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LETTER TO THE EDITOR

Spastic paraplegia in 'dominant optic atrophy plus' phenotype due to *OPA1* mutation

Elena Pretegiani, Alessandra Rufa, Gian Nicola Gallus, Elena Cardaioli, Alessandro Malandrini and Antonio Federico

Department of Neurological, Neurosurgical and Behavioural Sciences, University of Siena, 53100 Siena, Italy

Correspondence to: Antonio Federico,
Department of Neurological,
Neurosurgical and Behavioural Sciences,
University of Siena,
Siena, Italy
E-mail: federico@unisi.it

Sir, We read the papers by Yu-Wai-Man *et al.* (2010) and Marelli *et al.* (2011) with much interest. The authors described three families with dominant optic atrophy plus phenotype due to *OPA1* mutations presenting spastic paraplegia among the extra-ocular neurological features.

Two families, reported by Yu-Wai-Man *et al*. (2010), harboured a deletion c.876-878del(TGT) and a nonsense GTPase mutation c.899C>T, respectively, both resulting in premature termination codons. The affected members presented neuropathy in addition to spastic paraplegia and dominant optic atrophy. Marelli *et al.* (2011) described a third family in which a missense mutation c.1652G>A in the dynamin domain was associated with Behr syndrome.

We report here, a patient in whom a deletion c.2708_2711delTTAG of *OPA1* was associated with dominant optic atrophy, spastic paraplegia, Duane retraction syndrome, migraine with atypical aura, patent foramen ovale and muscle fibre abnormalities. Considering the previous reports, we extend the mutations of *OPA1* as possibly responsible for dominant optic atrophy plus phenotypes presenting spastic paraplegia, and identify some features shared by patients with optic atrophy plus and spastic pyramidal involvement.

The proband, a 28-year-old Italian female belonging to a family from Sicily, has suffered from loss of central vision due to optic atrophy since childhood. She was referred to our unit for the onset, appeared a few years earlier, of slowly progressive gait impairment and recurrent episodes of lower limb weakness or hemiparesis. These episodes, lasting some hours, were frequently associated with sensory symptoms and often followed by headache. Her medical history, besides visual acuity loss, reported a diagnosis of Duane retraction syndrome type I of the left eye. Upon admission to our department, the neurological evaluation revealed mild spastic gait, brisk tendon reflexes, bilateral ankle clonus and diffusely slight muscle atrophy. The neuro-ophthalmological examination indicated bilateral visual acuity (Snellen charts) of 3/10 (0.50 LogMAR), colour sensitivity of 13/15 (Ishihara plates) and abnormal eye movements according to Duane retraction syndrome type I. Optic disks showed normal cup to disc ratio with slight neuralrim pallor. Bilateral small paracentral scotomas were evident on Goldmann field perimetry. A reduced peripapillary retinal nerve fibre layer thickness particularly prominent in the temporal and inferior quadrants was measured by ocular coherence tomography. Pattern visual evoked potentials indicated increased latency of cortical responses, while motor, somatosensorial and brainstem auditory evoked potentials, audiological and nerve conduction tests were within normal range. Transcranial Doppler and transoesophageal echocardiography evidenced a marked right-to-left shunt due to patent foramen ovale. Spinal cord and brain MRI confirmed the isolated bilateral optic nerve atrophy, without parenchymal lesions, gadolinium enhancement or metabolic changes at spectroscopy. Cyto-proteic analysis and oligoclonal band research on cerebrospinal fluid were normal, as well as the basal serum lactate level.

The sequential analysis of *OPA1* identified an already reported deletion c.2708_2711delTTAG in exon 27 determining a premature termination codon in position 905 (p.Val903GlyfsX905). Her father and sister proved to be asymptomatic carriers of the same mutation.

The skeletal muscle biopsy showed abnormalities in muscle fibre size and the presence of atrophic fibres at haematoxylin–eosin stain; there was no evidence of ultrastructural mitochondrial abnormalities except for a small size (Fig. 1). Long-range

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