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Case Report

A case of congenital insensitivity to pain with anhidrosis with sensitivity reactions to the electric pulp test

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ABSTRACT

Background/Purpose: Congenital insensitivity to pain with anhidrosis (CIPA) is a rare autosomal recessive disorder characterized by anhidrosis, lack of pain sensation, and mental retardation. Mutations in the *NTRK1* gene are responsible for this disorder and cause the apoptosis of A-δ and C nerve fibers.

Methods and Results: A 6-year-old boy with CIPA showed sensitivity reactions to the electric pulp test in some teeth.

Conclusion: If A-β nerve fibers respond positively to the electric pulp test, it could potentially be used to diagnose the pulp vitality of CIPA individuals. However, it is possible that this is an exceptional CIPA case that retained sensitivity to some stimuli.

1. Introduction

Congenital insensitivity to pain with anhidrosis (CIPA) is an autosomal recessive disorder characterized by anhidrosis, lack of pain sensation, and mental retardation [1–8]. CIPA is also known as hereditary sensory and autonomic neuropathy type IV. It is extremely rare in most populations except in the Japanese and Israeli Bedouins. The prevalence of CIPA in Japan is estimated to be 1 in 600,000–950,000 [7,8].

The decreased perception of pain and temperature observed in CIPA patients extends to the entire body. The

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characteristic symptoms include oral self-mutilation such as biting of the tongue, lips, buccal mucosa, and fingertips, recurrent bone fractures, joint trauma, and fever episodes [8].

As many vitality tests for dental pulp usually utilize thermal or pain sensation, methods for diagnosing the pulp condition of CIPA individuals are very limited.

CIPA results from mutations in the *NTRK1* gene, which encodes the receptor tyrosine kinase for nerve growth factor [2,3,9]. This mutation causes apoptosis of nerve growth factor-dependent nerve fibers, including the thinly myelinated A-δ and unmyelinated C fibers, which are associated with nociceptive sensitivity [4,6,10]. By contrast, thick myelinated nerves such as A-β fibers, which are associated with non-nociceptive fibers, have been reported to be normal in CIPA patients [10,11]. Here, we report a case of a CIPA patient with sensitivity reactions for the electric pulp test (EPT) in some teeth.

The patient's guardian provided informed consent for publishing this study. This study was approved by the institutional review board of the National Center for Child Health and Development, Tokyo, Japan (Approval number 976).

2. Case report

The patient was a 6-year-old boy who had experienced frequent fevers since infancy. The orthopedist identified signs of previous bone fractures in the boy at age 4 years, but the boy had no complaints of pain. The patient had previously consulted a dermatologist for the symptom of high heat retention on hot days. Although sweat glands were present in the dermis, sweat was absent on the whole body except between the fingers. The skin reaction and itchiness in response to the histamine test were normal. His gene tests revealed mutations of the *NTRK1* gene: exon 17 c.2303C>T(p.P768L) and exon 14 c.1660delC. He was diagnosed with CIPA and referred to our dental clinic.

At the initial visit, his right ankle was fractured (Fig. 1A), but he could run in the waiting room without a brace. There were no signs of fingertip biting (Fig. 1B), and no ulcers or wounds on his cheek, lips, or tongue (Fig. 1C). However, he had undergone dental treatment for tooth pain, and some teeth needed treatment (Fig. 2). Before treatment, an EPT was conducted on the anterior teeth using an electric pulp tester (Pulppen B1000 analogue; Dental Electronics, Ballerup, Denmark) except for teeth that were classified as 2 or 3 on Miller's mobility index (Fig. 2B). The sensitivity level scale of the Pulppen B1000 ranges from 0 to 18, with 18 indicating a complete absence of pain sensation. The normal incisor sensitivity level is from 2 to 4. A sensitivity level of 4 was observed for teeth 53, 21, and 83, a level of 14 was observed for teeth 31 and 32, and the other teeth did not respond (Fig. 2B). Although tooth 65 had been restored by composite resin and metal band, there was decay at the margin between the tooth surface and the metal band. This was filled by composite resin. Since some of his teeth reacted to the electric stimulation, tooth 64 was restored by composite resin under local anesthesia. Tooth 75 was provided with root canal treatment, but the treatment was interrupted for family reasons.

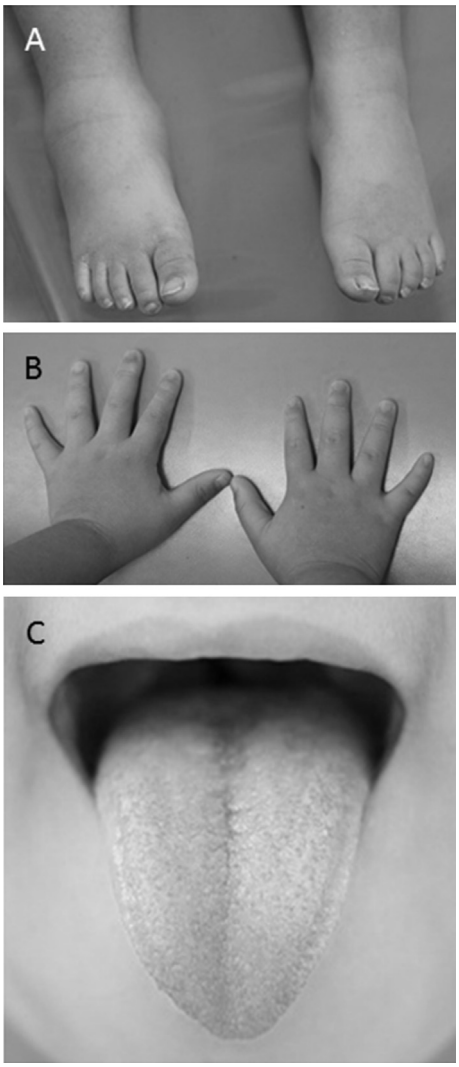

Fig. 1 – A bone fracture on the patient's right ankle; despite the fracture, the patient did not complain of pain (A). No signs of fingertip biting were observed (B). No signs of self-mutilation were found on his lips or tongue (C).

One year after the initial visit, he returned to resume the treatment. We acquired an orthopantomogram (Fig. 3A) and performed an EPT on the anterior teeth (Fig. 3B). A sensitivity level of 3 was recorded for teeth 31, 32, and 41, a level of 4 was recorded for tooth 21, a level of 5 was recorded for tooth 11, and the other teeth did not respond (Fig. 3B). We provided the root canal treatment for teeth 75 and 85, and restored teeth 65, 75, and 85 using preformed crowns.

3. Discussion

The A-type pulp sensory fibers are grouped into A-β and A-δ fibers [12,13]. A-β fibers, which are stimulated at a lower electrical threshold [12,14,15], are present in CIPA patients [10,11]. However, A-β fibers only make up approximately 10% of A-type fibers; the other 90% are A-δ fibers [13], which are not present in CIPA patients. The response threshold of the EPT relies on activating an adequate number of nerve terminals to

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