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SHORT REPORT

Occurrence of eye movement disorders in motor neuron disease

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Abstract

The diagnosis of amyotrophic lateral sclerosis (ALS) relies on symptoms and signs related to upper and lower motor neuron injury. Preservation of normal ocular motor movements is an important criterion for making this diagnosis as oculomotility pathways are classically spared in ALS. However, some authors report eye disturbances resulting from nuclear and supranuclear ophthalmoplegia in autopsy-proven ALS. Here, we report a case in which eye movement disorders were an early sign associated with a bulbar-onset ALS. The association of progressive ophthalmoplegia, dysexecutive syndrome and automatico-voluntary dissociation of eyelid occlusion suggested a 'progressive supranuclear palsy variant' of ALS caused by a disturbance in the descending frontal projections, even though morphological imaging was normal. Motor neuron disease with eye movement disorders must not be considered as a distinct clinical entity and must not exclude a diagnosis of ALS.

Key words: *Ophthalmoplegia, amyotrophic lateral sclerosis, frontal lobe*

Introduction

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease affecting both upper and lower motor neurons of the brainstem and spinal cord. Oculomotility pathways are classically spared in ALS (1).

We report a case of a patient with bulbar-onset ALS, early eye movement disorders and paralysis of voluntary eyelid occlusion. We discuss the diagnosis of atypical bulbar-onset ALS, taking into account a clinical analysis of oculomotor dysfunction and previously reported anatomo-clinical correlations.

Case report

A 71-year-old female without a history of neurological disorders was admitted for progressive dysarthria and dysphagia that had been present for one year and were associated with weight loss. She also complained of the inability to voluntarily close her eyelids for a period of one month.

Clinical examination was marked by a severe bilateral limitation of vertical gaze (Figure 1). Although she could blink spontaneously, she was unable to close her eyelids voluntarily or on command. Clinical examination also revealed muscular atrophy and fasciculations in the tongue, exaggerated jaw jerk, fasciculations in the upper limbs and severe dysarthria. She was unable to protrude her tongue or purse her lips. Manual muscle testing was normal. Deep tendon reflexes were present in the four limbs, and plantar responses were both extensor. There was no extrapyramidal syndrome.

Electromyography revealed diffuse denervation in the tongue and lower limbs. The amplitudes of motor evoked potentials and cortical silent periods were decreased for the right lower limb. Electro-oculography with standard oculomotor tests (WIN8000F Metrovision®) revealed abnormalities in vertical and horizontal pursuits with decreased amplitude and microsaccades (Figure 2). Horizontal optokinetic nystagmus was normal in both left-right and right-left directions and in vertical upward and downward directions.

Spinal fluid analysis was normal. Biochemical and immunological screening ruled out ALS mimic

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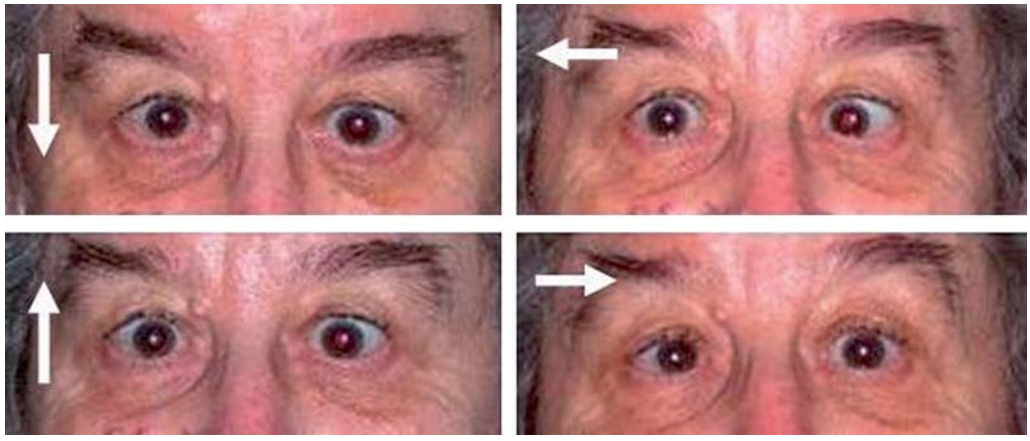

Figure 1. Severe limitation of vertical gaze (left), and incomplete limitation of horizontal gaze (right).

syndromes. There were no mutations in the SOD1 and TARDBP genes. Brain magnetic resonance imaging and perfusion tomoscintigraphy were normal.

A neuropsychological assessment revealed an isolated dysexecutive syndrome with impairments in planning and mental flexibility, perseverations and difficulties during tasks of motor inhibition.

After two years, a follow-up clinical examination revealed mild muscular weakness in the lower limbs, difficulties in walking and complete ophthalmoplegia. Abnormal imitation behaviour and perseverations were observed. Six months later, a percutaneous gastrostomy was required due to progressive dysphagia and severe weight loss. The patient died 54 months after the first onset of her symptoms.

Discussion

Despite the presence of oculomotor disturbances, clinical examinations, electromyography results and the clinical course were strongly suggestive of an ALS diagnosis.

