

Congenital Insensitivity to Pain with Anhidrosis (CIPA) Syndrome; A Rare Genetic Disorder Case Story



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ABSTRACT

Congenital insensitivity to pain with anhidrosis (CIPA) is the subtype four of hereditary sensory and autonomic neuropathy (HASN IV), caused by a defect in the NTRK1 gene and presenting early in life. We report a ten-year-old boy with gait problems and an inability to put weight on his feet. Four days before the visit, a trauma entered his right knee during a football match. He had swelling and erythema in his right knee and multiple scars on his torso and limbs. Magnetic resonance imaging (MRI) offered osteomyelitis and soft tissue periosteal abscess. The patient underwent an operation, and based on the pathology results, myositis ossificans (MO) was reported. Moreover, he was treated with antibiotics and supportive measures and was discharged with partial recovery. According to our knowledge, this is the first report of MO due to recurrent trauma in children with CIPA syndrome.

Introduction

Congenital insensitivity to pain with anhidrosis is an inherited and autonomic type IV neuropathy that occurs early in life [1, 2]. Other disease symptoms include recurrent episodes of hyperpyrexia, lack of sweating, mental retardation and self-harming behavior [3].

Myositis ossificans is a benign, self-limiting bone lesion that affects any type of soft tissue, including

tendons, subcutaneous fat and nerves. It is mainly seen in the muscle as a single lesion [4, 5].

Myositis ossificans can be categorized into nonhereditary and hereditary types [4, 6]. The pathophysiology of this disease is not completely clear, but it is believed to occur through improper differentiation of fibroblasts into bone cells [4]. It most often occurs in areas at high risk for injuries, such as the quadriceps, flexor muscles of the arm and abductor thigh muscles [7].

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The disease is divided into three types: myositis ossificans circumscripta or traumatica (MOT), myositis ossificans progressiva (fibrodysplasia ossificans progressive (FOP)) and myositis ossificans without a history of trauma (non-traumatic or malignant MO). MO is commonly seen in adults between the ages of 20 and 40 and is very rare in children under ten years old [6, 9].

Diagnosis is made by evaluating the patient’s medical history and family history and clinical, radiological and postoperative data [9, 10].

Radiological findings, including plain radiography, CT, MRI and bone scintigraphy are diagnosed [11]. Its differential diagnosis is bone and soft tissue malignancies [12].

This report aimed to introduce myositis ossificans in a child with CIPA syndrome which according to our knowledge, has not been reported yet.

Case presentation

In September 2021, a 10-year boy was referred to our center with pain and swelling in his right knee. He also mentioned the history of hitting four days ago during a football game. The child’s knee pain and swelling had intensified during this time, and the mother also reported an increase in body temperature from the previous two days. The patient was unable to weigh herself on her right leg (Fig. 1).

The patient was the first child in the family and was born by cesarean delivery. He had completed all the necessary vaccinations and was growing normally. His

parents were not related and did not mention a family history of a specific illness.

On initial examination, multiple scars were observed on all parts of the body, especially the limbs, which in the first place made us think of child abuse (Fig. 2)

From birth, he did not sweat and did not respond to painful stimuli. Throughout childhood, the patient presented multiple infections and fractures in various body sites and growth disturbances.

At baseline, the patient had a heart rate of 110, a body temperature of 39 ° C, a blood pressure of 95/55, a respiratory rate of 20 and a blood oxygen saturation of 97. On examination of the swelling and warmth of the right knee, Balutman’s sign was positive. The patient had taken the analgesic position of external rotation and abduction. The pulse of the right lower limb was weaker than the opposite.

They did not have a clear diagnosis or any support until they came to our clinic.

For more investigation, necessary laboratory tests were requested and the results were as follows:

CBCdiff: (WBC = 9800 cmm, Neut = 80%, Lymph = 16%, Hb = 9.9 g/dL, Plt =

242000 MI), TSH = 3.3 mlu/l, CRP = 2 +, ESR = 98 mm/h

Synovial Analyse: (Glu = 81, LDH = 3286 , Protein = 5, Albumin = 2.5 , Wbc = 640 , Neut = 8 , Lymph = 92 , Rbc = 13760)



