Hereditary sensory and autonomic neuropathy type II: a case report

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INTRODUCTION

Hereditary sensory and autonomic neuropathies (HSAN) encompass rare heterogeneous disorders of the peripheral nervous system. Sensory disturbances represent the predominant features, with a variable degree of autonomic involvement.

MATERIALS

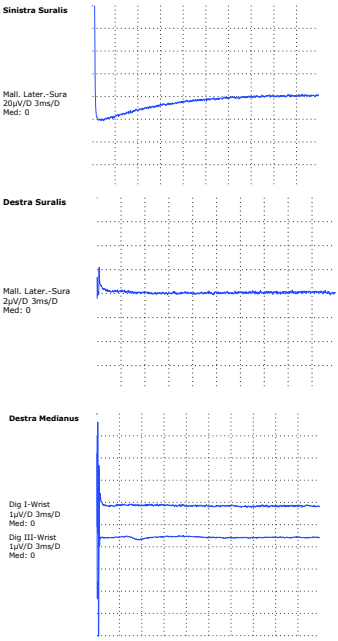
The patient is a male who came to our attention at the age of 33 years old, born to non-consanguineous parents, with a negative family history for neurological disorders. The patient reported childhood-onset of symmetric distally predominant limb tactile, thermal and pain hypoesthesia and thermal-pain anesthesia in the plantar surface of feet, which had led to distal amputations in the lower limbs due to unnoticed traumas. He reported dryness of the palms of the hands and soles of the feet, without sweating alterations and occasional gait instability. Previous genetic testing for mutations associated with Charcot-Marie-Tooth neuropathy type 2 (CMT2) in *MFN2*, *NEFL* and *GDAP1* genes were negative.
The neurological examination showed tactile and thermal-pain hypoesthesia of the hands and lower limbs and hypo-pallesthesia with distally predominant gradient, absent proprioception and upper limb sensory ataxia. Deep tendon reflexes were unelicitable with bilateral absence of the plantar reflex and multidirectional oscillations during the Romberg test.

METHODS

The patient underwent blood exams including autoimmune and microbiological screening, anti-neuronal antibodies, anti-gangliosides antibodies IgG and IgM, autoimmune encephalitis antibodies panel. The patient consented to exome next generation sequencing for hereditary neuropathies panel. Additionally, the electromyography (EMG), the valuation of autonomic control of cardiovascular reflexes and the skin biopsy were performed.

RESULTS

The blood exams did not reveal notable alterations. The EMG confirmed a severe predominantly sensitive polyneuropathy. The skin biopsy showed a severe autonomic small fiber neuropathy and absence of epidermal somatic fibers. The evaluation of autonomic control of cardiovascular reflexes reported normal responses. The exome sequencing identified the presence of the homozygous pathogenic variant c.3526_3529del_p.Thr1176CysfsTer21 in the WNK1 gene.



Bilateral Sural Nerve and Right Median Sensory Nerve Studies Using the Orthodromic Near-Nerve Technique (NNT)

DISCUSSION

HSANII is associated with biallelic pathogenic variants in *KIF1A*, *RETREG1* (FAM134B), *SCN9A*, or *WNK1* (1) genes. The pathophysiology is characterized by early impairment of large and small myelinated sensory fibers development with clinical onset before puberty (2). We report a pathogenic variant associated with truncation of the WNK1/HSN2 nervous system-specific isoform, as previously described (3). The pathogenetic mechanism may be related to dysregulation of the TRPV4 vallinoid receptor, involved in nocipeption (3).

CONCLUSION

Molecular studies and identification of new genetic correlations for HSAN are ongoing. Knowledge about the pathophysiology of these disorders is limited. Diagnostic delay predisposes to disease-related disability.

Bibliography

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