

CASE REPORT

AMYOTROPHIC LATERAL SCLEROSIS PLUS SYNDROME: A RARE CASE REPORT

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ABSTRACT: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder. In 1994, the El Escorial criteria were proposed for the diagnosis of ALS. These criteria include ALS-plus syndromes, which are defined by an association of ALS with extrapyramidal features or dementia. we present a case report of 31 years young man presented with weakness of lower limbs since one and half years and slurring of speech since 8 months and on examination patient had scanning of speech, eye saccades were slow, upper motor neuron type of quadriparesis with cerebellar ataxia and dysmetria with no sensory or bowel bladder involvement. Routine blood investigations were normal and MRI Brain showed features of atrophy of cerebrum and cerebellum and ENMG shows neurogenic pattern of fasciculations and spontaneous activity. Clinically cerebellar ataxia and dysmetria with pure motor neuron disease suggests the possibility if ALS Plus syndrome especially ubiquitinated forms of TDP-43 and ubiquitinated p62-positive inclusions were frequently observed. As such it is the rare presentation in young adults, further studies over ALS plus syndrome will bring additional information about neuropathological details and its effect on outcome.

KEYWORDS: Amyotropic lateral sclerosis, Quadriparesis, Escorial criteria, fasciculations and ubiquitinated inclusions.

INTRODUCTION: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that affects the upper and the lower motor neurons in the cerebral cortex, brainstem, and spinal cord.¹ The clinical features can be considered in relation to neurological regions or levels. Physical signs of this disorder encompass both, the upper and the lower motor neuron findings. Atrophy and weakness of respiratory muscles eventually lead to respiratory failure and death. Amyotrophic lateral sclerosis (ALS)-Plus syndromes meet clinical criteria for ALS but also include 1 or more additional features such as dementia, geographic clustering, extrapyramidal signs, objective sensory loss, autonomic dysfunction, cerebellar degeneration, or ocular motility disturbance. According to the revised El Escorial criteria, the described unusual combination of upper and lower motor neuron signs in association with cerebellar ataxia with dysmetria can be classified as a specific form of ALS-plus syndrome.^{2,3}

CASE REPORT: We are presenting a case of 31-year-old man who had weakness of limbs for 1 ½ years which was asymmetrical in onset ,started in right lower limb ,after 6 months progressed to upper limbs ,6 months later progressed to left lower limb. Patient also presented with Slurring of speech since 8 months. No history of fasciculations, radicular pain, sensory symptoms, bladder and bowel involvement. Family history is not contributing.

NEUROLOGIC EXAMINATION: The patient was awake, alert, and had dysarthria-scanning speech and could appropriately respond to questions and follow commands. His writing was illegible. Pupils

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were 2 to 3 mm in diameter and reactive to light and near vision. Horizontal and vertical saccades were slow. The uvula was midline and Gag reflex was normal. The sternocleidomastoid muscles and tongue was normal, no atrophy or fasciculations. Rapid tongue movements were normal. Tone was rigid in all the limbs. Power was Medical Research Council (MRC) grade 5 in the deltoid, biceps, and triceps muscles but MRC grade 4 in the right and left wrist flexors and extensors and intrinsic muscles of the hand. There was atrophy of the forearm and hand intrinsic muscles. Leg power was MRC grade 4, he was able to rise from a chair without using his hands, and heel and toe walking was difficult. No fasciculations were noted. Reflexes were exaggerated in the arms with bilateral Hoffman sign. Pendular knee jerk was present with well sustained clonus. Cutaneous abdominal reflexes were present. Babinski sign was positive. Palmomental reflex was present. Sensory examination found to be normal. Cerebellar ataxia with dysmetria was present.



Fig. 1: Showing wasting of Intrinsic muscles of both hands

Clinical and Laboratory Investigations: Magnetic resonance images of the brain demonstrated diffuse cerebral and cerebellar atrophy changes. An electromyogram demonstrated ongoing chronic partial denervation and fasciculations in muscles of the arm and leg (Biceps & vastus lateralis). Complete blood cell count, thyroid function studies, serum parathyroid hormone and vitamin B12, electrolytes values found to be normal and HIV-negative.

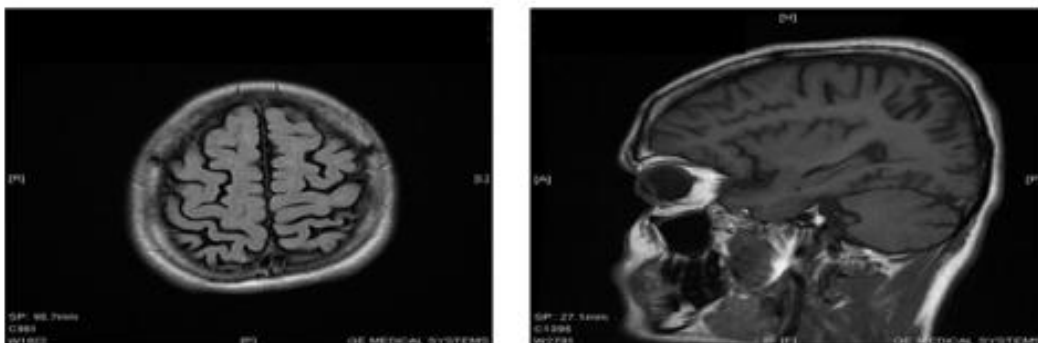


Fig. 2: MRI of brain axial T2 image showing diffuse cerebral atrophy

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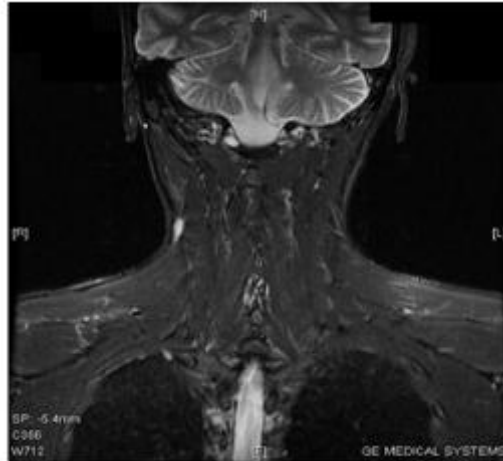


Fig. 3: MRI of brain and c-spine coronal stir image showing diffuse cerebellar atrophy

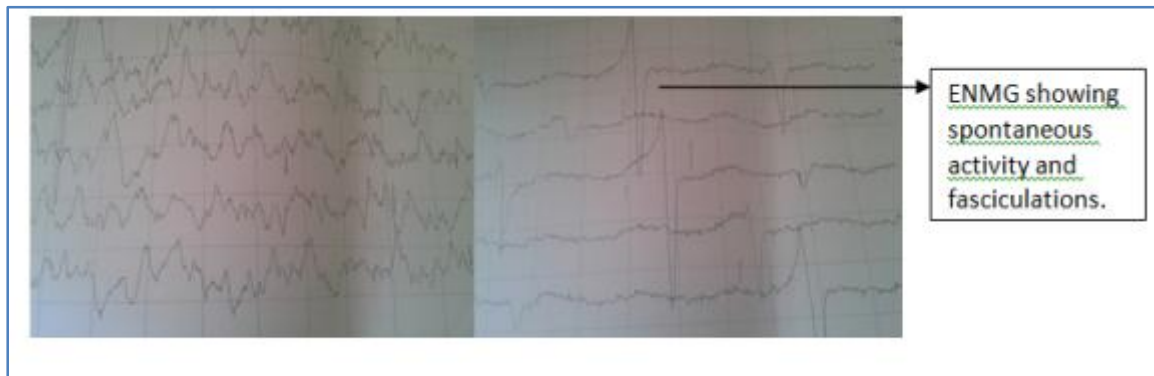


Fig. 4: ENMG showing spontaneous activity and fasciculations which are neurogenic pattern

The patient was given Tab. Riluzole 50 mg twice a day therapy and advised follow up.

DISCUSSION: ALS is a fatal neurodegenerative disease. Patients with ALS become progressively paralyzed, while remaining fully alert mentally, due to degeneration of the upper and the lower motor neurons in the brain and spinal cord. Brain stem involvement produces dysarthria (Slurred speech), dysphagia, and aspiration. Our patient had presented with features of pure motor system involvement affecting upper and lower motor neurons involving limb musculature and cerebellar ataxia.^{4,5} Electromyography, MRI images and nerve conduction further confirm the diagnosis. According to revised E1 Escorial criteria the combination of upper and lower motor neuron disease with cerebellar ataxia fits specific form of ALS plus syndrome. Literature review showed very few cases of ALS plus syndrome involving cerebellum. Herein, imaging and neuropathological evidence for involvement of the cerebellum, which to date is not thought to be involved in ALS, is reviewed.

Evidence for involvement of the cerebellum in ALS comes from several neuropathological studies. Especially ubiquitinated forms of TDP-43 and ubiquitinated p62-positive inclusions were frequently observed.

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The widely used transgenic SOD1-G93A ALS mice model showed prominent cerebellar immunostaining of pERK and alterations of tau expression.^{6,7} Studies using advanced MRI techniques demonstrated that several cerebral areas, including the cerebellum, were recruited in order to compensate for functional motor decline. Functional MRI, voxel based morphometry, and diffusion-tensor imaging showed these cerebellar alterations as being of functional and structural nature.

CONCLUSION In summary, we presented an interesting case of a patient with ALS Plus syndrome involving cerebellum which is rare association. After review of the available literature, it was felt that these were chance occurrences and that treatment entities do not affect the course of progressive ALS/MND.^{8,9} Clinically cerebellar ataxia with pure motor neuron disease suggests the possibility if ALS Plus syndrome especially ubiquitinated forms of TDP-43 and ubiquitinated p62-positive inclusions were frequently observed. As such it is the rare presentation in young adults, further studies over ALS plus syndrome will bring additional information about neuropathological details and its effect on outcome.¹⁰

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