




## Case Study

# Case report of a 7-year-old CIPA child with multiple debridement's and amputations.

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Doi: 10.29052/IJEHSR.v9.i4.2021.529-533

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**Received** 02/06/2021

**Accepted** 07/10/2021

**First Published** 25/10/2021



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## Abstract

**Background:** Background: Congenital Insensitivity to Pain (CIPA), otherwise known as Hereditary Sensory and Autonomic Neuropathy Type IV (HSAN IV), is a rarely occurring autosomal recessive disorder encompassed by a group of hereditary and sensory autonomic neuropathies, which was initially described as pure analgesia present congenitally. Its clinical manifestation includes recurrent episodes of infections with unexplained behavior, anhidrosis, mental retardation, and damage to oral structures.

**Case Presentation:** In this case report, we have demonstrated the signs and symptoms of a 7-year-old boy presented to the pediatric out-patient department of Memon Medical Institute Hospital with complaints of multiple fluid-filled blisters since the age of 1 year. He had a history of multiple hospital admissions due to infections, where he was diagnosed with a case of CIPA.

**Management & Results:** Since the diagnosis of this medical condition, the child has undergone multiple debridements of his wound and amputations. The treatment plan was aimed to manage the blisters, prevent self-injuries, and treat orthopedic problems by regular dermal and orthopedic follow-ups.

**Conclusion:** There is no cure for CIPA patients, the families that have CIPA patients must undergo prenatal testing and screening to prevent the birth of another affected child.

## Keywords

Congenital Insensitivity to Pain, Amputations, Debridement.



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## Introduction

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Congenital insensitivity to pain (CIPA) is an exceptionally rare neuro-pathological disorder that is characteristically termed as a patient's insensitivity towards pain and painful tactile perception or even due to self-mutilation<sup>1,2</sup>. Clinical features also include recurrence of unrelenting and unexplained fever, mental retardation, loss of sweating (anhidrosis), and abnormally functioning autonomic nervous system right from birth. CIPA patients usually undergo trauma, osteomyelitis, and bone fractures due to pain insensitivity<sup>3</sup>. As a result, such patients tend to undergo multiple operations like amputation after the failure of the osteotomy. Due to its rarity, behaviors and patterns of CIPA patients are difficult to find in the reported literature. The incidence of CIPA is predicted to be around 1 in 25,000<sup>4</sup>.

The classification of CIPA or HSAN is done into five types in total based upon multiple factors such as time at presentation, the pattern of inheritance, clinical and electrophysiological characteristics, specific genetic markers, and metabolic defects<sup>5</sup>.

Another name for CIPA is familial dysautonomia type II, occurring due to mutated Neurotrophic Tyrosine Kinase receptor type I (NTRK1) gene, which is present on chromosome 1 and contains a growth receptor factor for nerves. CIPA's diagnosis is made on a combination of clinical presentations, the neuro-pathological examination done on electron microscopy (shows absent unmyelinated fibers, reduced small myelinated fibers but normally distributed large myelinated fibers), and on pharmacological testing, i.e., intradermic reaction to 1:10,000 of histamine). The last method of diagnosis is the detection of mutation in the NTRK1 gene<sup>6</sup>.

Along with the sensation of pain, the sensation of temperature is also lost entirely over the body. Even on placing boiling tubes of water on the skin, no reaction takes place. Because of pain and temperature insensitivity, children can usually be self-mutilated, biting themselves, and suffer from fractures or burns. A minimum of 3 families is observed to be affected among family members,

with 2 or more siblings affected. The modes of transmission suggest that the mode of inheritance is autosomal recessive<sup>7</sup>. Tendon reflexes are found to be varied, being normal or being depressed. Blood pressure remains normal in most cases. Moreover, cold pressure testing consisting of a forearm submerged in ice water exhibits a failure to report any blood pressure or heart rate alteration. Fungiform papillae on the tongue are seen to be absent. In some cases, hypotrichosis of the scalp is reported<sup>8</sup>.

A skin biopsy shows normal organelles of the ectoderm, namely sweat glands. Nonetheless, injecting pilocarpine and neostigmine intradermally for induction of local sweating has shown to be a failure. Only some amount of sweating is observed in simultaneous injections of acetylcholine along with epinephrine. A normal response is observed in terms of lacrimation when the Schirmer test is performed. Injecting histamine phosphate intradermally produces an expected wheal but without any flaring of axons that normally should<sup>9</sup>.

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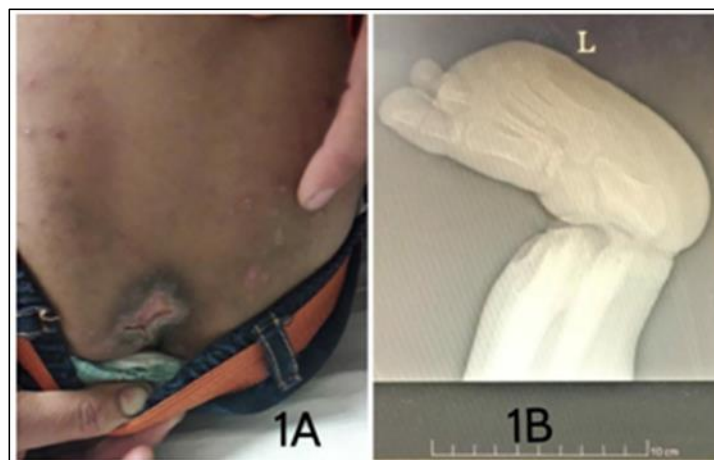
## Case Presentation

