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CASE REPORT

Successful Management of a Complicated Forearm Fracture in a Patient with Congenital Insensitivity to Pain: A Case Report

Anas Alrusan[1], Suhaib Bani Essa[2], Saif Aldin Naif Rawabdeh[3], Yazan Anaqreh[2], Modather Hatamleh[1], Mohammad Alradaideh[1], Mohammed Baker[4], Abdelwahab Aleshawi[4]

[1]Department of Anesthesiology, Faculty of Medicine, Jordan University of Science and Technology, Irbid, 21110, Jordan; [2]Division of Orthopedics, Department of Special Surgery, Faculty of Medicine, Jordan University of Science and Technology, Irbid, 22110, Jordan; [3]Department of Pediatrics, Faculty of Medicine, Jordan University of Science and Technology, Irbid, 22110, Jordan; [4]Division of Ophthalmology, Department of Special Surgery, Faculty of Medicine, Jordan University of Science and Technology, Irbid, 22110, Jordan

Correspondence: Anas Alrusan, Department of Anesthesiology, Faculty of Medicine, Jordan University of Science and Technology, Irbid, 22110, Jordan, Email amalrusan@just.edu.jo

Background: Congenital insensitivity to pain (CIPA) is an extremely rare syndrome that is caused by a mutation in the NTRK gene. CIPA is characterized by recurrent episodes of unexplained fever, infections, skeletal complications, anhidrosis, mental retardation, and ocular injuries due to the absence of reaction to painful stimuli. Several musculoskeletal complications have been reported and included fractures, avascular necrosis, joint dislocations, soft tissue, and bone infections. The severity of these complications presented complex diagnostic and therapeutic dilemmas. The collaboration of medical professionals from different specialties to provide appropriate medical care is needed.

Case Presentation: We present a case of a 1-year-old girl, diagnosed with CIPA, admitted to our center complaining of wound discharge and fever from a previously repaired left forearm fracture with nail insertion, which was found to be infected after a failed trial of nail removal. A multidisciplinary- management from anesthesia, orthopedics, ophthalmology, and pediatrics was conducted. The patient underwent successful nail removal, wound debridement, and radius bone reduction with the appropriate anesthetic protocol that did not include analgesic medications. The follow-up course was uneventful with proper alignment and virtually stable health status, with no apparent skeletal or ocular complications.

Conclusion: This report shows a case of CIPA with complicated forearm fracture. Patients with CIPA should be afforded a multidisciplinary healthcare approach in order to improve their quality of life and decrease the rate of complications. Parents and patients should be educated promptly. Orthopedics complications imply significant morbidity and require prompt surgical intervention with intense follow-up.

Keywords: congenital insensitivity to pain with anhidrosis, HSAN-IV, CIPA

Introduction

In 1932, Congenital Insensitivity to Pain (CIP) is a term that describes a group of extremely rare genetic diseases, which was first described by Dearborn as congenital pure analgesia due to the fact that CIP patients cannot feel pain.[1] CIP was classified by Dyck in 1983 within a wider classification of Hereditary Sensory and Autonomic Neuropathies (HSAN). In this classification, they categorized this entity into five subcategories based on clinical manifestations and pathological findings.[2] Congenital Insensitivity to Pain with Anhidrosis (CIPA) is the most described subtype and numericized as "Hereditary Sensory and Autonomic Neuropathy Type IV" (HSAN-IV).[3] CIPA is caused by mutations in the NTRK1 (neurotrophic tyrosine kinase receptor type 1).[4,5]

CIPA is featured by the inability to sweat and to perceive pain. The most common clinical presentation of this syndrome is unexplained episodes of hyperpyrexia, in addition to self-inflicted trauma, especially to fingers, which is

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caused by the inability to sense pain in their extremities. Furthermore, CIPA often presents with frequent skeletal fractures and deformities, and many cases also exhibit Charcot joints. Moreover, CIPA may be associated with severe ocular impairments.[6,7] Although skeletal complications are more common in the lower limbs, almost all bones and joints may be affected by CIPA patients. Fractures occurred in the early years of life, especially in toddler years. Surgical treatment of skeletal complications may not always be advisable because of the progressive nature of joint dislocation and the presence of cardiovascular complications such as bradycardia, in patients with CIPA.[3] In this article, we present the first case of successful management of a girl diagnosed with CIPA who presented with a complicated nail insertion after a left forearm fracture that was reported in Jordan.

Case Presentation

A 1-year-old girl, known to have CIPA syndrome; presented to the emergency department with a repaired left Monteggia fracture after falling down, which was managed with Open Reduction and Internal Fixation (ORIF) two months ago outside our institution. She presented with fever, wound discharge, and an exposed radial head, indicating a failed trial of nail removal that was placed previously. The child was diagnosed with CIPA at the age of 2 months outside our institution after she presented with recurrent attacks of fever of unknown origin. Due to the previous history of a sister diagnosed with CIPA, genetic testing was carried out and showed a mutation in the NTRK1 gene, consistent with CIPA. Neurological examination at our hospital showed clinical characteristics consistent with CIPA. She was a product of normal vaginal delivery with a full-term pregnancy without a history of neonatal intensive care unit admission. There was no previous history of fractures or other complications before this event was reported.

On physical examination, she had normal vital signs and neurological examination, including normal muscle tone and power. There was a small tongue laceration due to self-inflicted pitting without bleeding, edema, or swelling. Moreover, there was a burn on the dorsum of her hand that predated the fracture. The ocular examination was normal. Her X-ray showed malalignment of forearm bones and a deviated radius, with callus formation on the site of the ulnar fracture Figure 1. The laboratory results were normal except for high potassium (5.87 mmol/L), low hemoglobin (10.5 g/dl), and low mean corpuscular volume (70.4 femtoliters). Upon pediatric hematological consultation, she was diagnosed as having iron deficiency anemia, which necessitated the commencing of her on antibiotics and oral iron supplements. The patient's weight was 11.2 Kg, and her recumbent length was 73 cm.

Therefore, the decision was to admit the patient as a case of an infected left ulnar nail and dislocated radial head for nail removal and debridement under general anesthesia. In the operation room, the anesthetic management was optimized as follows: monitorization was applied with standard electrocardiography (ECG), noninvasive blood pressure

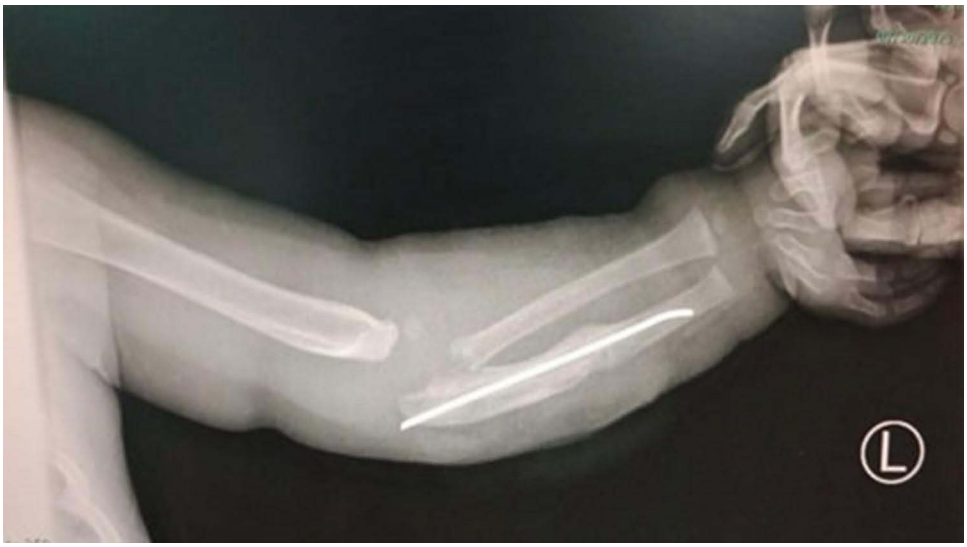

Figure 1 Preoperative X-ray for the left arm showed malalignment of forearm bones and a deviated radius, with callus formation on the site of the ulnar fracture. L: left.

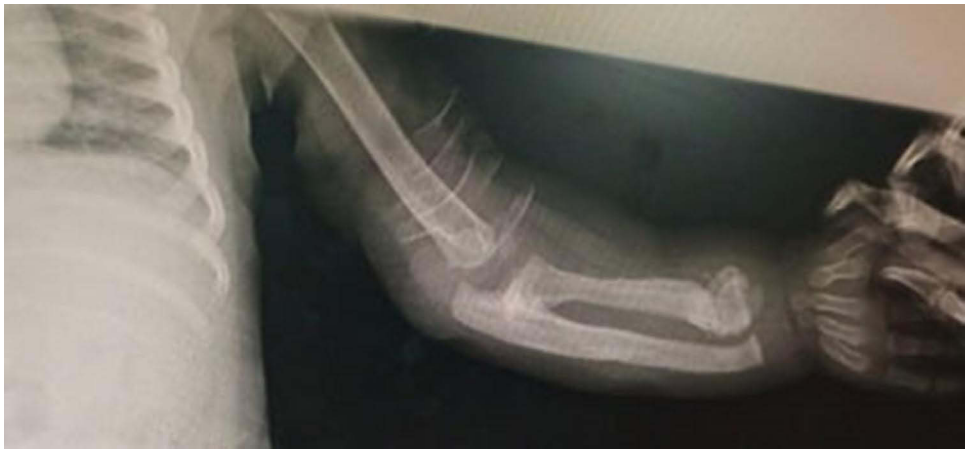

Figure 2 Six months postoperatively X-ray for the left arm demonstrated aligned bones without nail.

measurements (NIBP), oxygen saturation (O2 sat), and end-tidal CO2 (EtCO2). Her vitals were as follows: heart rate: 113 bpm, blood pressure: 87/55 mmHg, O2 sat: 98% on room air, respiratory rate: 28 bpm, ECG: normal sinus rhythm. The operation lasted for 2.5 hours. Intravenous induction was achieved using 2 mg/Kg of propofol and 0.5 mg/Kg atracurium. No analgesia was given. Maintenance was done using a mixture of 50% O2 and 50% room air (administered at a 3 L/min flow) with inhalational sevoflurane 3% throughout the procedure. Ringer lactate was used for fluid deficit and maintenance without giving analgesia or subsequent muscle relaxant doses. Vital signs and blood sugar levels were stable throughout the procedure, with no spikes in heart rate or blood pressure during intubation or surgery. There was no sweating or tearing. Urine output was around 20 mL/Kg/hour. The surgical procedure commenced with painting and toweling followed by opening the previous surgical wound. A tissue culture was taken which was positive for methicillin-resistant staphylococcus aureus. Aggressive debridement and nail removal were carried out. Radial head reduction was successfully achieved under X-ray. Cast and dressing were applied at the end of the operation.

Postoperatively, the patient was sent to the recovery room. The patient was stable, and slightly sedated, but responded to her mother's voice, opened her eyes, and moved her other arm and legs. She was not in pain during her stay in the recovery room and therefore did not receive analgesia. She was transferred to the pediatric ward with no postoperative complications. The mean score of Humpty Dumpty Pediatric Fall Scale was 14.88 (0.47) indicating a moderate to high risk of falling. She was hospitalized for the next 17 days and was managed with piperacillin and tazobactam due to the isolated species until no signs of infection and stable vitals were obtained. The cast was removed 1 month postoperatively with a clear wound, full motility, and function. Figure 2 shows an X-ray view of a follow-up visit. Six months later, she was presented with a normal orthopedic examination. She was also examined by a pediatrician and ophthalmologist with reassurance examination results.

Discussion

We present a case of a patient with CIPA presented with a complicated ulnar fracture. The fracture was repaired primarily with a nail insertion and then complicated by severe infection. Successful collaboration of anesthetic, orthopedics, pediatrics, and ophthalmology teams was achieved. Zhang and Haga presented the skeletal complications among 91 Japanese patients with CIPA. They found that fractures occurred in 65%, about 91% of them were in the lower limbs, and joint dislocations developed in 30%. Bone and joint infection developed in 22 patients (24%). Toddlers are among the most common age group to encounter fractures. According to their study, the leading factor of bone disorders was minor trauma, such as falling down. Conservative therapy was utilized more frequently than operations to.[3]

CIPA is a rare autosomal recessive disorder that belongs to a broader family of neuropathies called HSAN, which affects the small myelinated nerve fibers responsible for nociception, leading to the inability to perceive any noxious stimuli, including inflammation and heat.[8] Although the exact incidence of this disorder remains unclear, Hage et al estimated a prevalence of 1 in 600000–950000 live births a year.[9] Mutations other than NTRK gene include those in

SCN9A which affect the function of voltage-gated sodium channels in sensory neurons, and those in PRDM12 that lead to a defect in the normal development of nociceptive sensory neurons.[7] The SCN9A gene play crucial roles in the transmission of pain signals in CIPA. SCN9A encodes the NaV1.7 sodium channel, present in sensory neurons. This channel amplifies small voltage changes and is essential for initiating pain. Inactivating mutations in SCN9A prevent NaV1.7 from functioning, preventing the generation of action potentials in response to painful stimuli, resulting in complete insensitivity to pain.[10,11] Regarding the transcriptional regulator PRDM12, it has indispensable role in pain perception, and the mutated variants could disrupt the development of nociceptive sensory neurons.[12]

Most patients with HSAN are diagnosed during their infancy.[8] Clinical presentations of HSAN are characterized by self-mutilating injuries of the fingers (biting off fingertips) and oral cavity, in addition to burns due to impaired temperature sensation.[8] Older children may manifest with painless fractures and joint damage (as Charcot's joint) due to repetitive falling and unnoticed trauma.[8] Regarding upper limb skeletal injuries, a series by Mifsud et al was conducted and they concluded that upper limb skeletal injuries can be divided into two categories. The first category were spontaneous or posttraumatic fingertip ulcers that often required community care and oral antibiotics, but sometimes required formal surgical debridement and eventually phalangeal amputation. The second category was those related to the use of walking aids.[13] The mainstay of treatment should be conservative with pressure-free casts, strict nonweight bearing, regular wound review and debridement as necessary. The use of antibiotics should be avoided as much as possible unless evidence of cellulitis. Surgical debridement should be reserved for those patients in whom a strict period of rest, elevation and wound cleaning has failed to prevent the development of osteomyelitis.[13] Other manifestations include corneal injuries due to absent corneal reflexes, normal development or mental retardation according to the gene defect, or chronic anemia of unknown cause.[7,8]

In this child, CIPA was caused by a mutation in the NTRK1 gene that impairs the survival of nociceptive sensory neurons and sympathetic ganglion neurons that rely on nerve growth factor (NGF).[14] The signs and symptoms of CIPA appear early, and usually present in infancy as unexplained episodes of hyperpyrexia due to the core difference of anhidrosis in contrast to other entities of HSAN.[15] However, with careful medical attention, affected individuals can live into adulthood[9].

Conclusion

In conclusion, patients with CIPA may present with life-threatening and site-threatening complications such as complicated fractures. Those patients should receive proper management for their complications with the collaboration of medical professionals from different specialties. Adequate education for those patients and their families, regular follow-up visits, and prompt and multidisciplinary healthcare approaches may protect them and enhance their quality of life.

Ethics and Patient Consent

Written informed consent was obtained from the patient's parents for publication. Institutional review board approval is not required for this type of article.

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Disclosure

There are no conflicts of interest to declare.

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