

A Rare Case of Adult-Onset Leukoencephalopathy with Brain Stem and Spinal Cord Involvement and Normal Lactate

Dr. Nihaal Reddy¹, Dr. Harpreet Singh Grewal², Dr. Santosh Patil³

^{1,2}Resident, Department of Radiodiagnosis, KLE University's Jn Medical College, Nehru, Nagar, Belgaum.590010, India

²Associate Professor, Department of Radiodiagnosis, KLE University's Jn Medical College, Nehru, Nagar, Belgaum.590010, India

Abstract: *Aims & Objectives:* To review the clinical presentation and imaging findings in detection of Adult-Onset Leukoencephalopathy with Brain Stem And Spinal Cord involvement and Normal Lactate Level. *Materials & Methods:* A 19 year old female patient, presented with complaints of sudden onset of paraplegia, with gait spasticity and fever for duration of two weeks prior to the scan. Patient underwent MRI Brain and Spine. *Result:* Patient underwent MRI Brain and spine and showed confluent T2, FLAIR and restricted diffusion symmetrical hyperintensities in periventricular, peritrigonal, corpus callosum, cerebral white matter (sparing of subcortical U fibres), internal capsule, brainstem (pyramidal and medial lemniscus) on both sides in brain. Ill defined T2, FLAIR and Diffusion weighted hyperintensities were seen in the dorsal columns and lateral corticospinal tracts over the entire length of spinal cord. MRS showed normal lactate levels. *Conclusion:* LBSL is a recently described rare autosomal recessive disorder with gradual onset, usually in childhood or adolescence, but occasionally in adulthood. It is caused by mutations in DARS2 gene on chromosome 1, encoding mitochondrial aspartyl tRNA synthase. MRI findings often suggest the diagnosis. For an MRI-based diagnosis of LBSL, all the major criteria and one of the supportive criteria need to be fulfilled. Major criteria - signal abnormalities in the following: (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 in the medulla oblongata. Supportive criteria: signal abnormalities in splenium of the corpus callosum, posterior limb of the internal capsule, medial lemniscus in the brainstem, superior cerebellar peduncles, inferior cerebellar peduncles, intraparenchymal part of the trigeminal nerve, mesencephalic trigeminal tracts, anterior spinocerebellar tracts in the medulla, cerebellar white matter with subcortical preponderance.

Keywords: LBSL, Lactate, Leukoencephalopathy, Brainstem, Spinal Cord

1. Introduction

Leukoencephalopathy with brainstem and spinal cord involvement and elevated lactate (LBSL) is an autosomal recessive white matter disorder, first described in 2003 by its unique pattern of MRI abnormalities (van der Knaap et al., 2003). LBSL typically involves the cerebral and cerebellar white matter and specific tracts in the brainstem and spinal cord (van der Knaap et al., 2003; Scheper et al., 2007). The signal changes are often inhomogeneous and spotty. Proton magnetic resonance spectroscopy shows elevated lactate in the affected white matter in most patients. Slow neurological deterioration with signs of pyramidal, cerebellar and dorsal column dysfunction generally starts in childhood (van der Knaap et al., 2003), but adult onset has also been reported (Petzold et al., 2006; Labauge et al., 2007). In 2007, the related gene, DARS2, was found, which codes for mitochondrial aspartyl transfer RNA synthetase (Scheper et al., 2007). The pathological basis of the disease is unknown. We describe the clinical and radiological features of a patient with adult-onset LBSL and normal lactate levels on MRS.

2. Materials and Methods

A 19 year old female patient, presented with complaints of sudden onset of paraplegia, with gait spasticity and fever for duration of two weeks prior to the scan. Patient underwent MRI Brain and Spine. MRI of the brain and spine and proton magnetic resonance spectroscopy (1H

MRS) on the abnormal white matter was performed to all patients using Magnetom Symphony TIM System1.5 T machine. Our brain MRI protocol included sagittal spin echo (SE) T1-weighted images (TR 550, TE 8), axial and coronal fast spin echo (FSE) T2-weighted images (TR 4200, TE 97), axial fluid-attenuated inversion recovery (FLAIR) (TR 9000, TI 2500, TE 82), axial spin echo (SE) T1-weighted images (TR 535, TE 13) and axial diffusion weighted images (b0-1000). A post gadolinium sagittal and axial T1-weighted image was performed.

