The painless eye: Neurotrophic keratitis in a child suffering from hereditary sensory autonomic neuropathy type IV

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Hereditary sensory autonomic neuropathy (HSAN) is a group of inherited disorders (total 5 types) that are associated with sensory dysfunction and varying degrees of autonomic dysfunction. HSAN type IV (HSAN-IV) or *congenital insensitivity to pain and anhidrosis (CIPA)* is a rare genetic disorder inherited in an autosomal recessive manner. We report a case of this very rare genetic disease in a 3-year-old girl child, born to a family in north India with ocular features of neurotrophic keratitis. The diagnosis was made clinically based on the hallmark features of insensitivity to pain and temperature, anhidrosis, self-mutilating behavior with multiple recurrent oral ulcers, nasal bleeds, multiple trophic ulcers over joints, and decreased intellect.

Key words: Anhidrosis, autonomic neuropathy, congenital insensitivity to pain and anhidrosis, Hereditary sensory autonomic neuropathy, neurotrophic keratitis

HSAN are a group of very rare genetic disorders characterized by axonal atrophy and degeneration, primarily affecting peripheral sensory and autonomic neurons.[1] HSAN is sub classified into types I–V based on age-at-onset, inheritance pattern, and several other features.[2]

HSAN-IV is distinguished by its cardinal features comprising of extensive involvement of ectodermal structures and marked decreased sweating. It commonly is autosomal recessive in genetic distribution.[3,4] Patients exhibit prominent distal sensory loss with manifest insensitivity to pain, frequently leading to self-mutilating behavior, sometimes resulting in severe complications.[2] Neurotrophic keratitis is the more commonly associated ocular feature.

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Case Report

A 3-year-old girl, born from a non consanguineous marriage, presented to us with complaints of blurred vision, redness, and watering in both eyes for 3 weeks.

She had a past history of multiple injuries and self-inflicting traumas. Parents gave a strong history of, lack of response to any painful stimuli and insensitivity to extreme temperature stimuli. She also had lacking intellectual ability.

On general examination, there were multiple ulcers all over her extremities, more over pressure areas and multiple healed abrasions [Fig. 1a-e]. She had decreased sensations in distal parts of both extremities and skin appeared thickened. Various signs of self-mutilation like recurrent nosebleed, ulcers over the tongue, nail marks, and mutilations of digits were noted [Fig. 2a]. She presented with a large café au lait spot on her right cheek [Fig. 2b].

Her visual acuity was found to be 6/6, N6 in the right eye and 6/24, N12 in the left eye. Slit lamp examination [Figs. 2c and 3], at the time of presentation, revealed mild, nonspecific changes, with staining of inferior palpebral conjunctiva in the right eye. In the left eye, severe conjunctival congestion, follicles, with significant superficial punctate keratitis (SPKs) along with a nebulo-macular corneal scar was noted. Features suggestive of neurotrophic keratitis were graded into stage 1 in RE and stage 2 in the LE (Mackie classification). *Tear Film Break Up Time* was found to be below lower limit. Schirmer's 1 test was found to be at the lower range.

Laboratory investigations were found to be within normal limits. MRI brain and spinal cord was normal. The child further underwent nerve biopsy, which showed absence of small unmyelinated fibers, decrease in neuronal population, and abnormally enlarged mitochondria.

Discussion

HSAN is caused by mutations in NTRK1,[4] which gets auto phosphorylated in response to nerve growth factor (NGF).[5] Neuropathological studies report absent unmyelinated nerve fibers in sural nerve biopsies.[2,6] Severe anhidrosis and absence of sympathetic skin responses, can be accounted for by the lack of sweat gland innervation.[7]

Even though there is gene identification, gene analysis is not routinely used for diagnosis because of interference of

