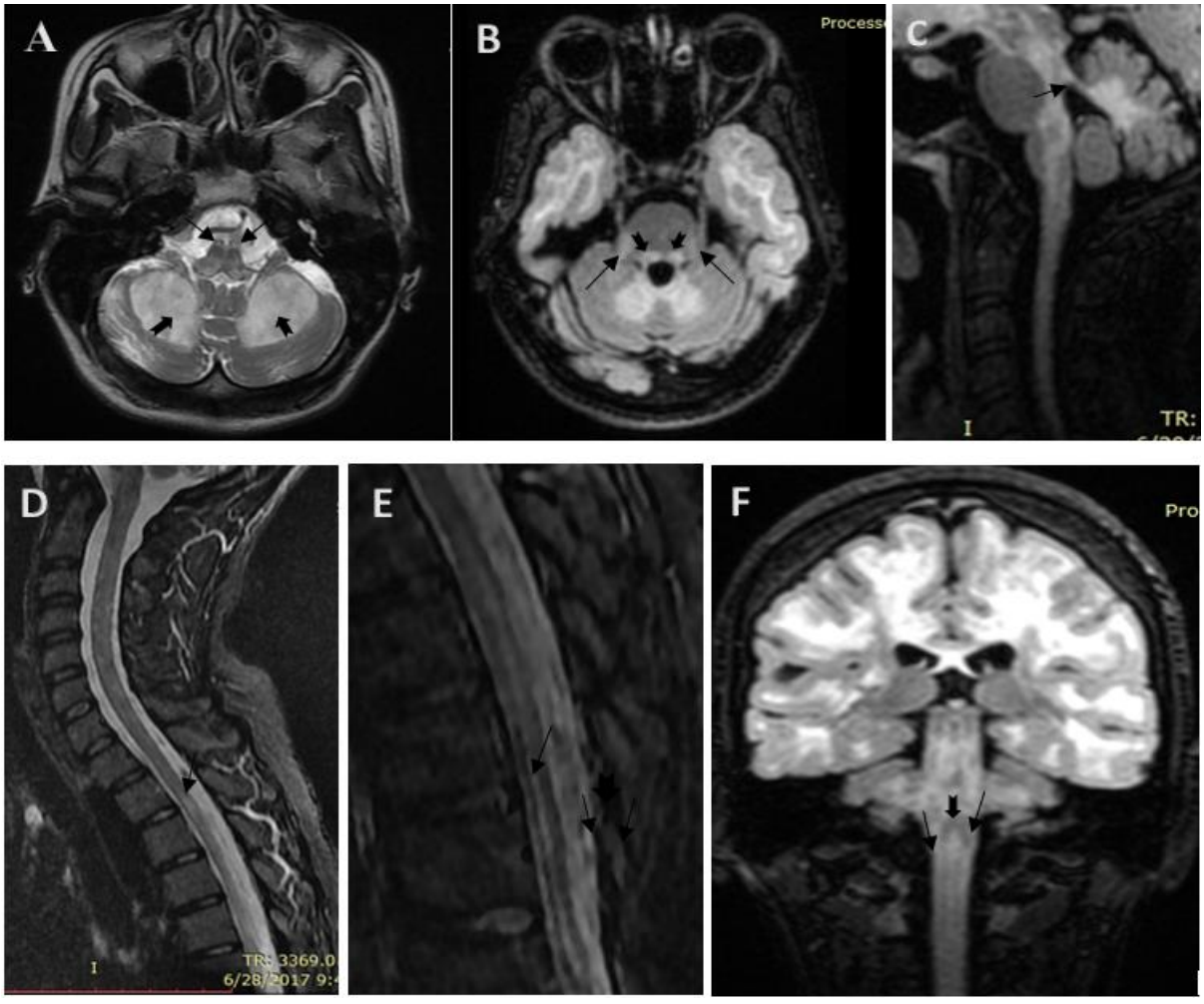

Fig. 2. (A) Pyramidal tract of the medulla oblongata (thin arrows) and cerebellar white matter involvement (thick arrows) in axial T2-weighted and Flair. (B) Intra-parenchymal part of the trigeminal nerves(thin arrows) and medial lemniscus involvement (thick arrows). (C) Superior cerebellar peduncle involvement. (D, E) Lateral corticospinal tracts of the spinal cord involvement. (F) Lateral corticospinal tract (thin arrows) and dorsal column involvement(thick arrow).

