Acta Neurol Belg (2016) 116:401–403
DOI 10.1007/s13760-015-0531-z

LETTER TO THE EDITOR

Brait–Fahn–Schwarz disease: Parkinson's disease and amyotrophic lateral sclerosis complex

Asiye Mukaddes Erol[1] · Ahmet Kasim Kilic[2] · Aykut Celik[1] · Canan Celik[3] · A. Nazli Basak[4]

Received: 2 July 2015 / Accepted: 11 August 2015 / Published online: 29 August 2015

Introduction

Neurodegenerative diseases such as Parkinson's disease (PD) and amyotrophic lateral sclerosis (ALS) are sometimes present together, as in the Parkinsonism-dementia complex of Guam. Outside the specific geographical regions, the combination of ALS and PD is rare [1]. This neurodegenerative complex was first described by Brait et al. [2] and clinically presents with levodopa responsive parkinsonism followed by ALS.

Hereby, we report the case of a patient who presented with clinical findings of both PD and ALS. We will review the clinical features of the patient and briefly discuss the common underlying mechanisms of two rarely accompanying disorders.

Case report

A 70-year-old woman admitted to hospital with weakness on her left side of the body and diagnosed as stroke 6 years ago. Although the patient was walking with a cane after stroke, then she began to walk with small, wide-based steps and was slower in her movements. A diagnosis of Parkinson's disease was made based on resting tremor, bradykinesia and rigidity. She initially responded well to antiparkinsonian medications. About 18 months later, she began to notice shrinking in the muscles of her hands, and developed uncomfortable cramps and muscle twitching. She became dysphagic and was hospitalized once due to aspiration pneumonia. Over the course of last year, she became wheelchair bound.

Her medical history was unremarkable except for hypertension. Familial history for extrapyramidal disorders was negative. She had facial masking. Her speech was slow and slurred. Resting tremor of both hands was observed. She had tongue atrophy and fasciculations were observed in her hands and tongue. Decreased gag reflex, bilateral increased deep tendon reflexes, Hoffman's and Babinski's signs were present. She had rigidity with bilateral cogwheeling. Her sensory examination was intact. Neuropsychological assessment was performed using the Standardized Mini Mental test. Although her responses were delayed, no severe cognitive deficits could be noted. She had muscle atrophy in intrinsic muscles of hand. Laboratory evaluation was normal.

The electromyogram (EMG) revealed decrease of compound muscle action potential (CMAP) and relatively decreased motor nerve conduction velocity (NCV) but normal sensory NCV's and sensory nerve action potential (SNAP) amplitudes. Needle EMG showed frequent fasciculations, fibrillations, and high-amplitude polyphasic motor-unit potentials in the upper and lower extremities. These findings were considered compatible with motor neuron involvement. The presence of pyramidal damage was evaluated by MR spectroscopy (Fig. 1). Decreased *N*-acetylaspartate (NAA) and choline (Cho) were obtained.

✉ Asiye Mukaddes Erol
drasmyilmaz@yahoo.com.tr

[1] Department of Physical Medicine and Rehabilitation, Bursa Şevket Yılmaz Training and Research Hospital, Yildirim, 16800 Bursa, Turkey

[2] Department of Neurology, Bursa Şevket Yılmaz Training and Research Hospital, Yildirim, 16800 Bursa, Turkey

[3] Department of Physical Medicine and Rehabilitation, University of Giresun, Giresun, Turkey

[4] Department of Molecular Biology and Genetics, Boğaziçi University, Bebek, 34342 Istanbul, Turkey

