with persistence of the bowel lesion, followed by necrosis and perforation(4,8). We recognized the clinical findings of neutropenic enteropathy on an average of 4 days after the onset of chemotherapy-induced neutropenia. Persistence of neutropenia should also be noted in our patient in whom surgical intervention did not provide regression of the process. The ongoing ileus with impaired vascularity, severe cell mediated immune defect with or without infection with *Candida albicans* or other opportunistic organisms, would not permit healing of the anastomosis.

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Hereditary Sensory Autonomic Neuropathy Type IV

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Hereditary sensory autonomic neuropathy Type IV is an autosomal recessive disorder due to lack of maturation of small myelinated and unmyelinated fibers of peripheral nerves, which convey sensation of pain and temperature, therefore, resulting in self mutilation. There is anhidrosis due to lack of innervation of normal sweat glands resulting in recurrent episodes of hyperpyrexia. The clinical presentation of two children with this rare disease is described.

Key words: *Hereditary sensory autonomic neuropathy, Insensitivity to pain, Self-mutilation.*

Hereditary sensory and autonomic neuropathy (HSAN) is a rare syndrome

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characterized by congenital insensitivity to pain, temperature changes and by autonomic nerve formation disorders. HSAN is classified into five types: sensory radicular neuropathy (HSAN I), congenital sensory neuropathy (HSAN II), familial dysautonomia or Riley Day Syndrome (HSAN III), congenital insensitivity to pain with anhidrosis (HSAN IV) and congenital indifference to pain (HSAN V)(1).

HSAN type IV inherited as an autosomal recessive trait, is characterized by recurrent episodes of unexplained fever, failure to thrive, absence or decreased perspiration (despite normal sweat glands), insensitivity to pain, self mutilation and mental retardation(2). Only few case reports of HSAN are available from India(3-8). We report two patients with HSAN type IV. The purpose is to introduce this rarely encountered disease, and to present information related to diagnosis and management.

Case Report

A six-year-old female child, first product of a non-consanguineous marriage, presented with painless ulceration of soles of both feet since 2 years of age. The child was unable to tolerate the high summer temperatures. On exposure to sun she would become extremely hot. According to the mother, the child had no sweating and also never seemed to feel pain. Her motor milestones were delayed though her mental development was appropriate for age. There was no family history of paraesthesias, leprosy or tuberculosis. Examination revealed pallor with multiple ulcers on both feet. Her tongue was mutilated beyond recognition. She was conscious, oriented with no cranial nerve deficit and normal muscle bulk and power. There was generalized hypotonia with absent deep tendon reflexes. The touch sensation was normal while pain and temperature sensations were absent. There were no hypopigmented patches or thickened, palpable nerves. The parents and an eleven-month-old female sibling were normal.

Investigations revealed hemoglobin of 6.5 g/dL with microcytosis and hypochromia on peripheral smear. Total and differential leucocyte count, liver and renal function tests were within normal limits. No sweat was formed on sweat induction though skin biopsy showed presence of normal sweat glands. On subcutaneous injection of pilocarpine the wheal and flare reaction was absent. Electrophysiological studies were suggestive of a peripheral neuropathy, which was predominantly axonal, sensory, and showed involvement of lower limbs more than upper limbs. *X*-rays of the limbs revealed evidence of chronic osteomyelitis. Pus culture from the leg ulcers grew Pseudomonas and was treated appropriately. Sural nerve biopsy was not done in view of chronic osteomyelitis affecting the same region.

Case 2

The second case was a one-year-old boy brought to our hospital for evaluation for cause of self-mutilation. There was history of consanguinity with parents being first cousins. Parents noticed multiple episodes of fever and absence of sweating since the child was 2 months old. None of these episodes of hyperpyrexia had any localization for fever. The child started biting his tongue and fingers after his teeth erupted at the age of six months. There was also history of absence of crying after painful stimuli. His developmental milestones were normal. The child had an elder male sibling with a similar illness who died at 1½ years of age from a chest infection and a 7-year-old sister, who is asymptomatic. On physical examination the child had mild

pallor with bites marks over the tongue and tips of the fingers. On neurological examination, there was hypotonia with normal deep tendon reflexes. The child responded to touch but there was no response to pain and temperature.

Hereditary sensory autonomic neuropathy was suspected and further investigations were conducted. Nerve conduction velocity studies in sural and median nerves revealed normal SNAP latency, conduction velocity and amplitude. There was no sweat production on pilocarpine iontophoresis. Sural nerve biopsy showed feature suggestive of focal segmental demyelination.

Discussion

The classification of various types of HSAN is based on the inheritance pattern, clinical features, and systems of neurons predominantly affected. HSAN I is autosomal dominantly inherited with symptoms begin in the second decade or later. There is loss of pain and temperature sensation but preservation of tactile sensation. Sural nerve biopsy shows loss of unmyelinated fibres more than myelinated fibres. HSAN II is an autosomal recessive disorder with onset in infancy. There is generalized pansensory loss. Autonomic disturbances included bladder dysfunction, impotence and distal anhidrosis. Motor function is preserved but tendon reflexes are lost. There is loss of myelinated fibres in the sural nerve biopsy. HSAN III is also autosomal recessively inherited affecting mostly Ashkenazi Jews. The clinical manifestations usually present at birth and are suggestive of defective autonomic control. Nerve biopsy shows reduced number of unmyelinated fibres. HSAN IV is an autosomal recessive disorder associated with bouts of pyrexia, anhydrosis and mental retardation. Nerve biopsy reveals absent unmyelinated fibres. HSAN V is an autosomal recessive disorder with onset at birth and normal sweating. Motor functions and tendon reflexes are normal. Sural nerve biopsy shows selective reduction in the number of smaller myelinated fibres(1,8).

The clinical picture of our patients suggests the diagnosis of HSAN type IV. Impaired sense of pain and temperature, absence of sweating, signs of self-mutilation and presence of recurrent fever with onset in infancy supports the diagnosis. Mental retardation in HSAN IV is variable, from severe to mild, and some patients were initially reported to be apparently normal, but later mild retardation was showed by a formal assessment(9). Unfortunately, no formal assessment was done in our cases to detect the presence of mild 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 syndrome, Tourette syndrome and de Lange syndrome. Absence of nail and hair abnormalities and presence of normal sweat glands on skin biopsy exclude the anhidrotic ectodermal dysplasia.

As nerve conduction studies test only 1-2% of the large myelinated fibres, they may not be sensitive enough to detect abnormalities of small fibers as was evident in the second case. Focal segmental demyelination seen on nerve biopsy in the second case has not been reported so far. Presence of normal number of sweat glands on skin biopsy is consistent with previous reports(10).

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