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Case Report

Hereditary sensory autonomic neuropathy type V: a rare case report

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ABSTRACT

Hereditary sensory autonomic neuropathy (HSAN) type V is a rare autosomal recessive condition caused by mutation in neurotrophic tyrosine kinase receptor type 1 gene located on chromosome 1 (1q21-1q22). It is characterized by pain insensitivity, partial anhydrosis without mental retardation and unimpaired touch and pressure sensitivity. Self-mutilation injury involving teeth, lips, tongue, ears, eyes, nose and fingers are invariable feature of this disorder. This rare disorder can be extremely challenging for the physicians as the symptoms like pain, tenderness is absent and hence most of the symptoms and injuries are frequently missed. Here we report a case of 1-year old female child with HSAN type V, having the typical clinical manifestations of pain insensitivity causing self-mutilation. Apart from the classical manifestations of HSAN type V, our case also had bilateral corneal opacity.

Keywords: Congenital insensitivity to pain, Corneal opacity, Hereditary sensory autonomic neuropathy

INTRODUCTION

Hereditary sensory autonomic neuropathy (HSAN) type V is a rare autosomal recessive condition caused by mutation in neurotrophic tyrosine kinase receptor type 1 gene located on chromosome 1 (1q21-1q22). It is characterised by pain insensitivity, partial anhydrosis without mental retardation and unimpaired touch and pressure sensitivity. Self-mutilation injury involving teeth, lips, tongue, ears, eyes, nose and fingers are invariable feature of this disorder. This rare disorder can be extremely challenging for the physicians as the symptoms like pain, tenderness are absent and hence most of the symptoms and injuries are frequently missed

CASE REPORT

One-year old female child presented with a history of self-mutilating behaviour which was noticed by mother since 1 month. Child was first born to a third degree consanguineously married couple. On further questioning there was no history of developmental delay. Family history did not reveal similar complaints in other family members. Antenatal history, birth history and postnatal history was uneventful.

Figure 1: Self mutilation of tongue.

Figure 2: Self mutilation of lower lip.

On examination child had signs of extensive self-mutilation. Major bulk of oral tissues including tip of the tongue was missing with fissures over lower lip due to extensive self-mutilation as shown in Figure 1 and 2. Neurological examination revealed absent pain and temperature sensations. Fine touch was intact. Tendon reflexes and plantar response were normal. Other systemic examination were unremarkable. Ophthalmoscopic examination showed bilateral corneal opacity (Figure 3).

Figure 3: Bilateral corneal opacity.

Hematological and biochemical investigation including uric acid levels were normal. Nerve conduction study was normal. Sural nerve biopsy showed severe fibre loss and Schwann cell proliferation with semithin section showing predominantly small fibre loss in all funicles with relative preservation of large myelinated fibres with no evidence of regenerating clusters consistent with the diagnosis of HSAN type V.

Hence in light of the classical clinical manifestation along with examination of nerve biopsy specimens, the diagnosis of HSAN type V was made in the absence of genetic analysis.

DISCUSSION

Hereditary sensory autonomic neuropathy occurs less frequently than hereditary motor sensory neuropathies. HSAN has been categorized into 5 types based on inheritance pattern, time of presentation, clinical and electrophysiological features, metabolic defects and specific genetic markers.[1] HSAN type V is similar to HSAN type 4 but is relatively mild without mental retardation and less severe anhydrosis.[2]

HSAN type I is the most common type with autosomal dominant inheritance. The onset of symptoms occurs in second to fourth decade of life with progressive sensory loss and chronic perforating ulcers of feet and progressive destruction of underlying bones.

HSAN type II is autosomal recessive condition. Onset of symptoms is seen in early infancy or childhood with loss of pain, temperature, pressure and light touch sensation and chronic ulcerations and multiple injuries to fingers and feet. Deep tendon reflexes are reduced.