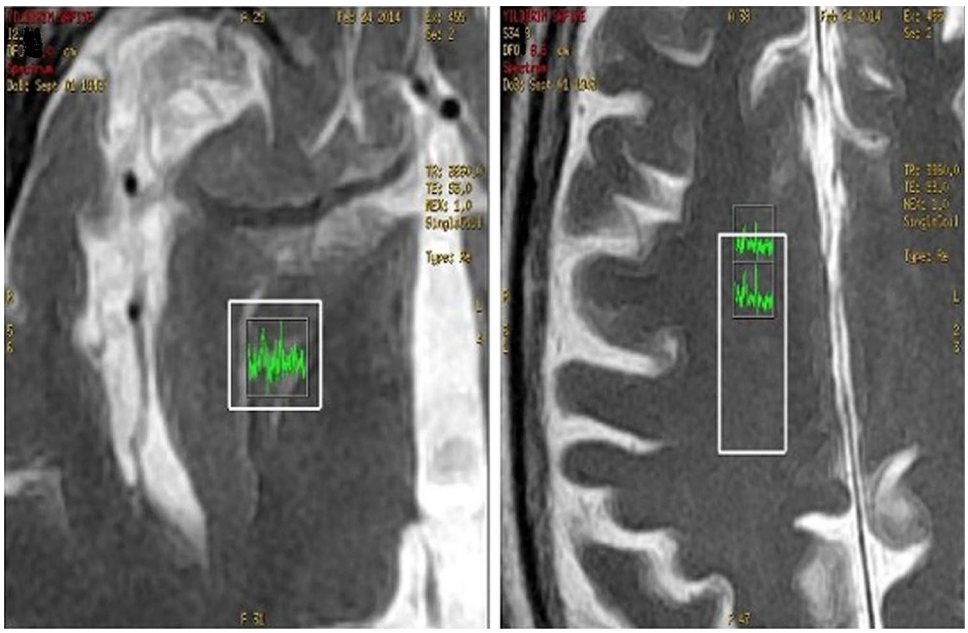

Fig. 1 The posterior limb of the right internal capsule, and normal appearing white matter (NAWM) were compared for neuronal damage by MR spectroscopy. Decreased *N*-acetylaspartate (NAA) and choline (Cho) were obtained from internal capsule. Creatinin (Cr) levels did not differ. NAA/Cho and NAA/Cr ratios were decreased. Cho/Cr levels were increased

NAA/Cho and NAA/Cr ratios were decreased. Cho/Cr ratio was pathologically increased. These findings confirmed the neurodegeneration in pyramidal tract. Genetic screening for SOD1, C9orf 72 and UBQLN2 was negative.

She had bulbar, upper and lower motor neuron involvement. A diagnosis of definite ALS, according to El-Escorial-revised criteria, was made and riluzole medication was started [3]. Range of motion, progressive-resistive, and breathing exercises were performed. With the assistance of the physical therapist, the patient practiced sitting balance. During clinical follow-up, the patient's oral feeding progressively impaired; therefore, percutaneous endoscopic gastrostomy (PEG) was planned. She refused feeding through a PEG device. The clinical course of patient became worse so she was transferred to neurology clinic. The patient died 6 months later because of respiratory failure. An autopsy was not performed.

Discussion

We report a patient presenting with levodopa responsive parkinsonism who then developed upper and lower motor neuron degeneration signs. The syndrome of parkinsonism and motor neuron disease without other neurological symptoms was first described by Kenneth Brait and Stanley Fahn [2]. Our patient was cognitively normal and showed clinical features consistent with a clinical diagnosis of PD and ALS. A good response to treatment with levodopa distinguishes this case from ALS-plus. Unlike parkinsonism accompanying ALS, before the appearance of motor neuron degeneration, there was a definite clinical progression of the extrapyramidal symptoms.

Signs of motor neuron diseases have been reported to accompany parkinsonism in different neurodegenerative disorders. ALS is associated with parkinsonism with a frequency ranging from 5 to 17 %, during the course of disease [1]. Imaging studies revealed a progressive dopaminergic deficit in ALS patients even in the absence of extrapyramidal signs [4]. Evidence of neuronal loss with Lewy body inclusions in the basal ganglia has been demonstrated in some ALS patients. In this case, at the beginning, the clinical picture was characterized by bradykinesia and rigidity but the clinical course did not differ from that expected in ALS without parkinsonism.

The neuropathological similarities between ALS and PD suggest that these disorders may share common pathophysiological pathway [1]. Insoluble aggregates of disease-related proteins can be deposited as intraneuronal inclusions which are histopathological hallmarks of both diseases [5]. Beside toxic proteins, there is overwhelming evidence of impaired mitochondrial dysfunction, axonal transport defects and neurotoxic effects of free radicals as a causative factor [5, 6]. However, the real pathogenesis still remains to be proved.

Conclusion

Other associated neurodegenerative diseases should take place within differential diagnoses in the presence of clinical symptoms which cannot be explained by PD.

Further epidemiologic studies are needed to address the relationship of the neurodegenerative diseases.

Compliance with ethical standards

Conflict of interest Asiye Mukaddes Erol, Ahmet Kasım Kılıç, Aykut Çelik, Canan Çelik and A. Nazlı Başak declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Written informed consent was obtained from the patient for publication of this case report andaccompanying image.

References

1. Manno C, Lipari A, Bono V, Taiello AC, La Bella V (2013) Sporadic Parkinson disease and amyotrophic lateral sclerosis complex (Brait–Fahn–Schwartz disease). J Neurol Sci 326:104–106
2. Brait K, Fahn S, Schwarz GA (1973) Sporadic and familial parkinsonism and motor neuron disease. Neurology 23:990–1002
3. Brooks BR, Miller RG, Swash M, Munsat TL, World Federation of Neurology Research Group on Motor Neuron Diseases (2000) El Escorial revisited: revised criteria for the diagnosis of amyotrophic lateral sclerosis. Amyotroph Lateral Scler Other Motor Neuron Disord 1:293–299
4. Zoccolella S, Palagano G, Fraddosio A, Russo I, Ferrannini E, Serlenga L, Maggio F, Lamberti S, Iliceto G (2002) ALS-plus: 5 cases of concomitant amyotrophic lateral sclerosis and parkinsonism. Neurol Sci 23:23–24
5. Roy S, Zhang B, Lee VM, Trojanowski JQ (2005) Axonal transport defects: a common theme in neurodegenerative diseases. Acta Neuropathol 109:5–13
6. Johri A, Beal MF (2012) Mitochondrial dysfunction in neurodegenerative diseases. J Pharmacol Exp Ther 342:619–630