Neurol Sci (2013) 34:1813–1814
DOI 10.1007/s10072-013-1296-x

LETTER TO THE EDITOR

Considerable post-partum worsening in a patient with CMT2E

Luca Gentile · Federica Taioli · Gian Maria Fabrizi · Massimo Russo · Claudia Stancanelli · Anna Mazzeo

Received: 14 November 2012 / Accepted: 5 January 2013 / Published online: 15 February 2013

Dear Editor,

Mutations in neurofilament light polypeptide gene (NEFL) have been reported to cause autosomal dominant (AD) axonal CMT2 (CMT2E), AD demyelinating CMT1 (CMT1F) [1] and autosomal recessive CMT2 [2].

We report clinical, neurophysiological and pathological findings of a patient belonging to a three-generational family that carries the p.Glu396Lys mutation in NEFL gene. Other members of the family (mother and uncle) have been previously described [3]; they presented a moderate to severe sensory–motor neuropathy, with onset between the first and the second decade, and prominent sensory ataxia with hearing loss in the female patient.

Our patient is a 32-year-old woman who has complained of mild balance impairment since childhood without any clinical evidence of progression until 3 years ago when, since the 5th week of her first pregnancy, she noticed a rapid worsening with severe walking difficulty and balance impairment. In fact, she started to walk with a stick, especially outdoor. She also had distal numbness and paraesthesias at the four limbs.

Neurological examination at the 14th week of her pregnancy revealed ataxic gait with bilateral foot-drop and positive Romberg's test, along with moderate distal wasting of upper and lower limbs, and bilateral pes cavus. In upper limbs, there was mild weakness of wrist extensors (MRC 4) and severe weakness in hand muscles (MRC grade 1–3). In lower limbs, weakness of ankle dorsiflexion (MRC 3) and severe weakness of extensor hallucis longus (EHL) (MRC 1) was seen, and the patient was areflexic. Sensory examination showed reduction of pinprick sensation below wrists and knees, and reduction of vibration sense below wrists and ankles. Joint position sense was reduced at the toes.

Nerve conduction study showed an intermediate sensory-motor neuropathy, with motor conduction velocity which ranged from 27 m/s in the median nerve to 42 m/s in the ulnar, and absent motor action potential in lower limbs. Sensory action potentials were diffusely absent. Normal or negative results were found for haematological and biochemical tests, including ANA, ANCA, C3, C4, hepatitis C markers, glucose tolerance test and thyroid hormones.

Similar to other members of this pedigree, there was a delay in BAEP and MEP central components.

Due to atypical progression, sural nerve biopsy was performed, to rule out inflammatory processes, and moderate loss of myelinated fibres was seen. There were neither amyloid deposits nor the presence of inflammatory cells. A moderate endoneurial and perineurial edema was seen.

Sequencing of the NEFL gene confirmed the same mutation (p.Glu396Lys) as the patient's mother. Neurological improvement started a few months after delivery even if she continued to complain of moderate weakness at lower limbs with slight difficulty in walking.

Previous studies have shown that mutations in NEFL gene can cause a high-variety of peripheral neuropathy phenotype, with clinical impairment ranging from mild to severe and with electrophysiological features that make classification in a specific CMT type (CMT1, CMT2) difficult [1]. Similarly to the family previously described with

L. Gentile (✉) · M. Russo · C. Stancanelli · A. Mazzeo
Department of Neurosciences, Psychiatry and Anesthesiology, AOU "G. Martino", Messina, Italy
e-mail: lucagentile84@yahoo.it

F. Taioli · G. M. Fabrizi
Section of Neuropathology, Department of Neurological, Neuropsychological, Morphological and Movement Sciences, University of Verona, Verona, Italy

this mutation [4] and to other members of the family, our patient showed a sensory-motor polyneuropathy with MCV in an intermediate range and prominent sensory ataxia. Interestingly, the patient had a considerable worsening immediately after first pregnancy. Atypical episodic worsening of clinical features related to feverishness in patients with CMT2E/1F has been previously reported [3, 4].

A superimposed inflammatory neuropathy in patients with CMT has been reported by many authors [5, 6]. Although rapid progression of symptomatology was suggestive of a superimposed neuropathy in our patient, no other cause of polyneuropathy, except mutation in the NEFL gene, has been found.

Exacerbation of weakness and other neuropathic symptoms during pregnancy have been reported in about 40 % of women with CMT1. In particular, 50 % of women with early onset CMT1 had pregnancy-related exacerbation, which persisted in about 2/3 [7].

As a possible pathomechanism, it has been supposed that oestrogen–related peripheral nerve oedema is exaggerated in CMT as a result of recurrent demyelination and remyelination. Pregnancy induced axonal degeneration through uterine adrenergic nerves and metabolic changes have also been hypothesized [8].

In conclusion, we observed a pregnancy-related worsening in a CMT2E patient, as already described in CMT1. We suggest that CMT patients who wish to have children should undergo a closer neurological follow-up during pregnancy, and should be informed of a possible benign deterioration of their condition.

References

1. Jordanova A, De Jonghe P, Boerkel CF, Takashima H, De Vriendt E, Ceuterick C (2003) Mutations in the neurofilament light chain gene (NEFL) cause early onset severe Charcot–Marie–Tooth disease. Brain 126:590–597
2. Yum SW, Zhang J, Mo K, Li J, Scherer SS (2009) A novel recessive *NEFL* mutation causes a severe, early-onset axonal neuropathy. Ann Neurol 66:759–770
3. Fabrizi GM, Cavallaro T, Angiari C, Cabrini I, Taioli F, Malerba G et al (2007) Charcot-Marie-Tooth disease type 2E, a disorder of the cytoskeleton. Brain 130:394–403
4. Züchner S, Vorgerd M, Sindern E, Schröder JM (2004) The novel neurofilament light (NEFL) mutation Glu397Lys is associated with a clinically and morphologically heterogeneous type of Charcot–Marie–Tooth neuropathy. Neuromuscul Disord 14:147–157
5. Vital A, Vital C, Lagueny A, Ferrer X, Ribière-Bachelier C, Latour P, Petry KG (2003) Inflammatory demyelination in a patient with CMT1A. Muscle Nerve 28(3):373–376
6. Ginsberg L, Malik O, Kenton AR, Sharp D, Muddle JR, Davis MB (2004) Coexistent hereditary and inflammatory neuropathy. Brain 127(Pt 1):193–202
7. Rudnik-Schöneborn S, Röhrig D, Nicholson G, Zerres K (1993) Pregnancy and delivery in Charcot-Marie-Tooth disease type 1. Neurology 43(10):2011–2016
8. Pollock M, Nukada H, Kritchevsky M (1982) Exacerbation of Charcot-Marie-tooth disease in pregnancy. Neurology 32(11): 1311–1314