Congenital Insensitivity to Pain (Hereditary Sensory and Autonomic Neuropathy Type V): A Rare Case Report

Shilpy Singla, Post Graduate Student
Nikhil Marwah, BDS, FAGE, MDS
Samir Dutta, MDS

ABSTRACT

Congenital insensitivity (**HSAN**) to pain is a rare disorder, which affects the body's pain-protective mechanism and predisposes the patient to increased risk and incidence of traumatic injuries. Currently, 5 types of hereditary sensory and autonomic neuropathies have been identified, depending upon different patterns of sensory and autonomic dysfunction, peripheral neuropathy, clinical features, and genetic abnormalities. The purpose of this report is to present the case of a 10-year-old boy with congenital insensitivity to pain (hereditary sensory autonomic neuropathy [HSAN] type V) with dental implications. History, clinical features, nerve conduction studies, and electron microscopy revealed no reaction to painful stimuli, a self-mutilating habit, multiple missing teeth, and an absence of small, unmyelinated fibers, thus indicating HSAN type V. Management included patient counseling and use of a mouthguard to prevent further damage and restore function. (**J Dent Child 2008;75:207-11**)

Received March 27, 2007; Last Revision August 9, 2007; Revision Accepted December 9, 2007.

KEYWORDS: HEREDITARY SENSORY AUTONOMIC NEUROPATHY, INSENSITIVITY TO PAIN, SELF-MUTILATION, PERIPHERAL SENSORY NEUROPATHY

Hereditary sensory autonomic neuropathy (**HSAN**) represents a collective group of disorders that affect the number and distribution of small myelinated and unmyelinated nerve fibers. HSAN is characterized by diminished or absent sensitivity to pain, touch, and pressure on the extremities and varying parts of the trunk.[1] HSAN is classified into 5 types.[2] (Table 1)

Type I—hereditary sensory radicular neuropathy—is the most common of hereditary, sensory, and autonomic neuropathies transmitted by autosomal dominant trait. It is characterized by a sensory deficit in the distal portion of the lower extremities, chronic perforating ulcerations of the feet, and progressive destruction of the underlying bones. Symptoms appear in late childhood or early adolescence. Many patients have accompanying nerve deafness, atrophy of the peroneal muscles, and a reduction in the number of unmyelinated nerve fibers. Motor nerve conduction velocities are normal, but sensory nerve action potentials are absent.

Type II—congenital sensory neuropathy—presents an onset of symptoms in early infancy or childhood. Upper and lower extremities are affected, with chronic ulcerations and multiple injuries to the fingers and feet. Pain sensation is predominantly affected, and deep tendon reflexes are reduced. Auto-amputation of distal phalanges and neuropathic joint degeneration is quiet common. There is a total loss of myelinated fibers and a reduced number of unmyelinated fibers.

Type III—familial dysautonomia or Riley-Day syndrome—is an autosomal recessive disorder seen mostly in

Dr. Singla is a postgraduate student, Dr. Marwah is assistant professor, and Dr. Dutta is professor and head, all in the Department of Pedodontics and Preventive Dentistry, Government Dental College, Rohtak, Haryana, India. Correspond with Dr. Singla at shilpy1_singla@yahoo.co.in

Table 1. Classification of Hereditary Sensory and Autonomic Neuropathy (HSAN) Subtypes[7]

Condition (HSAN type)	Inheritance pattern	Onset	Genetic abnormality	Clinical features
I	Autosomal dominant	Late onset—after second decade	Mutation in SPLTCI gene at locus 9q22.1-q22.3	Progressive sensory loss, no autonomic dysfunction, hearing loss
II	Autosomal recessive	In infancy	Unknown	No autonomic dysfunction, global sensory loss,
III (Riley-Day syndrome)	Autosomal recessive	In infancy	Mutation in IKBKAP (inhibitor of kappa light polypeptide gene enhancer in B-cells) at locus 9q31	Ashkenazi Jewish disease, profound autonomic dysfunction, loss of pain and thermal sensation, absent deep tendon reflexes, and fungiform papillae
IV	Autosomal recessive	In infancy	Mutation in NTKR1 (neurotrophic tyrosine kinase receptor type 1) gene at locus 1q21-q22	Self mutilation, impaired sweating with hyperpyrexia, absent thermal sensation, severe learning disability
V	Autosomal recessive	In infancy	Invariable may be unknown—mutation in NGFB (nerve growth factor B) gene in some cases	Tactile, vibratory, and thermal sensations usually intact, no autonomic dysfunction, deep tendon reflexes intact