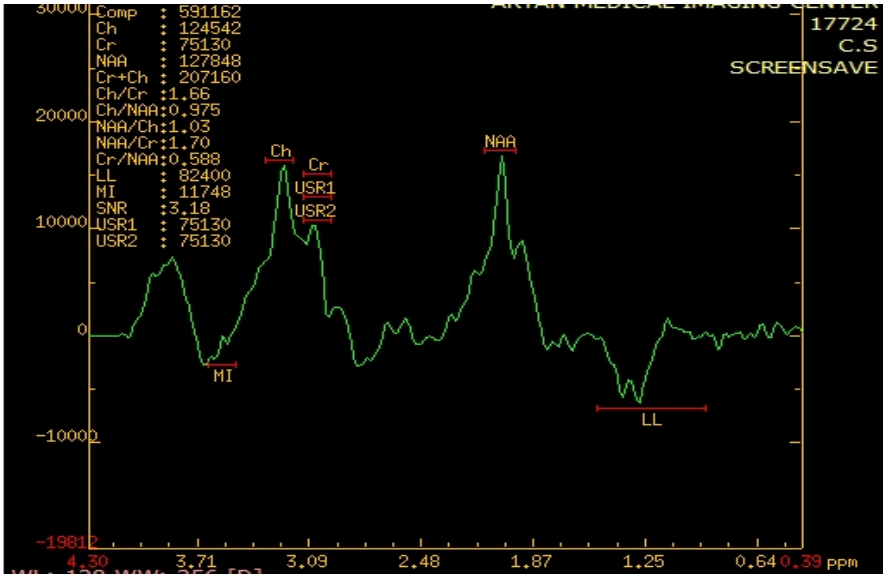

Fig. 3. MRS: inverted doublet lactate peak indicating elevated lactate level in the brain parenchyma.

Following the patient's workup, MRS shows low peaks of N-acetyl aspartate (NAA) as a marker of degeneration and abnormal inverted doublet lactate peak (Fig. 3), indicating elevated lactate level in brain parenchyma.

3. Discussion

Our 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 DARS mutation like as in some reported cases.[1, 2] Leukoencephalopathy with brain stem and spinal cord involvement and lactate elevation (LBSL) is a rare autosomal recessive disorder recently described in 2003 as an inherited leukodystrophy caused by a mutation in the DARS2 gene that reduced production of an enzyme called mitochondrial aspartyl-tRNA syntheses. Due to the recent recognition of the disease, the number of actual cases seems to be higher. Some are often undiagnosed among patients with leukodystrophy of unknown origin.[3, 4] The age of the disease onset varies from childhood to adulthood. Major clinical symptoms are spasticity in the lower and upper extremities, gait ataxia, and decreased sense of position, which is developed by the cerebellum, pyramidal tract, and posterior column involvements. The disease course is usually progressive, but the rate of progression and prognosis depend on the age of onset. Clinical symptoms of the late-onset disease are milder than earlier forms. Our patient also followed this mild pattern of disease with small cognitive involvement. Interestingly, despite the widespread signal change of white matter, the cognitive impairment is mild.[4, 5] Familial types of the disease[6] and asymptomatic person[7] have also been reported. Our diagnosis is based on characteristic MRI abnormalities in selective areas. According to revised 2012 MRI criteria, major criteria include signal abnormalities in the following areas: 1-cerebral white matter (which is either nonhomogeneous and spotty or homogeneous and confluent,) with relative sparing of the 'U' fibers;[2] Dorsal columns and lateral corticospinal tracts of the spinal cord;[3] Pyramids at the level of the medulla oblongata or decussation of the medial lemniscus or both. Minor criteria include signal abnormalities in the splenium of the corpus callosum, posterior limb of the internal capsule, superior cerebellar peduncles, inferior cerebellar peduncles, intra-parenchymal part of the trigeminal nerve, mesencephalic trigeminal tracts, anterior spinocerebellar tracts in the medulla, cerebellar white matter. In MRI-based diagnosis of LBSL, the imaging findings should meet all major criteria and at least one minor criteria. In the absence of spinal cord MRI, both pyramidal tracts and the medial lemniscus decussation should exist.[3, 8] Atypical MRI findings such as U fibers and basal ganglia involvement have also been described.[9] Brain involvement is often confluent in younger age, but in older ages, we can observe "spotty" cerebral white matter T2-hyper intense lesions that are hypointense in T1 so that the lesions may be included in the differential diagnosis of multifocal acquired lesions such as multiple sclerosis.[3] Sometimes lesions are hyperintense in diffusion-weighted imaging (DWI) with a corresponding restricted apparent diffusion coefficient (ADC) map due to cytotoxic edema.[10] Initially, regarding the name of the disease, high lactate in the magnetic resonance spectroscopy (MRS) image was diagnostic in almost all patients,[4] but later, patients with normal lactate MRI were also reported.[10, 11]

According to the reported cases, the possibility of high lactate detection by MRS is high in acute lesions with diffusion-weighted imaging -apparent diffusion coefficient (DWI-ADC) restriction but decreases overtime during the disease.[6, 10] There is no specific treatment for LBSL patients so far. Symptomatic therapy such as anti-spastic medications and conservative therapy (physiotherapy) could improve some suffering symptoms like spasticity and pain. Partial steroid response with unknown mechanism was reported in DARS-associated leukoencephalopathy. In LBSL, there is only one adult-onset case report with steroid response of bladder symptoms in the literature.[2] Interestingly our case had a partial response to 3 days' intravenous methylprednisolone pulse that persisted for several months. Clinical response to steroids in our patients raises diagnostic suspicion of superimposed inflammatory or demyelinating disease, leading to misdiagnosis and unnecessary treatment in these patients.