HSAN type III is an autosomal recessive condition which is evident from birth as a poor or absent suck reflex, hypotonia and hypothermia. Reduced or absent tears, absence of fungiform papillae, absent corneal reflexes, anhidrosis, decrease or absent deep tendon reflexes (DTR), postural hypotension, decreased response to pain and temperature perception but normal touch perception is seen. Many patients die during infancy or childhood.

HSAN type IV is a rare autosomal recessive disorder described initially by Swanson in 1963.[3] HSAN type IV or CIPA (Congenital Insenstivity to Pain with Anhidrosis) is secondary to mutation in the neurotrophic tyrosine kinase receptor type 1 (NTRK 1) gene located on chromosome number 1 which encodes one of the receptor for nerve growth factors. Child presents with recurrent episodes of hyperthermia and unexplained fever. Other symptoms include anhidrosis, profound loss of pain insensitivity, mild to moderate mental retardation. Mental retardation and insensitivity to pain is known to cause self-mutilation in these patients especially in the fingers, lips and tongue. Corneal ulcerations are very common. It is not uncommon to see non-painful fractures in these patients which can cause chronic osteomyelitis and septic arthritis. Autonomic deficits include inability to sweat in response to heat or chemical stimuli.

HSAN type V is an autosomal recessive condition similar to HSAN type IV characterised by lack of pain perception, partial anhydrosis without mental retardation with preservation of all other sensory modalities including normal touch perception, proprioception, warm

and cold temperature discrimination and vibration.[4] It is caused by mutation in NTRK1 gene located on chromosome 1 coding for nerve growth factor B (NGFB) gene.[4,5] Self-mutilation is invariable feature of this disorder most often involving the teeth, lips, tongue, ears, eyes, nose and fingers.

HSAN type V resembles HSAN type 4. These two neuropathies can be differentiated on the basis of clinical features and nerve biopsy. Greater severity of anhydrosis is present in HSAN type IV compared to type V. Mental retardation is not seen in HSAN type V which is always seen in HSAN type IV.[6-8]

In HSAN type V, there is severe reduction of unmyelinated nerve fibres and a moderate loss of thin myelinated nerve fibres whereas HSAN type IV show reduced small myelinated nerve fibres and normal large myelinated nerve fibres.[9,10]

Self-mutilation and impairment of pain sensation is also seen in conditions such as Lesch-Nyhan syndrome and de Lange syndrome.[11] However HSAN type V can be differentiated from these syndromes by the presence of partial anhydrosis, absence of peripheral nerve thickening and dysmorphic features, a normal serum uric acid level and electrophysiological studies and histopathological findings of nerve fiber loss.[11]

Only few cases of HSAN type V has been reported due to rarity of the condition. Though in the case we report here, genetic analysis was not done but however classical clinical manifestations and nerve biopsy examination has led to the diagnosis of HSAN type V.

There is no definite treatment for HSAN type V. Medical management is supportive and aimed at controlling hyperthermia, prevention of self-mutilation and treatment of orthopedic problems. Typical oral manifestations in HSAN type V are ulcers seen on the ventral surface of the tongue due to repeated biting during infancy (resection of anterior portion of tongue), auto-extraction of the teeth and tearing wounds mostly on the lower lip.

Oral management of these patients should focus on preventing injury to the tongue, lips, teeth, and oral mucosa. Children may require grinding of the teeth or extraction of all teeth or bite guard to prevent self-mutilation injury to the tongue and lips.

HSAN type V is extremely dangerous and in most of the cases the patient does not live over the age of 25. But with better understanding of the disorder and helping patient to achieve independent function with minimal physical limitations we can increase the life span of these patients.

CONCLUSION

Prenatal diagnosis should be done in all families with HSAN type V patient to prevent birth of an affected child. Early diagnosis, patient education for prevention of trauma, skin and eye care, proper management of local infections forms the main stay of management in preventing the frequency and severity of complications.

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