HEREDITARY SENSORY AUTONOMIC NEUROPATHY - A CASE REPORT

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Abstract:
ABSTRACT Hereditary Sensory Autonomic Neuropathies (HSAN) are rare inherited genetic disorders, affecting predominantly the sensory system and to a variable extent the autonomic nervous system. It consists of 5 main sub-types (type 1 to 5). Here we report two children from a family who presented in their 2nd decade with clinical features of sensory changes manifesting in the form of multiple painless ulcers, erosive lesions of distal phalanges in toes, mutilating arthritis, autonomic involvement in the form of loss of sweating with relative preservation of motor functions. Electro diagnostic tests revealed absent Sensory Nerve Action potentials (SNAPs) and normal Compound muscle action potential (CMAPs). The mode of inheritance age at onset, clinical phenotype were suggestive of HSAN type 2. The aim of reporting this rare disorder is to recognize this disorder early so as to minimize the disabling complications as there is no treatment.

Keyword:
Key words HSAN- Hereditary sensory autonomic neuropathy , AR- autosomal recessive , autonomic neuropathy

INTRODUCTION:
Hereditary sensory and autonomic neuropathy (HSAN) is a slowly progressive neurological disorder characterized by predominant distal sensory loss, and autonomic nervous system involvement. The exact prevalence is not known, though it is reported to be low. There are five subtypes of HSAN ( type 1 to 5). There are certain distinguishing phenotypic differences among the subtypes. HSAN type 1 exhibits autosomal dominant pattern of inheritance, with age of onset in 2nd to 5th decade with motor weakness in addition to the sensory and autonomic involvement. HSAN type 2 has early childhood or rarely juvenile age of onset, autosomal recessive pattern of inheritance and has predominant distal sensory and autonomic involvement.
HSAN types 3-5 are inherited in an autosomal recessive pattern with age of onset in infancy. HSAN type 3 has predominant autonomic involvement with postural hypotension and episodic hypertension. HSAN type 4 presents as congenital insensitivity to pain with anhidrosis. They present with recurrent episodes of unexplained fever. HSAN type 5 presents as congenital insensitivity without anhidrosis.

This classification of HSAN proposed by Dyck et al\(^2\) was done based on basis of mode of inheritance, clinical symptoms and age at onset. Absence of pain and self-mutilation are characteristic findings of all the subtypes of HSAN. Though being categorized into types one through five, some children do not fit well into this classification. We report 2 cases of HSAN type 2.

**CASE REPORT OF 2 SIBLINGS FROM THE SAME FAMILY**

**CASE 1:**
An eighteen year old boy 1st child born out of consanguinous parentage with a normal birth and developmental history developed numbness and progressive non-healing ulcers over plantar aspect of the feet of 8 yrs. duration. The ulcers extended from the ball of the great toe up to the distal phalanx on the right side. On the left side the ulcers extended from the ball of the great toe and caused erosive lesions of distal phalanx of the left great and 2\(^{nd}\) toes. Subsequently he developed mutilating arthritis, and loss of sweating in legs and feet. He had relatively preserved motor functions. There was no history of recurrent episodes of fever. The bladder and bowel habits were normal. The course of the disease was slowly progressive. His younger brother was affected with similar illness. His parents were phenotypically normal.

A detailed neurological evaluation revealed normal cognitive functions, loss of all modalities of sensation, more marked on the distal parts of the limbs. Multiple ulcerations (fig 1& fig2) were present on feet with mutilating acropathy in the form of partial loss of toes with anhidrosis (fig. 3). There was total (deep) areflexia. The peripheral nerves were not palpable. The motor functions were well preserved.

Fundus examination was normal. The remainder of the central nervous system and other systemic examinations including blood pressure were normal.

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INVESTIGATIONS:
Hematological evaluation done was within normal limits. Serum B12 estimation, thyroid profile was normal. Split skin smear was negative for lepra bacilli. HIV by ELLISA was negative. He was worked up to exclude connective tissue disease and vasculitis. Electrophysiological studies revealed absent SNAPs and normal CMAPs amplitudes. The autonomic study revealed abnormal heart rate response on valsalva maneuver and deep breathing.