Jews of eastern European descent. Patients present with sensory and autonomic disturbances, such as a weak suck reflex, hypotonia, hypothermia, retarded physical development, poor motor coordination, reduced tears, depressed deep tendon reflexes, absent corneal reflexes, postural hypotension, and scoliosis. Peripheral nerves show a reduced number of myelinated and unmyelinated axons. The prognosis of this type is very poor, with most patients dying in early infancy or childhood.

Type IV—congenital insensitivity to pain and anhidrosis (CIPA)—infants present with hyperthermia unrelated to environmental temperatures, anhidrosis, and insensitivity to pain. Palmar skin is thickened, and Charcot's joints are commonly present. Peripheral nerve biopsy reveals absence of small, unmyelinated fibers with abnormally enlarged mitochondria.

Type V—congenital insensitivity to pain—is an autosomal recessive condition with onset in infancy. Features include profound insensitivity to pain with tactile, vibratory, and thermal sensations usually intact and a severe reduction in unmyelinated fibers.

Congenital insensitivity to pain is a rare disorder grouped under HSAN type V, and was first described in 1932 by Dearborn as congenital pure analgesia.[3] It is characterized as an autosomal recessive disorder with onset at birth and is associated with profound insensitivity to pain with normal tactile, vibratory, and thermal sensations. Motor and tendon reflexes are intact in most of the cases. Although these patients are sensitive to thermal stimuli, they are not aware of the pain normally associated with high temperatures. Hence, burns often occur. Fractures and other orthopedic injuries are also very frequent. Self-mutilation is an almost invariable feature of this disease, most often involving the teeth, lips, tongue, ears, eyes, nose, and fingers.[4]

The purpose of this paper is to present a case report of congenital insensitivity to pain (HSAN type V) and outline its dental implications.

CASE REPORT

A 10-year-old boy reported to the Department of Pedodontics and Preventive dentistry, Government Dental College, Rohtak, Haryana, India, with the chief complaint of missing teeth. He was born of a nonconsanguinous marriage and was the only child. He was born at term without any complications and with no family history of similar illness. History revealed that he exhibited an absence of normal reaction to painful stimuli such as falls and cuts. He also did not cry during vaccinations.

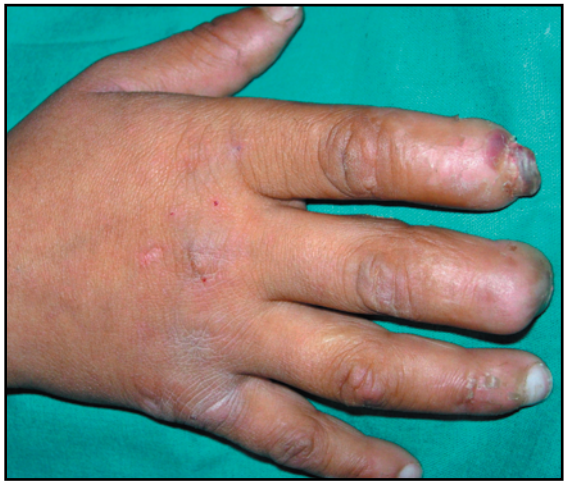

Figure 1. Fingers are short with stubby blunt ends; notice the loss of terminal phalanges and loss of nails with ulceration.