The diagnostic criteria of the World Federation of Neurology (2) state that the oculomotor system is spared in ALS and that abnormalities in eye

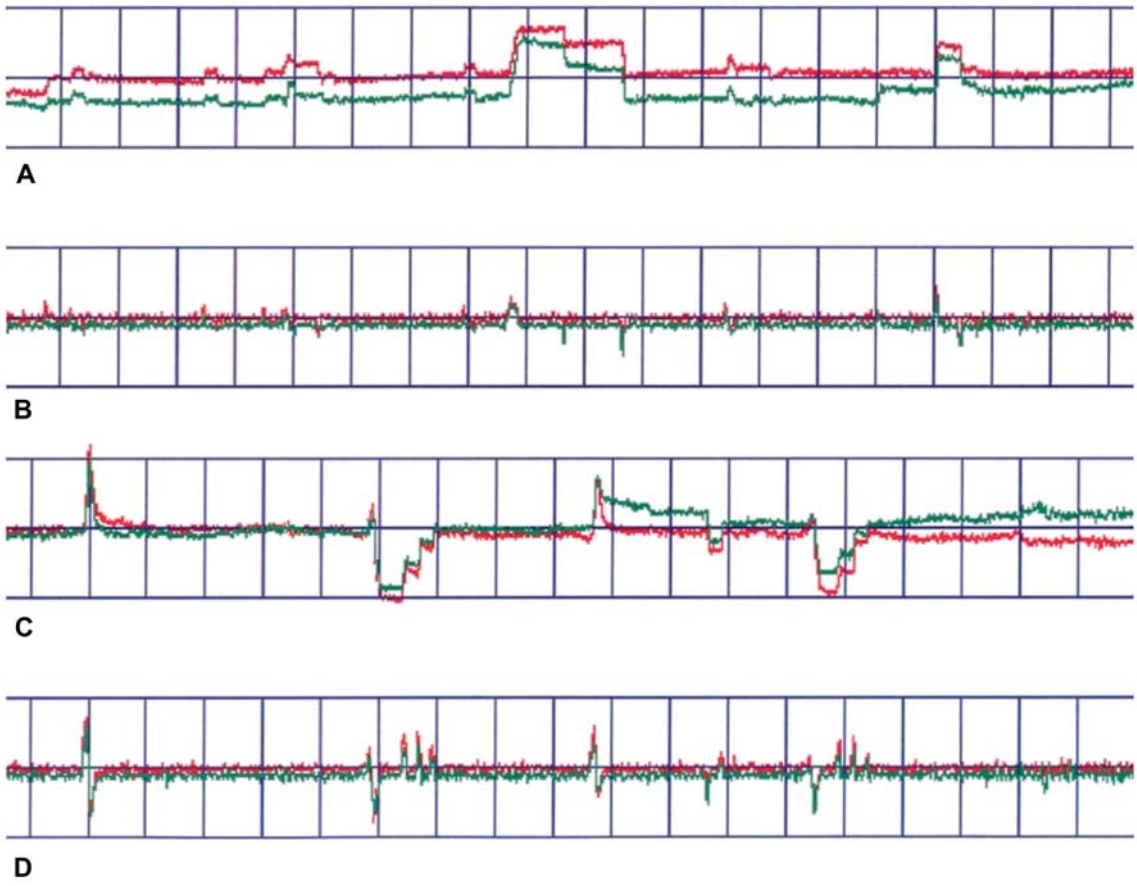

Figure 2. Electro-oculogram during 10° horizontal (eye position A, velocity B) and vertical (eye position C, velocity D) saccades. Note microsaccades and abnormal vertical pursuit to the upward position.

movements should lead to the questioning of an ALS diagnosis. However, in the NNIPPS study (3), an anatomopathological report revealed autopsy-proven ALS in a patient with a clinical diagnosis of progressive supranuclear palsy. Moreover, patients with ALS and ventilation support who survive beyond the usual natural history of the disease are known to develop ophthalmoplegia (4).

Several anatomopathological reports have shown the heterogeneity of eye movement disorders resulting from nuclear and supranuclear ophthalmoplegia in ALS (1). Sunohara et al. (5) reported a case of an ALS patient unable to close his eyes either voluntarily or on command. Post mortem examination disclosed lesions of the precentral areas on both sides. As in our case, this may suggest that the inability to initiate eyelid movements in ALS derives from degeneration of the corticogeniculate tracts.

Here, we report a case in which eye movement disorders were an early sign associated with ALS. Our case presented with dysexecutive syndrome, progressive ophthalmoplegia and automatico-voluntary dissociation of eyelid occlusion. This association suggested a disturbance in the descending frontal projections even though morphological imaging was normal.

In the frontal lobe, three main areas are involved in eye movement control (6): the frontal eye field, the supplementary eye field and the dorsolateral prefrontal cortex. Massive degeneration of the corticogeniculate tracts, which is likely to be accompanied by a severe supranuclear palsy of the pontine and bulbar muscles, can be followed by a spectrum of supranuclear ocular motor diseases (7).

Moreover, recent studies of eye movements in ALS found that saccadic intrusion amplitude, antisaccade errors and reduced smooth pursuit velocity gain were correlated with neuropsychological measures sensitive to lesions of the frontal lobe (8). Throughout the course of the disease, these abnormalities can lead to a clinical pattern of complete ophthalmoplegia or, more frequently, supranuclear gaze palsies, thus presenting as a 'progressive supranuclear palsy variant' of ALS (7). Our case illustrates this peculiar form with an early and severe development of eye movement abnormalities. Furthermore, eyelid apraxia, a feature present in our case, is often seen in progressive supranuclear palsy (8).

Conclusion

This case adds to the increasing evidence for the clinical heterogeneity of motor neuron disease. The association of ALS and eye movement disorders must not be considered as a distinct clinical entity and must not lead to the exclusion of an ALS diagnosis.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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