HEREDITARY SENSORY AUTONOMIC NEUROPATHY TYPE 1 – A RARE CASE REPORT

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ABSTRACT
Hereditary sensory and autonomic neuropathies (HSAN’s) are inherited group of disorders with loss of sensory, autonomic and sometimes motor function. They are classified by Dyck into 5 types of which we report a case of type 1 HSAN in a 22 years male who presented with impaired sensations over both feet and a trophic ulcer over right foot.

INTRODUCTION
HSAN type 1 is an autosomal dominant disorder with late onset of symptoms usually in 2nd decade. The defect is localized to chromosome 9q22, with the affected gene being identified as serine palmitoyltransferase long chain base subunit-1 (SPTLC1) (Dyck et al., 1993; Sinead M Murphy et al., 2013) affecting spingolipid synthesis pathway, leading to progressive degeneration of dorsal root ganglion with loss of both myelinated and unmyelinated nerves especially of lower limbs leading to distal sensory and mild motor impairment (Axelrod et al., 1996).

CASE REPORT
A 22 years male, born out of 2nd degree consanguinity, came to our OPD with complaints of altered sensation over both feet of 6 years duration and ulcer over the right foot of one month duration. History of minor trauma to the right foot 1 month back, following which he developed erosion and ulceration over plantar aspect. Initially small in size and progressed within days to current size, associated with serous discharge, redness and swelling over right 2nd toe. There was history of flat feet since birth. There is no history of pain, itching, fever, blister formation and topical application. No history suggestive of hypo-pigmented, hypo-anaesthetic patches. No history suggestive of proximal or distal muscle weakness. There is similar history of ulceration over left foot 6 years back. He underwent medical management and the ulcer resolved. History of trauma to both second toes 2 years back for which he underwent fish mouth surgery.

On examination, bilateral flat feet noted, surgical scars seen over bilateral 2nd toes. A single ill-defined ulcer of size 5x4 cm is present over the plantar aspect of right foot overlying 2nd metatarsal. Edges are sloping with no active discharge. Warm, erythematous, oedematous and dry skin is seen over the dorsal aspect of the right foot towards 2nd toe. No hypo-pigmented, hypo-anaesthetic patch seen over the body. All modalities of sensation over both the feet are impaired and intact elsewhere. Bilateral greater auricular and ulnar nerves were just palpable, but not thickened or tender. Examination of gait, motor system and deep tendon reflexes were normal.

Complete blood picture, fasting and postprandial sugars, renal function test, liver function test, thyroid function test, RF factor, ANA titre, routine urine investigation, radiography of bilateral feet, slit skin smear for Lepra bacilli, screening MRI to rule out compression...
neuropathy were done and were within normal limits. Nerve conduction studies was done and revealed sensory and motor axonal neuropathy in lower limbs and mild sensory axonal neuropathy in upper limbs. Right sural nerve biopsy was taken to rule out pure neuritic leprosy and showed normal histology. Thus we conclude to the diagnosis of hereditary sensory and autonomic neuropathy type 1.

**Figure 1:** Clinical photograph showing the trophic ulcer over plantar aspect of right foot. Surgical scars over both 2nd toes are seen.

**Figure 2:** Clinical photograph showing erythema and edema over dorsal aspect of the right foot.

**Figure 3:** Histopathology of right Sural nerve (at high power- 400X) reveals normal histology

**DISUSSION**

Hereditary sensory neuropathy type 1, (also referred as HSAN-1, Hereditary sensory radicular neuropathy, Mutilating acropachy and Acrodystrophic neuropathy) is a dominantly inherited degenerative disorder of sensory dorsal root ganglia. In addition, loss of small myelinated and unmyelinated nerves is seen resulting in the development of distal sensory and motor loss, predominantly involving lower limbs. Comparatively the clinical symptoms manifests late, than being congenital.

HSAN-1 occurs as a result of mutation in the gene serine palmitoyltransferase long chain base subunit-1 (SPTLC1) on chromosome 9q22.1-q22.3 (Nicholson et al., 1996). Serine palmitoyltransferase (SPT), an enzyme catalysing the rate limiting step in denovo synthesis of sphingolipid, is located at the outer membrane of endoplasmic reticulum. This step involves the condensation of L-serine and Palmitoyl Coenzyme A. Recently mutation in SPTLC2 gene was also found to contribute to HSAN1. As a result, shift in substrate specificity of SPT occurs, leading to use of L-alanine and L-glycine alternatively. It results in the formation of 1-deoxysphingolipids, which is neurotoxic in nature resulting in blockage of neurite formation (Dawkins et al., 2001).

Mutations occurring in exon 5(C133Y, C133W) and exon 6(V144D) on chromosome 9 of SPTCL1 leads to increase in denovo synthesis of glucosylceramide in
lymphoblast cell lines. This triggers apoptosis which produce massive cell death during closure of neural tube. Ceramide induced neural degeneration is proposed to be one among the causes of HSAN1. 

With the evolution of molecular genetics, seven gene loci and six disease causing genes for autosomal dominant and recessive HSAN have been recognized. These genes play an essential role in metabolism of lipids and regulation of intracellular vesicular transport, as a nerve growth factor and presumptive transcriptional regulator (Auer-Grumbach et al., 2010).

Clinical features manifests in late childhood or adolescence with the development of progressive loss of sensation in lower extremities, primarily pain and temperature. Frequently manifests as chronic trophic ulcer over weight bearing areas of feet which may lead to distal muscle wasting, weakness and mutilating deformity. This condition may be associated with lancinating pain in lower extremities, extension of sensory symptoms to upper extremities, neural deafness, congenital cataract and mental retardation occasionally (Heckman et al., 1995; Berginer et al., 1984). During the late stage of the disease, neuropathic arthropathy, spontaneous fractures, osteomyelitis and extrusion of bone fragments particularly metatarsals can occur, which often necessitate amputation. Nerve conduction studies for motor fibres are usually normal. HSAN1 can mimic Charcot-Marie-Tooth syndrome when there is severe distal muscle weakness and wasting. It should be differentiated from Hansen’s disease, Diabetic neuropathy, Heredofamilial amyloidosis, Tabes dorsalis, Syringomyelia, Familial progressive hypertrophic neuropathy of Dejerine and Sottas”.

Management is often supportive including usage of good fitting shoes, regular dressings and lessening of weight bearing if ulcers form.

CONCLUSION
This has thrown light over the fact that, it is of paramount importance to consider all possible causes, when a patient presents with trophic ulcer, before pertaining to a definitive diagnosis.

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CONFLICT OF INTEREST
The authors declare that they have no conflict of interest.

STATEMENT OF HUMAN AND ANIMAL RIGHTS
All procedures performed in human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

REFERENCES