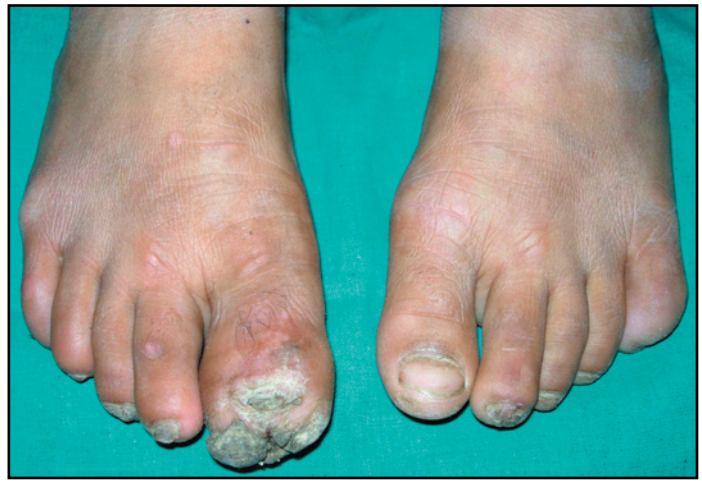

Figure 2. The littlest toes are deformed, and necrosis is seen on the left foot's big toe.

A general examination revealed the presence of normal deep tendon reflexes and normal reactions to light touch, tickling, and pressure. He also responded normally to thermal stimuli, although there was no reaction to painful stimuli. There was no alteration in taste and no history of flushing, temperature lability, or altered lacrimation, which suggested normal autonomic function.

Physical examination of his extremities showed that his fingers were short with stubby blunt ends; there was a loss of terminal phalanges and nails on the index and middle fingers of both hands with ulceration (Figure 1). His littlest toes were also deformed, and necrosis was seen on the big toe of his left foot (Figure 2). Other distinguishing features included bilateral corneal opacities (Figure 3) and hypoplasia of the nipples (Figure 4).

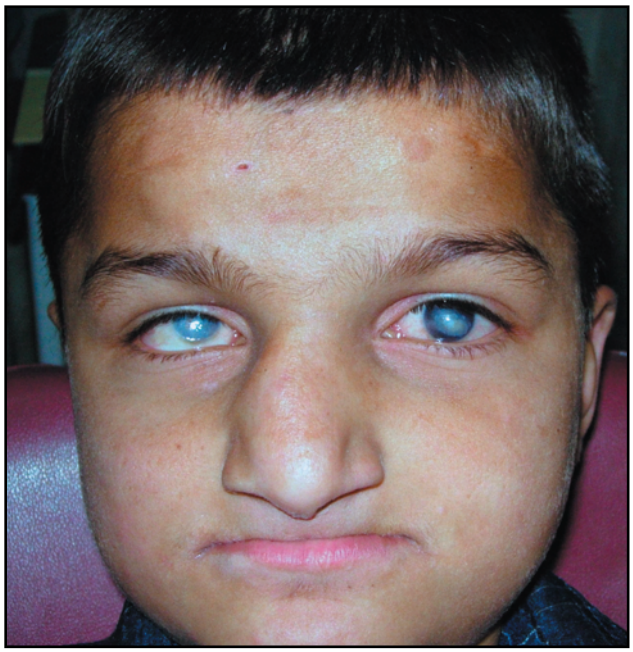

Figure 3. Bilateral corneal opacities.

Intraoral examination revealed absence of all the permanent maxillary teeth, with the exception of the first molars and presence of severe maxillary ridge resorption. There was a full complement of teeth present in the mandibular arch, which were normal regarding the patient's dental and chronological. The panoramic radiograph (Figure 5), showed congenitally missing permanent maxillary teeth, except for the permanent maxillary first and second molars. Dental history further revealed that all primary teeth in the maxillary arch had initially erupted at a normal age, but were auto-extracted by the patient or abnormally loosened by him and subsequently exfoliated.

Our provisional diagnosis based on history and clinical findings suggested HSAN. To further strengthen our belief, we decided to conduct definitive nerve investigations to support our diagnosis. Nerve conduction studies demonstrated that distal and motor nerve conductions were within a normal range and no consistent sensory potentials were obtained from nerve trunks following surface stimulations at the digits. A concentric needle electromyography from extremity muscles revealed no spontaneous activity and presented a normal recruitment pattern. Electron microscopy, however, revealed an absence of small unmyelinated fibers to confirm our diagnosis of congenital insensitivity to pain (HSAN type V).