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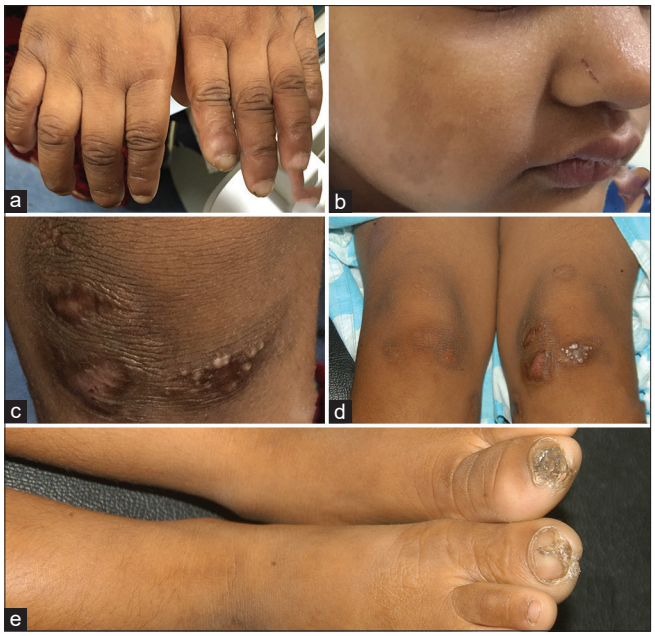

Figure 1: Self mutilating marks and non healing ulcers on distal digits. (a) Hands. (b) Nose. (c and d) Knees and lower limb. (e) Toes

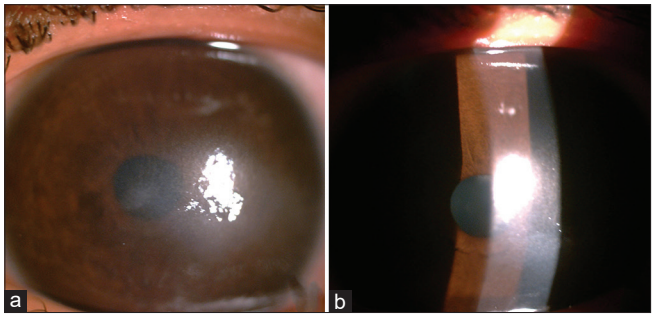

Figure 3: (a and b) Slit lamp photography showing left eye Neurotrophic Keratitis (Epithelial Keratopathy) with corneal scarring

numerous mutations.[4] Diagnosis usually is clinical, like in our case, requires three criteria – *anhidrosis, decreased pain perception, and delayed or reduced intellectual ability*.[4,7,8]

Due to corneal denervation, there occurs a suppression in the secretion of tears and mucin expression on the corneal epithelium.[9] Thus, SPKs may be the initial finding in these patients.[9] Though, another study found that, decrease in tear breakup time (TBUT) was not a consistent finding.[10]

Conclusion

HSAN-IV may present to the ophthalmologist first with signs and symptoms of neurotrophic keratitis. A detailed history and general examination may aid to the diagnosis and appropriate therapy. We present one such rare case requiring regular follow up and counseling to avoid further avoidable damage both physical and psychological.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients

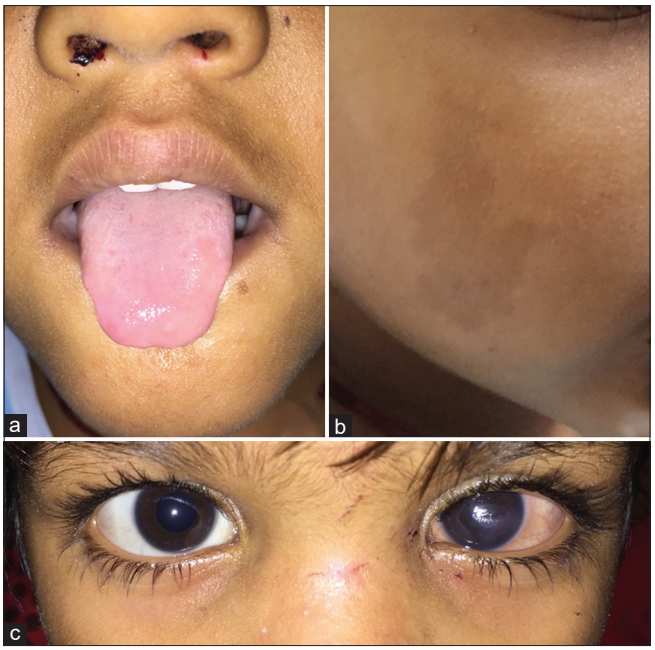

Figure 2: (a) Shows Recurrent multiple oral ulcers (tongue) and Recurrent nosebleeds – Highlighting the Self Mutilating Behavior. (b) Shows the café – au – lait spots and nail marks on the skin – Again Highlighting the self-mutilating behavior. (c) Shows neurotrophic keratitis in the left eye with congestion and corneal scarring

understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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