Fig. 1. Swelling in the lower right thigh and scarring of old ulcers



Fig. 2. Ulcerative lesion of the toe

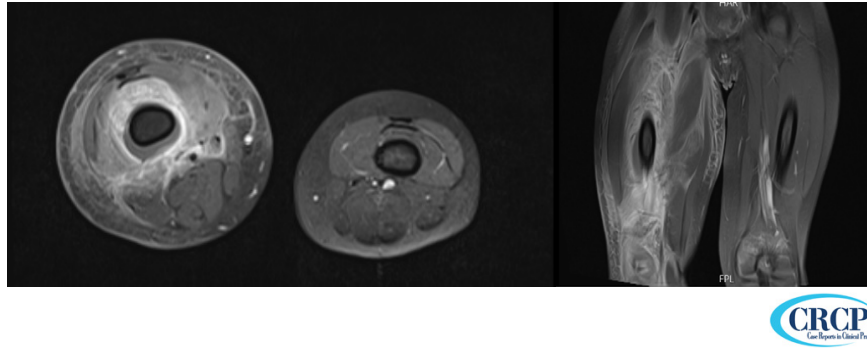


Fig. 3. MRI finding of Myositis ossificans in a 10- year- old boy with CIPA syndrome

MRI of the knee was requested to rule out osteomyelitis. MRI was performed on soft tissue collection and osteomyelitis (Fig. 3).

The patient was treated with injectable antibiotics ceftriaxone and clindamycin. About 200 ml of yellow discharge was removed during surgery, and samples of suspicious muscle tissue were sent for pathology, culture and smear.

The pathological response of the patient was reported to be myositis ossificans. The patient was treated with injectable antibiotics for ten days. Then due to the improvement of symptoms, the patient was discharged with the recommendation to visit an outpatient clinic, continue oral antibiotic treatment, and perform genetic testing to diagnose CIPA syndrome. Due to the high cost of genetic testing, parents did not agree to it.

After the diagnosis of myositis ossificans, antibiotic therapy was continued. Moreover, necessary recommendations were given to the patient's family to prevent recurrent trauma.

In addition, the patient received NSAIDs (ibuprofen) and underwent physiotherapy. He was followed up regularly without any signs of deterioration. Ten weeks later he was able to walk well.

Discussion

Congenital insensitivity to pain with anhidrosis (CIPA, MIM 256800), known as hereditary sensory and autonomic neuropathy type IV (HSAN-IV), is a rare congenital autosomal recessive disorder was described about 50 years ago for the first time [13].

CIPA is determined by variable and distinctive features that appear early in birth or during infancy, including a lack of natural responses to painful stimuli, the absence of significant reduction in

sweating (anhidrosis), and varying degrees of mental retardation [13]. Other senses, such as touch and pressure are preserved. This lack of sensitivity to pain and heat sensations can lead to recurrent bone fractures, burns, and sometimes self-injury of fingers, tongue and lips [3]. These injuries may be neglected or mistaken as child abuse because they are associated with repeated injuries that may lead to constant damage [14]. Significant orthopedic complications such as osteomyelitis, nonunion, avascular necrosis, and heterotopic ossification are common and, in some cases, are early manifestations of the disease [15].

Diagnosis is generally clinical and based on impaired pain and temperature perception [14].

Myositis ossificans (MO) is an uncommon benign disorder involving heterotopic bone formation in muscle or other soft tissue (tendons, ligaments, fascia and connective tissue). [4, 8]

There are three types of the disease: Myositis ossificans progressiva, myositis ossificans circumscripta or traumatica and MO with no history of trauma (non-traumatic MO) [8].

The patient presents with soft tissue pain and stiffness following trauma. MO is most common in adolescents and young adults, especially in the third decade of life. It is infrequent in children under ten years old, and few cases have been reported in the paper [6, 8, 9].

Diagnosis of MO is based on history, physical examination, imaging and pathology. An important differential diagnosis is osteosarcoma and osteomyelitis [9, 10].

The disease is self-limiting and benign, and treatment is usually conservative. Except in cases of painful mass with nerve compression, surgical removal of the mass is recommended [8].

Conclusion

Because no treatment is available for CIPA, prenatal screening is the only option available to prevent the birth of an infected child in families with the disease.

Early recognition of these patients, prevention of accidental injuries, and timely diagnosis of orthopedic complications can help to restrict the frequency and severity of complications of this disorder.

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Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Authors' contributions

Definite diagnosis of case and Critical revision of the manuscript for important intellectual content: **Zahra Nafei**;

Contributing in case management and writing the article: **Marjan Jafari**

Conflict of interest

Authors declare that there is no conflict of interest.

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