The focus was on oral rehabilitation, prevention of further injury to oral structures and other body parts, and restoring the oral apparatus' functionality. Treatment options considered ranged from counseling, selective grinding, and the provision of preventive appliances like an oral screen and mouthguards to aggressive management, such as extraction of teeth.

The management strategy was formulated, and the patient was initially counseled. The patient had an overwhelming response and could understand the problem. He wanted to give a conscious effort to correct it. Among the treatment options, we felt that selective grinding would not help much as no teeth (except for molars) were present

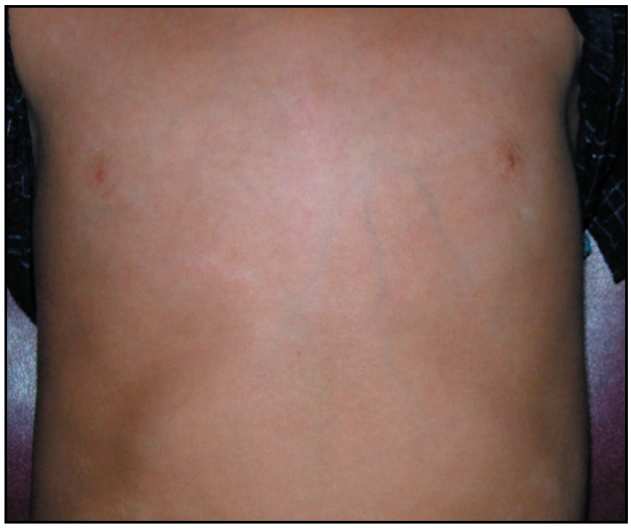

Figure 4. Hypoplasia of the nipples.

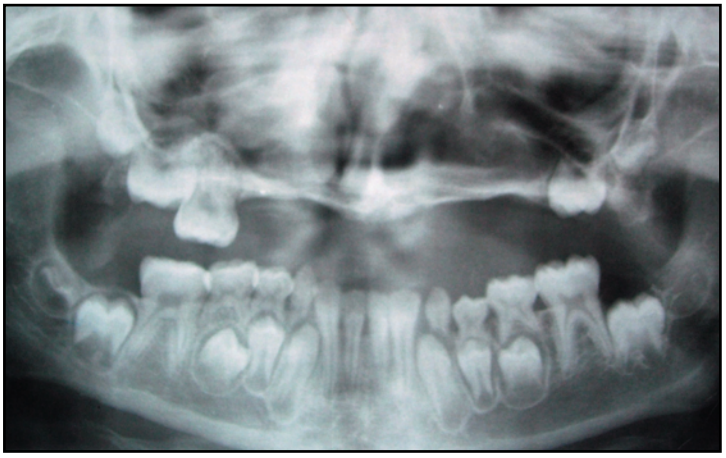

Figure 5. Orthopantomogram radiograph exhibiting absence of all the permanent maxillary teeth, with the exception of first molars, and a full complement of teeth is present in the mandibular arch.

in the maxillary arch and the mandibular teeth would continue to injure the maxillary alveolar ridge. Extraction was considered to be too aggressive for this patient due to his young age. Mouthguard therapy was thought to be the best option based on 2 factors. First, the patient exhibited minimal oral soft tissue damage (due to a self-mutilating habit), which could be avoided by this appliance, thereby preventing auto-extraction and secondly, restore masticatory function.

The patient is on follow-up since 6 months using preventive protocol with periodic assessment and counseling.

DISCUSSION

Congenital insensitivity to pain is a rare disorder and oral manifestations may be a presenting complaint. Self-mutilating teeth injuries are a prevalent finding, and these injuries often begin as the primary dentition erupts. Auto extraction may be more frequent among subjects with mixed or permanent dentition, as both erupting and shedding teeth are mobile and can easily be removed, as reported in our case.[5] Frequently, the tongue and lips are also affected with resultant scarring and deformation associated with tooth eruption.[6] In this case, insensitivity to pain is evident from nerve conduction studies and there is a total lack of response to painful stimuli and unperceived injuries to fingers, leading to necrosis and destruction of nails.