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After attaining written and informed consent from the institute, patient, and parents/guardian, this case report was written. This study is of a 7-year-old boy visiting the Pediatric out-patient department of Memon Medical Institute Hospital with complaints of multiple fluid-filled blisters since the age of 1 year (Figure 1A). The starting of the blisters was when the child started to crawl. The parents observed the blisters to be progressive with variable size, filled with pus, and spread widely but mostly on the frictional areas of the body. Blisters used to become more prominent during the summer season. However, scarring or pruritus was not observed in the blisters. Auto amputation of multiple digits was also seen (Figure 1B). The child had a history of tongue bites and deep wounds leading to deformation of lips and angle of mouth. In addition, birth history showed delayed crying and delayed achievement of milestones. The family history suggested that parents having a consanguineous marriage. Moreover, the child had four siblings and one elder brother who died of

similar complaints at the age of 4. The child had a history of multiple hospital admissions where he was diagnosed as a case of CIPA.

Since diagnosis, the child has undergone multiple debridements of his wound as well as amputations.



**Figure 1 A: Multiple blisters can be seen on the child's lower back. B: Multiple digit amputations can be seen on the x-ray of the left foot.**

### Management & Results

Since the diagnosis of CIPA, the child has undergone multiple debridement of his wound and amputations. Previously, the patient was admitted in the hospital for the successful amputations of left lower limb digits. On presentation to the hospital this time, the patient's parents were advised to apply sudocrem and fucidin ointment on the blisters three times a day for 2 weeks. Moreover, they were also advised to bring their child for dermal and orthopedic follow-up in order to diagnose and manage skin and orthopedic problems and thereby preventing complications.

The treatment plan was aimed to treat the symptoms of patients involving blisters, preventing self-injuries and treating orthopedic problems with regular dermal and orthopedic follow-ups.

On follow-up after two weeks, improvement in the blisters were observed with no sign of scarring, however; there is no definitive cure of CIPA patients. Therefore, patients' parents were advised to bring the child for follow-ups regularly.

### Discussion

Congenitally, sensory functions can be affected by multiple disorders. Dick classified such congenital abnormalities (neuropathy) into five types viz. congenital sensory neuropathies, sensory radicular neuropathies, Riley-Day syndrome or familial dysautonomia, CIPA, and congenital indifference towards pain. Due to overlapping clinical signs and symptoms, differential diagnosis of such neuropathies is challenging and not straightforward diagnosis<sup>10</sup>.

Characteristics of CIPA include insensitivity towards superficial and deep painful stimuli but with an intact tactile perception, recurrent unexplained fever during infancy, self-mutilation, mental retardation, anhidrosis, normal lacrimation, and corneal reflex, hypoactive or absent deep tendon reflex, and abnormality of autonomic nervous system<sup>11</sup>. Similarly, in our study as well, the above features were observed.

A major and primary concern in anesthesia is impairment in control of temperature. In addition to pain insensitivity, the autonomic nervous system abnormalities include anhidrosis, i.e., the inability

to respond to sweat in response to heat or chemical stimulus<sup>12</sup>. The cause of this is the absent unmyelinated fibers and loss of small myelinated fibers where sweat glands demonstrate no innervation. It leads to death in around 20 % of CIPA patients within their initial 3 years of life. Therefore a strict and regular temperature control system is required for maintaining body temperature to around 37 degrees<sup>13</sup>.

Like in our and other studies have reported a regular occurrence of surgical procedures in CIPA patients. One of the studies reported a 5-year-old girl and her 2-year-old brother, both born from normal pregnancy and delivery to parents of non-consanguineous marriage with no prior history of CIPA in their family. However, both parents recalled a relatable history of self-mutilation and biting of tongue, wrists, fingers, and feet, leading to bleeding in their early months of life<sup>14</sup>.

Another case report of a 5 and a half-year-old boy reported extraction of his primary molars. From birth, the child showed hypoesthesia or insensitivity to pain completely. Additionally, parents did not observe any sweating. A skin biopsy of the child was taken without any local anesthesia. Other than dental abnormality, the child was also reported to have suffered from a fracture of the right leg that he kept mutilating for 18 months. The child was mentally disabled mentally even though he was social, and his behavior has improved previously<sup>15</sup>.

In yet another case report of a 2 and a half-year-old boy referred to the clinic with complaints of severe self-mutilation to the tongue, oral mucosa, hands, and feet because of biting unconsciously. He was an offspring of parents that were consanguineously married. The child was observed to suffer from fever and convulsions in the early months of life. The parents never observed any sweating of their child right from birth and did not tolerate exposure to the sun (warm weather). In such conditions, they became irritated and cried with normal tearing and lacrimation. Likewise, no complaint of pain, the feeling of hot or cold was reported<sup>16</sup>.

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## Conclusion

There is still no cure for CIPA patients, the families that have CIPA patients must undergo prenatal testing and screening to prevent the birth of another affected child. Therefore, early diagnosis of CIPA patients and its orthopedic complications with the prevention of accidental injuries can be achieved with regular dermal and orthopedic follow-ups, which could be useful in minimizing the frequency and severity of complications in this medical condition.

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## Conflicts of Interest

The authors have declared that no competing interests exist.

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## Acknowledgment

The authors would like to acknowledge the assistance and support of doctors and paramedical staff of Memon medical institute in this case report.

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## Funding

The author(s) received no specific funding for this work.

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