Case Report

Osteomyelitis in Congenital Insensitivity to Pain with Anhidrosis

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Abstract

Background: Congenital insensitivity to pain with anhidrosis (CIPA) is a rare autosomal-recessive disorder. Recurrent osteomyelitis is also a rare, severe and fatal finding in this disorder.

Case Presentation: We report a 4-year-old boy brought to Namazi Hospital with a pus draining fistula on his right foot. He was the first son of an Iranian consanguineous parent. He had a history of episodic hyperpyrexia since neonatal period, absence of sweating except emotional tear, insensitiveness to injections and trauma, multiple burn and fractures in both extremities, corneal ulceration in 3rd month of his life, hyperactivity, frequent constipation with rectal prolaps, oral scar on his lips and tongue because of self biting, multiple scars on palms and hands and several hospitalization history for debridement of necrotic tissue and bone due to recurrent osteomyelitis of right calcaneous bone. Electromyography of the extremities and nerve conduction velocity confirmed nociceptive fiber pathology compatible with CIPA which is the first diagnostic hypothesis when assessing a child with CIPA and undiagnosed infection.

Conclusion: CIPA is an untreatable illness, however the early diagnosis, cooperation and education of the parents will help us control its most severe and fatal complications.

Key words: Congenital Insensitivity to Pain with Anhidrosis (CIPA), Osteomyelitis, Hereditary Neuropathy

Introduction

Congenital insensitivity to pain with anhidrosis (CIPA) or hereditary sensory and autonomic neuropathy type IV is a rare autosomal-recessive disorder. Pathogenesis pathway of CIPA includes point mutations affecting both coding and non-coding regions of the neurotrophic tyrosine receptor kinase type 1 (NTRK1)/ nerve growth factor receptor gene. Defects in nerve growth factor (NGF) signals transduction at its receptor lead to failure to survive as various NGF-dependent neurons are not maintained, most probably due to apoptosis in nervous system development (1-3). Insensitivity to pain results in absence of reaction to painful stimuli, self- mutilation, neuropathic joints, risk of injury, burn, fracture, infection and corneal ulceration.

Anhidrosis, the inability to sweat, predisposes affected individuals to recurrent episodic high fevers and mental retardation (2,3) some of whom have severe self-mutilating injuries to their tongue, hands, lips and oral mucosa witch result in digital amputation and also premature loss of permanent tooth germ during the treatment(4).

Osteomyelitis is considered as a possible cause of destruction of the tarsal bone (5). We present here a 4-year-old boy with most of the above mentioned symptoms and signs and with a prominent pus draining fistula on the right foot due to calcaneous bone osteomyelitis which needed multiple surgical treatments.

Case Presentation

A 4-year-old boy was brought to Namazi Hospital with a pus draining fistula on his right foot. He was the first son of an Iranian consanguineous parent. He had history of episodic hyperpyrexia since the neonatal period, absence of sweating except emotional tear, insensitive to injections and trauma, multiple burn and fractures in both extremities. He also had history of corneal ulceration in 3rd month of his life and frequent constipation with rectal prolapse. There was no family history of metabolic or neurologic disorder. . He was hospitalized six months ago for debridement of necrotic tissue and bone due to osteomyelitis of the right calcaneous bone and had recurrent osteomyelitis and surgical treatments at the same site on admission which had resulted in walking difficulties (Figures 1 and 2).

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Figure 1: Radiograph of osteomyelitis on calcaneous bone with fistula

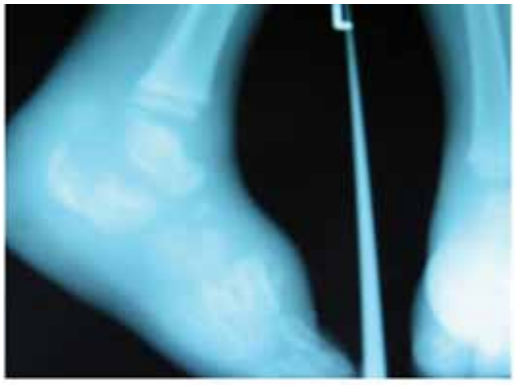

Figure 2: Osteomyelitis and soft tissue edema of left foot

On physical examination, he was hyperactive and had oral scar on his lips and tongue because of self biting, multiple scars on palms and hands, dry skin with hypopigmented scars on both forearms. Examination of chest, heart, spleen and liver was normal and there were no lymphadenopathies. Neurologic examination showed mild hypotonia and lack of response to painful stimuli such as pinpricks. Cell blood count, electrolytes, blood urea nitrogen, creatinin, thyroid and liver function tests were unremarkable. Investigation for metabolic and immunodeficiency disorders were negative but G6PD was deficient. Chest radiography and brain magnetic resonance imaging were normal. Sclerotic lesions caused by previous osteomyelitis were seen on both feet.

Electromyography (EMG) of the extremities showed absent sympathetic skin response in response to acoustic and electric stimuli applied to the peripheral nerves of upper and lower limbs. Nerve conduction velocity (NCV) revealed that the second component of blink response was absent that could confirm nociceptive fiber pathology on the left proneal, left posterior tibial and sural nerves compatible with CIPA. Surgical debridement was done and appropriate antibiotics were initiated for osteomyelitis which resulted in his problems were resolved. Before discharge, the parents were instructed how to take precautions against trauma to child and seek other supportive treatments as well.

Discussion

Characteristics of clinical, EMG and NCV findings of the patient revealed the diagnosis of CIPA. Congenital insensitivity to pain with anhidrosis is a rare disorder first described by Dearborne in 1932 (6). Dyck et al. recognized 5 types of hereditary sensory and autonomic neuropathies (HSAN) in 1993 (7): HSAN I-sensory radicular neuropathy, HSAN II-congenital sensory neuropathy, HSAN III- familial dysautonomia or Riley Day syndrome, HSAN IV-congenital insensitivity to pain with anhidrosis (CIPA) and HSAN V-congenital indifference to pain. When a child is referred with insensitivity to pain, anhidrosis and self-mutilation, three groups of disorders could be considered based on the dominant clinical findings (8). Firstly, CIPA is the only syndrome accompanied by anhidrosis, so it can be differentiated easily from other types of hereditary sensory and autonomic neuropathies. Second group are the hereditary anhidrotic ectodermal dysplasia and Fabry disease both of which are X-linked and occur in males. Fabry disease is also distinguished from CIPA by the presence of paroxysmal pain and paresthesia, fever, transient proteinuria and cutaneous angiokeratomas. Lesch-Nyhan syndrome is the third group, an X-linked recessive disorder clinically determined by self-mutilation scars and hyperuricemia. These findings are lacking in CIPA (8).

CIPA is a serious illness that may be fatal in the first year of life if hyperpyrexia is not properly treated (9). One of the most important and fatal complications of CIPA is osteomyelitis. Our patient had recurrent episodes of osteomyelitis and multiple surgeries for necrotic tissue debridement which did not result in amputation, however, in some reported cases osteomyelitis and bone or joint deformities demanded surgical treatments including amputation (8). Surgical treatment resulted in walking difficulties in our case. In contrast to other reports, rectal prolapse due to long lasting constipation caused by autonomic disorder was the prominent finding in our case.

There is no specific treatment for CIPA, however, the most important things of all are accurate diagnosis and special training of parents to prevent self-mutilation or accidental trauma (8). Most frequent injuries are caused by self-biting in CIPA. The severe nature of these injuries necessitates serial extraction of primary teeth soon after eruption, which leads to a cessation of the problem. Following the eruption of the permanent teeth, the mutilation will not return, indicating that they have learned not to bite themselves (10).

Conclusion

During the assessment of a patient with insensitivity to pain, anhidrosis, self-mutilation and recurrent infections, CIPA should be the first diagnostic hypothesis. CIPA is an untreatable illness, however, early diagnosis, cooperation and education of the parents will help

clinicians to control and prevent its most severe and fatal complications like osteomyelitis.

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Conflict of interest:

None declared

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