Single-voxel point-resolved proton spectroscopy sequences (PRESS) with echo time (TE) of 135 ms was obtained in our case. The voxels were located in the centrum semiovale and in the deep periventricular white matter. N-acetylaspartate (NAA) was assigned at 2.02 parts per million (ppm), choline (Cho) at 3.2 ppm, creatine (Cr) at 3.03 ppm and lactate (Lac) at 1.3 ppm. Metabolite ratios (NAA/Cr and Cho/Cr) were also measured. All data processing was performed by software provided by the manufacturer. Spinal cord MRI protocol included axial and sagittal T1-weighted (TR 400, TE 12), and T2-weighted (TR 3700, TE 103) images of the whole spine.

3. Result

Patient underwent MRI Brain and spine and showed confluent T2, FLAIR and restricted diffusion symmetrical hyperintensities in periventricular, peritrigonal, corpus callosum, cerebral white matter (sparing of subcortical U

fibres), internal capsule, brainstem (pyramidal and medial lemniscus) on both sides in brain. Ill defined T2, FLAIR and Diffusion weighted hyperintensities were seen in the dorsal columns and lateral corticospinal tracts over the entire length of spinal cord, with patchy enhancement on contrast study MRS increased choline and creatine and N-acetylaspartate levels. There was no evidence of lactate elevation.

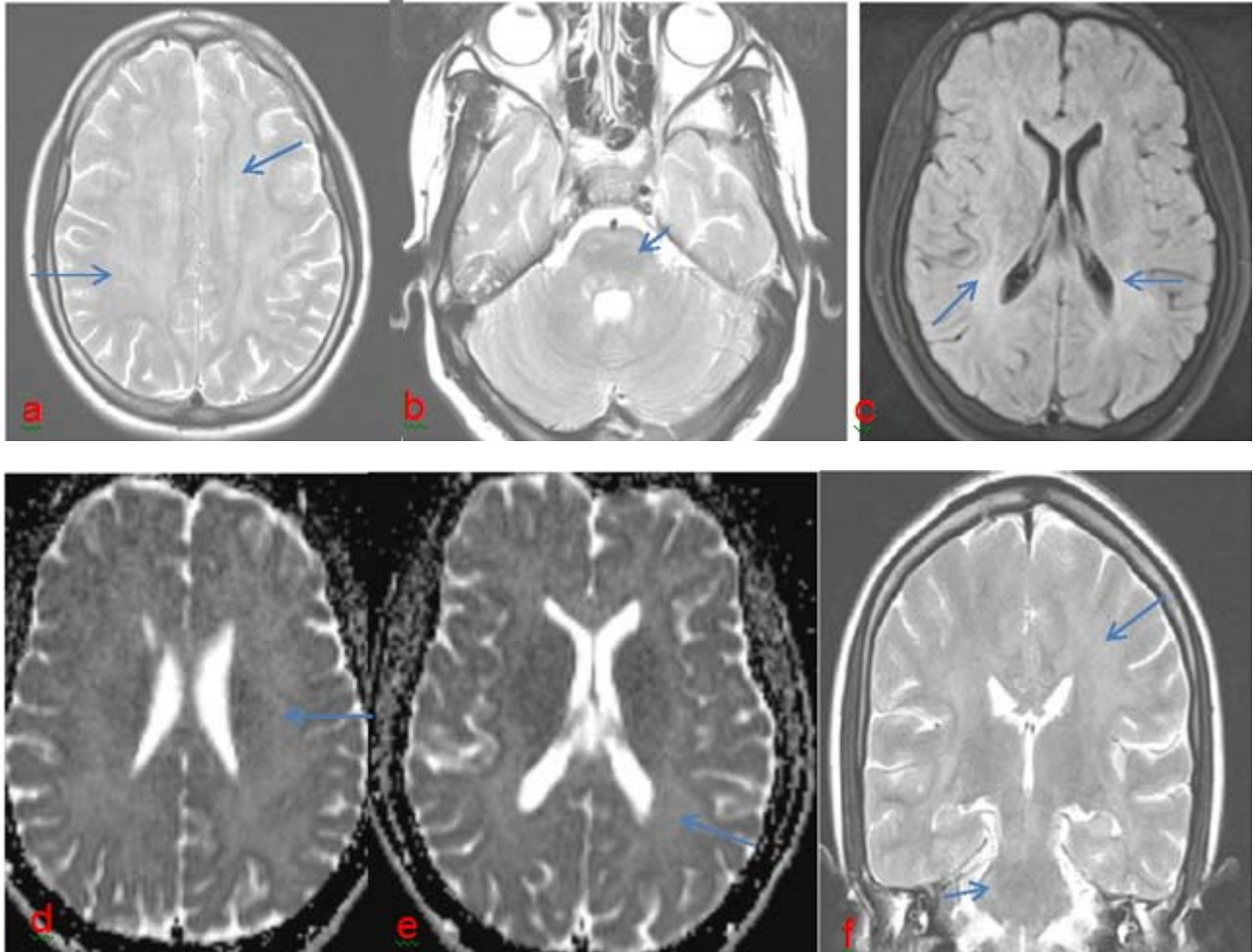


Figure 1

- a) T2 axial images shows symmetrical white matter hyperintensities in fronto-parietal region (arrows)
- b) T2 axial images shows hyperintensities in the pons (arrows)
- c) FLAIR axial image shows periventricular hyperintensities(arrows)
- d, e)DWI & ADC sequences show corresponding hyperintensities (arrows) which were evident on T2 sequences.
- f) Coronal T2 sequence showed periventricular and brainstem hyperintensities (arrows)

