Superimposed inflammatory neuropathy in patients affected by Charcot-Marie-Tooth neuropathy

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BACKGROUND: Superimposed inflammation may exacerbate the severity of hereditary neuropathy. We describe the frequency of this complication in a large population of patients monitored at the Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genova (DINOGMI).

PATIENTS: our first observation concerns a family in which three first cousins were affected by CMT2J. In two of them, a superimposed inflammatory neuropathy was previously diagnosed.

Patient 1: A 60-year-old man with subacute onset of distal lower limb neuropathy. Electrophysiological data demonstrated axonal and demyelinating damage and CSF underlined a mild increase of protein. After a cycle of endogenous immunoglobulin MRC score improved from 57 to 60. The patient was also successfully treated with steroid, azathioprine and plasmapheresis.

Patient 2: A 53-year-old female which began with lower limb proximal strength impairment, later associated with subacute distal neuropathy. The electrophysiology examination showed axonal and demyelinating damage with block of conduction while CSF was normal. After a cycle of endogenous immunoglobulin MRC score improved from 57 to 58. She was also treated successfully with steroid.

Patient 3: Female with proximal deficit of force, which began when she was 60 years.

To expand this interesting finding we decided to analyze 280 patients with a genetically diagnosed CMT selected from our database of 457 patients seen at the DINOGMI. 45.7% were affected by CMT1A, 12.1% by CMT1X and 10.7% had MPZ-related neuropathies.

Patient 4: Female with CMT2J who presented at the age of 74 a clear worsening of neuropathy and was diagnosed with AIDP.

Patient 5: Man affected by CMT2J. At 56 years old he was hospitalized for rapidly worsening AIDP which determined tetraplegia and respiratory failure. The patient was treated with IGIV with partial benefit. He died for internist complication.

Patient 6: Man with CMT1A diagnosed at the age of 37. 14 years later, suddenly appeared paresthesia in left hand and right lower limb, with simultaneous deficit of force. Such symptoms spontaneously improved.

Patient 7: Female with CMT1A. When 47 years old she complained paresthesia in both hands and distal weakness. CSF showed elevated protein (1 g/dl). After IGIV treatment MRC score improved from 50 to 58. She was effectively treated with steroids, too.

Patient 8: Female with CMT1A. When 47 years old she complained paresthesia in both hands and distal weakness. CSF showed elevated protein (1 g/dl). After IGIV treatment MRC score improved from 50 to 58. She was effectively treated with steroids, too.

Patient 9: A 56-year-old man presented weakness in right hand along with pes cavus and frequent falls. Electrophysiological test evidenced block of conduction in ulnar nerve. Diagnosis was CMT1A with MMN. After IGIV strength and neurophysiological data improved.

RESULTS: A confirmed inflammatory neuropathy was identified in 4 patients affected by CMT1A and in 5 with CMT2J neuropathy caused by Thr124Met mutation. The percentage of patients with superimposed inflammatory features was 3.1% in CMT1A group (2 CDIP, 1 MMN, 1 history suspected for inflammatory neuropathy) and 16.6% in CMT2J (2 CIDP, 1 with signs of inflammation at neuroimaging without respecting the criteria for a specific diagnosis, 2 dead for proven AIDP). Anti-gangliosides antibodies were performed and negative in patient 1,2,3,7,8 and 9. Anti-Neurofascin antibodies were performed in patient 1 and 3 and were negative, too.

CONCLUSIONS: inflammation may exacerbate a hereditary neuropathy, especially in patients affected by MPZ mutation Thr124Met. We suggest that alterations in protein P0 glycosylation site may be the underlying substrates of susceptibility in the immune system.

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