Sympathetic skin response was absent. Sural nerve biopsy shows (fig 4) fasicles with thick walled blood vessels in the epineurium on trichrome stain. High power examination (fig 5) reveals hypoplastic fascicles with perivascular inflammatory infiltrate. These findings are consistent with the diagnosis of HSAN.

CASE 2:
Fourteen years old boy who is the younger brother of case 1 with a normal birth and developmental history developed progressive non-healing ulcers over both feet present for 2 years duration. The ulcers extended upto the toes resulted in erosive arthritis and mutilation of his left great toe. He later developed hyperpigmentation of skin, and sweating disturbance in legs and feet.
Clinical examination revealed mental sub-normality with a IQ of 68 with absence of secondary sexual characters. He had graded sensory loss for touch, pain and temperature in upper and lower limbs. There was autonomic involvement in the form of sweating abnormalities, (fig.6) skin and hair changes in the lower limbs. Multiple ulcerations were present on feet with mutilating acropathy in the form of partial loss of toes with anhidrosis. There was total (deep) areflexia. The peripheral nerves were not palpable. The motor functions were well preserved. Fundus examination was normal. The central nervous system and other systemic examinations including blood pressure were normal.

INVESTIGATIONS:
Routine hematological work up was within normal limits. Serum B12 estimation, thyroid profile was normal. Split skin smear was negative for the lepra bacilli. HIV by ELLISA was negative. Endocrinology work up for sex hormones was normal. He was worked up to exclude connective tissue disease and vasculitis. Electrophysiological studies revealed absent SNAPs and normal CMAPs amplitudes. The autonomic study revealed abnormal heart rate response on valsalva maneuver and deep breathing. Sympathetic skin response was absent. Sural nerve biopsy (fig7) revealed total absence of myelin on Weigert-Pal stain (modified). This finding is consistent with the diagnosis of HSAN.

DISCUSSION:
HSAN type 2 is an inherited genetic disorder with autosomal recessive pattern of inheritance, with age of onset being early childhood. The common presenting manifestations being pan sensory loss, with autonomic involvement in the form of loss of sudomotor fibres to the extremities. All the characteristic features were present in our case except for the age of onset. The pattern of inheritance, age of onset, clinical phenotype and the electrophysiological studies are in favour of the diagnosis of HSAN type 2. Our patients developed their disease in second decade, which is rare but has been reported by Donaghy et al. HSAN type-II usually manifests at birth or in infancy. The usual autonomic disturbances in the form of bladder, bowel involvement and hypertension were absent in our cases, although both had distal anhidrosis. Sensory nerve action potentials are absent and Sural nerve biopsy shows loss of myelinated fibers more than the unmyelinated ones. Association of spastic paraplegia
with HSAN2 has been reported by Cavanagh et al. although such feature was absent in our cases. In India, Balachandran et al has reported type-II variety in siblings.

When faced with a child presenting with insensitivity to pain, impaired sweating, limb ulcers, and mutilation, HSAN should be considered in the differential diagnosis. The other causes of predominant small fibre involvement are diabetes, amyloidosis, HIV infection, paraneoplastic, connective tissue disease and vasculitis. HSAN can be differentiated from other diseases by the characteristic clinical and electrophysiological manifestations in accordance to its type. Lesch-Nyhan syndrome is an X-linked recessive disorder clinically characterized by lesions from self-mutilation. Hyperuricemia, a major diagnostic criterion for Lesch-Nyhan syndrome, is not found in HSAN.

Initial delay in diagnosis can occur due to similarity of the mutilating acropathy with that of leprosy, a more common disease in this area. Hence the leprosy should always be excluded prior to diagnosis of this rare disorder. There are no medical therapies available to treat these neuropathies, other than prevention and treatment of mutilating skin and bone lesions. Prevention of trauma to the anesthetized parts and appropriate management of the sequelae of autonomic neuropathy are the aims.

CONCLUSION:
Though rare a knowledge of hereditary sensory autonomic neuropathy type 2 which presents as pansensory loss, mutilating acropathy, total areflexia with normal motor functions and distal anhidrosis is necessary to differentiate this from the more prevalent hansen neuropathy. Prevention and treatment of the mutilating skin and bone lesions prevents further disabilities.

References:


