

Congenital Insensitivity to Pain: A Gift Or A Curse?

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Key points:

- Introduction
- Symptoms and Diagnosis
- Causes and Treatment
- Effect on daily life
- Conclusion

Introduction

Pain is a gift to human beings. It is a blessing in disguise. It is not only a pathological mechanism, but also an important protective signal to prevent further injuries. Insensitivity to pain leaves the body unprotected and vulnerable to injuries. Congenital insensitivity to pain is an extremely rare autosomal recessive disorder. It causes complete inability to perceive pain and temperature stimuli.¹

It has five types. The most well-described subtype to date is HSAN-IV (CIPA).²

The estimated incidence is 1 in 25,000 individuals.³

Symptoms and Diagnosis

Symptoms of diseases like this include lack of pain perception, inability to sweat, and absence of response to temperature stimuli. Other autonomic functions may also be disturbed. Some individuals may exhibit intellectual impairment and generalized or localized stunted growth. People with CIPA often go through recurrent fractures, deformities, and injuries that go unnoticed due to the absence of pain perception. The age of onset ranges from 6 months to 57 years.⁴

Corneal ulcers are shown to be a major symptom of the disease.⁵

Some injuries can be resolved with treatment, while others can lead to lifelong tissue defects if left untreated. CIPA also causes an increase in self-mutilation behavior. For example, the patient reported by Gaur et al. (2018) suffered from frequent self-mutilation behaviors due to insensitivity to pain. He was only a year old when he had severe corneal scarring, a lip defect, and a distal phalangeal injury caused by self-mutilation behaviors.⁶



Figure 1: (A, B) Conjunctival hyperemia and corneal ulcer; (C) tongue and lip defects with oral ulcers.¹²

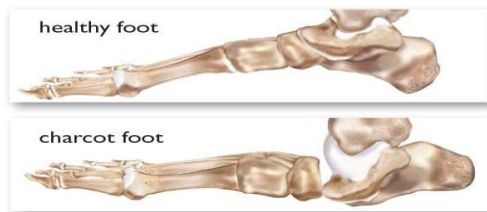


Figure 2: Charcot foot caused by repetitive fractures at the same anatomical site.¹³

The diagnosis of this condition relies on early recognition of its clinical symptoms, with genetic sequencing for confirmation. Prognosis depends on the disease's severity and the emergence of secondary complications, with a generally reduced life expectancy.⁷

Cause and Treatment

CIPA is caused by mutations in the NTRK1 (neurotrophic tyrosine kinase receptor type 1) gene, also known as TRKA. This gene codes for a protein that is a receptor tyrosine kinase, crucial for the development and survival of neurons in the sympathetic and sensory nervous systems.⁸

The absence of this protein causes developmental apoptosis of neurons, disrupting neurotrophic signaling. Along with NTRK1, mutations in the PRDM12 gene are a newly discovered cause of CIPA, leading to defective nociceptor development during embryogenesis.⁹

Treatment for such an unfortunate disease depends on treating symptoms. Education and preventive measures play a vital role. Patients and guardians are advised to maintain regular communication with healthcare providers. Currently, no gene therapy is available. Fifty percent of cases are associated with consanguinity.¹⁰

Effect on Daily Life

Daily life is greatly affected by this disease. As mentioned above, a patient will not perceive thermal stimuli (heat or cold), resulting in accidental burns. A toddler, in particular, may unintentionally injure themselves and be unable to perceive pain. Life

expectancy is significantly reduced because infections and injuries often go unnoticed due to the absence of pain. Counseling for rehabilitation is highly advised in these cases.

Conclusion

Despite the presence of scientific literature on this condition and its examination in various contexts to establish diagnostic and clinical criteria, there remains insufficient information on the contemporary impact of the disease. It is important for us to underscore the necessity of imparting knowledge not only to healthcare professionals but also to families, enabling the early detection of this condition and, in doing so, curbing the onset of intricate secondary complications. Of particular significance is the emphasis on preventing self-inflicted injuries. Hanson B et al., in 2019, designed a device to notify individuals of extreme temperature variations in their surroundings.¹¹

However, no further literature supporting this type of device or proposing new treatment options has been identified.

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