4. Conclusions

We hope that by increasing the reports of clinical and imaging findings, genetic study and follow-up of LBSL patients, and evaluation of their response to drugs such as corticosteroid, we will diagnose these patients more accurately and prevent misdiagnosis. In the future conducting therapeutic trials will provide useful solutions for the treatment and management of these patients.

Conflict of Interest

The authors declared that there is no conflict of interest.

Acknowledgements

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

[1] Távora DG, Nakayama M, Gama RL, Alvim TC, Portugal D, Comerlato EA. Leukoencephalopathy with brainstem and spinal cord involvement and high brain lactate: report of three Brazilian patients. Arquivos de neuro-psiquiatria. 2007;65:506-11. https://doi.org/10.1590/S0004-282X2007000300028.

[2] Muthiah A, Housley GD, Klugmann M, Fröhlich D. The Leukodystrophies HBSL and LBSL—Correlates and Distinctions. Frontiers in Cellular Neuroscience. 2021:478. https://doi.org/10.3389/fncel.2020.626610.

[3] Kassem H, Wafaie A, Abdelfattah S, Farid T. Leukoencephalopathy with brainstem and spinal cord involvement and lactate elevation (LBSL): assessment of the involved white matter tracts by MRI. European journal of radiology. 2014;83(1):191-6. https://doi.org/10.1016/j.ejrad.2013.09.023.

[4] Uluc K, Baskan O, Yildirim KA, Ozsahin S, Koseoglu M, Isak B, et al. Leukoencephalopathy with brain stem and spinal cord involvement and high lactate: a genetically proven case with distinct MRI findings. Journal of the neurological sciences. 2008;273(1-2):118-22. https://doi.org/10.1016/j.jns.2008.06.002.

[5] Alibas H, Koytak PK, Ekinci G, Uluc K. A case with leukoencephalopathy with brainstem and spinal cord involvement and elevated lactate (LBSL) with Its Characteristic Clinical and Neuroimaging Findings. Clinical neuroradiology. 2014;24(3):297-300. https://doi.org/10.1007/s00062-013-0250-x.

[6] Labauge P, Roullet E, Boespflug-Tanguy O, Nicoli F, Le Fur Y, Cozzone PJ, et al. Familial, adult onset form of leukoencephalopathy with brain stem and spinal cord involvement: inconstant high brain lactate and very slow disease progression. European neurology. 2007;58(1):59-61. https://doi.org/10.1159/000102171.

[7] Labauge P, Dorboz I, Eymard-Pierre E, Dereeper O, Boespflug-Tanguy O. Clinically asymptomatic adult patient with extensive LBSL MRI pattern and DARS2 mutations. Journal of neurology. 2011;258(2):335-7. https://doi.org/10.1007/s00415-010-5755-5.

[8] Steenweg ME, van Berge L, van Berkel CG, de Coo IF, Temple IK, Brockmann K, et al. Early-onset LBSL: how severe does it get?. Neuropediatrics. 2012;43(06):332-8. DOI: 10.1055/s-0032-1329395.

[9] Galluzzi P, Sacchini M, Bartalini G, Monti L, Cerase A, Lamantea E, et al. LBSL (leukoencephalopathy with brain stem and spinal cord involvement and high lactate) without sparing of the u-fibers and globi pallidi: A case report. European Journal of Radiology Extra. 2011;79(2):e73-6. https://doi.org/10.1016/j.ejrex.2011.06.002.

[10] Werner R, Daum E, Felber S, Wöhrle JC. Leukoencephalopathy with brain stem and spinal cord involvement and not always lactate elevation. Clinical Neuroradiology. 2018;28(3):451-3. https://doi.org/10.1007/s00062-017-0647-z.

[11] Petzold GC, Bohner G, Klingebiel R, Amberger N, Van der Knaap MS, Zschenderlein R. Adult onset leucoencephalopathy with brain stem and spinal cord involvement and normal lactate. Journal of Neurology, Neurosurgery & Psychiatry. 2006;77(7):889-91. http://dx.doi.org/10.1136/jnnp.2005.078568.

How to Cite this Article: Sahraian MA, Shahmohammadi A, Shahmohammadi S, Doosti R. Leukoencephalopathy with Brain Stem and Spinal Cord Involvement and Lactate Elevation (LBSL) Based on Typical MRI and MRS Findings: A Case Report. International Journal of Scientific Research in Dental and Medical Sciences, 2022;4(1):38-41. http://doi.org/10.30485/IJSRDMS.2022.325233.1241.