A diagnosis of HSAN type V (Table 1[7]) is suggested by the patient's absence of pain, self-mutilating auto-extractions, clinical insensitivity to pain, normal reaction to touch and thermal stimuli and the results of nerve conduction studies which show the absence of unmyelinated fibers. Motor functions and tendon reflexes are normal, thus differentiating the problem from HSAN type II in which there is generalized pansensory loss and abnormal temperature sensation.[8] HSAN type I is an autosomal dominant disorder, and symptoms begin in the second decade or later, whereas HSAN type V is autosomal recessive and begins in infancy. HSAN type III is autosomal recessively inherited, affecting mostly Ashkenazi Jews, and its manifestations usually present at birth and is suggestive of defective autonomic control. HSAN type IV is also congenital insensitivity to pain, but is associated with pyrexia, anhidrosis, absent thermal sensation, and mental retardation.

Though no disorder exactly mimics hereditary sensory autonomic neuropathy, impairment of pain sensation and oral mutilation have been reported in some syndromes, such as Lesch-Nyhan, Tourette, and De Lange syndromes, but all these show some degree of mental retardation. The absence of nail and hair abnormalities and the presence of normal sweat glands on a skin biopsy exclude anhidrotic ectodermal dysplasia.

Several methods of prevention of injuries have been suggested, such as elimination of sharp surfaces of teeth, use of mouthguards, and extraction of teeth. The degree of self-injury must be considered when deciding on appropriate management, and extractions may be unavoidable where the mutilation is particularly severe or where more conservative treatment options have proved ineffective. Prevention of dental diseases in the mandibular arch was important, as caries can progress to pulpal involvement without causing pain and may lead to infection and tooth loss. At the present time, there is no specific treatment for congenital insensitivity to pain or the other hereditary sensory and autonomic neuropathies. Recent molecular genetic advances in knowledge about the sensory and autonomic neuropathies, however, have improved diagnosis of the condition and genetic counseling for affected families.[9]

The dental team should, therefore, be involved in the management of these patients as soon as a diagnosis is made. Moreover, careful monitoring should continue throughout the patient's lifetime, along with comprehensive dental care to maintain the patient's social, psychological, and behavioral rehabilitation.

REFERENCES

1. Littlewood SJ, Mitchell L. The dental problems and management of patient suffering from congenital insensitivity to pain. Int J Paediatr Dent 1998;8:47-50.
2. Menkes JH, Sarnat HB. Child Neurology. 6th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2000:198-205.
3. Dearborn G. A case of congenital pure analgesia. J Nerv Ment Dis 1932;75:612-5.
4. Nicholoson GA, Dawkins JL, Blair IP, Kennerson ML, Gordon MJ, Cherryson AK, et al. The gene for hereditary sensory neuropathy type I (HSN-1) maps to chromosome 9q22.1-q22.3. Nat Genet 1996;13:101-4.
5. Amano A, Akiyama S, Ikeda M. Oral manifestations of hereditary sensory and autonomic neuropathy type IV. Congenital insensitivity to pain with anhidrosis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998;86:425-31.
6. Hall KH. Paediatric Orofacial Medicine and Pathology. London, UK: Chapman & Hall Medical; 1994: 330-5.
7. Dyck PJ. Neuronal atrophy and degeneration predominantly affecting peripheral, sensory, and autonomic neurons. In: Dick PJ, Thomas PK, Griffin JW, Low PA, et al, eds. Peripheral Neuropathy. Philadelphia, Pa: WB Saunders; 1993:1065-93.
8. Basu S, Paul DK, Basu S. Four siblings with type II hereditary sensory and autonomic neuropathy. Indian Pediatr 2002;39:870-4.
9. Auer-Grumbach M. Hereditary sensory neuropathies. Drugs Today (Barc) 2004;40:385-94.