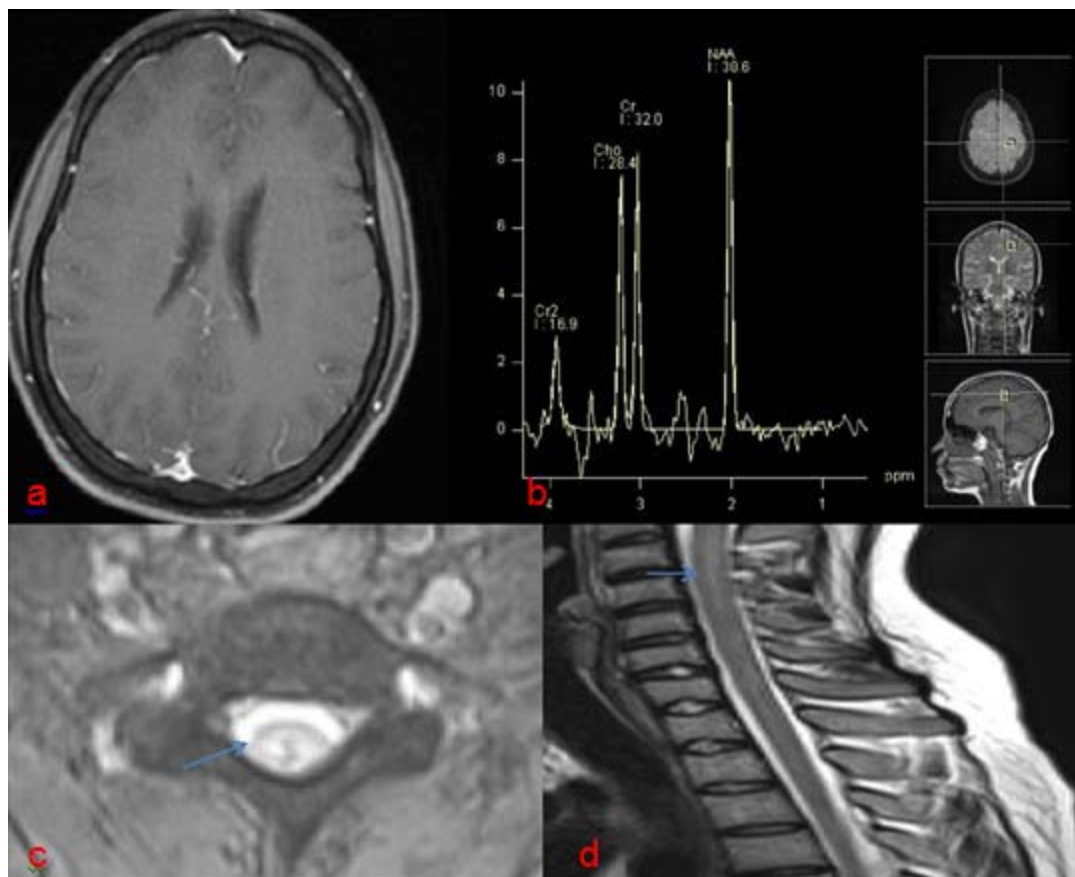


Figure 2

- a) T1 contrast image shows no enhancement
 b) MRS in periventricular white matter shows NAA, Cr and Co peaks, absence of significant Lactate or lipid peaks
 c) T2 axial image at cervical spinal cord shows dorso-lateral hyperintensities (arrows) in the cord.
 d) T2 sagittal image shows patchy hyperintensities (arrows) along the length of spinal cord

4. Discussion

Leukoencephalopathy with brain stem and spinal cord involvement and high brain lactate (LBSL) has recently been described in 2003 by Van der Knaap et al. This disorder is characterized by childhood onset of slowly progressive neurological symptoms including cerebellar ataxia, tremors, muscle weakness, spasticity and mild cognitive deficit or decline. In our case, patient was presented with complaints of sudden onset of paraplegia, with gait spasticity and fever for duration of two weeks prior to the scan. Patients usually present in the childhood period and showed consistent elevation of lactate on MRS. However our case showed normal lactate on MRS, as reported by Labauge et al. in adult onset form of LBSL in which, the level of lactate is normal. Labauge et al. also reported the first asymptomatic adult patient with a typical MRI aspect of LBSL. LBSL is an autosomal recessive disease, caused by mutations in the DARS2 gene, encoding the mitochondrial aspartyl-tRNA synthetase, which explains the persistent lactate peak found in LBSL patients at brain MRS analysis. Patients with LBSL have distinct clinical characteristics and MRI pattern, which are different from those seen in all other known leukoencephalopathies.

Galluzzi et al. have described distinctive features of LBSL as follows; first, white matter abnormalities and involvement of brainstem structures by brain MRI; second, sparing of the U-fibers was an invariant distinctive feature of the syndrome; third, whenever evaluated, spinal cord was always involved; fourth, brain [1H] MR spectroscopy failed to show a lactate peak in all cases. The MRI findings in our patient were diagnostic, but MRS did not show lactate elevation in the affected cerebral white matter. A few clinico-radiological LBSL cases with genetic confirmation have been reported before with normal or inconstant lactate levels. The reason why lactate is not always present is not yet known.

5. Conclusion

LBSL is a recently described rare autosomal recessive disorder with gradual onset, usually in childhood or adolescence, but occasionally in adulthood. It is caused by mutations in DARS2 gene on chromosome 1, encoding mitochondrial aspartyl tRNA synthase. MRI findings often suggest the diagnosis. For an MRI-based diagnosis of LBSL, all the major criteria and one of the supportive criteria need to be fulfilled. Major criteria - signal abnormalities in the following: (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 in the medulla oblongata. Supportive criteria: signal abnormalities in splenium of the corpus callosum, posterior limb of the internal capsule, medial lemniscus in the brainstem, superior cerebellar peduncles, inferior cerebellar peduncles, intraparenchymal part of the trigeminal nerve, mesencephalic trigeminal tracts, anterior spinocerebellar tracts in the medulla, cerebellar white matter with subcortical preponderance. Distinct MRI findings in the form of selective affection of subcortical and deep white matter tracts of the brain (involving the posterior limb of internal capsules and sparing the subcortical U fibers), dorsal column and lateral cortico-spinal tracts of the spinal cord should lead to the diagnosis of LBSL supported by the presence of lactate peak in 1H MRS. However lactate peak is not present in all cases, which was seen in case reported by us. The disease can be confirmed by the analysis of the disease gene DARS2.

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