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Post-herpetic neuralgia in a patient with congenital insensitivity to pain and anhidrosis

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Introduction

Congenital insensitivity to pain and anhidrosis (CIPA) is an inherited disease. CIPA is characterized by episodes of unexplained fever, systemic analgesia, anhidrosis, and mental distress. These symptoms occur because of an abnormality of the *trkA* gene, a receptor tyrosine kinase of nerve growth factor (NGF) [1]. Patients with CIPA often experience trauma, fracture, and even osteomyelitis because of their insensitivity to pain.

We experienced a patient who had been diagnosed with CIPA who complained of itching as a sequela of *Herpes zoster* infection. We believe that this itching was a symptom of post-herpetic neuralgia. Post-herpetic neuralgia is defined as persistent pain that follows a *Herpes zoster* infection; however, the mechanism of post-herpetic neuralgia is not known. We present a report of this patient and discuss the mechanism of post-herpetic neuralgia in this individual.

Case report

The patient was a 27-year-old man who had had a fever of unknown cause at birth. He was diagnosed with CIPA at 6 months of age. He had systemic analgesia, and post-traumatic scars were found all over his body. He had anhidrosis, and showed little sweat with various sweat stimulus tests, such as thermal stimulus. In autonomic functional tests, he showed a normal cardiovascular reaction to norepinephrine and methacholine tolerance tests. He showed no reaction on the axon reflex test. In the right ulnar nerve, the sensory nerve conduction velocity was 50 m/s, and the motor nerve conduction velocity was 36 m/s. The motor nerve conduction velocity was slighty delayed. Nerve biopsy had not been done. His intelligence was at the level of a 3-year-old boy.

On March 6, 1997, he experienced a *Herpes zoster* infection, at the Th 10–12 levels, and complained of feeling uncomfortable and having a burning sensation. He could not sleep at night because of the burning sensation. His cutaneous symptoms showed the typical aspect of *Herpes zoster* infection. He had a slight fever, and his appetite was decreased. On March 8, 1997, he was taken to consult a dermatologist. He was treated intravenously with the antiviral drug, aciclovir, and intradermally with the antiviral drug, vidarabine. No analgesics were prescribed by the dermatologist. He complained of "pain" in the involved cutaneous regions, but this complaint was not regarded as real pain by the parents, because he used to express discomfort as pain. One week later, on March 14, 1997, when the dermal symptoms and the burning sensation had almost subsided, he began to complain of itching, and was treated orally with an antihistamines chlorpheniramine maleate. The itching increased in severity for about 3 months.

At follow-up in August, 1998, when he was brought to our department, he was still experiencing some itching, but it had mostly subsided. His clinical course is shown in Fig. 1. All the dermal symptoms had resolved, except for pigmentation. He had never complained of a sense of "itching", and he had not scratched his body because of itching. Even when bitten by mosquitoes, he had never complained of itching.

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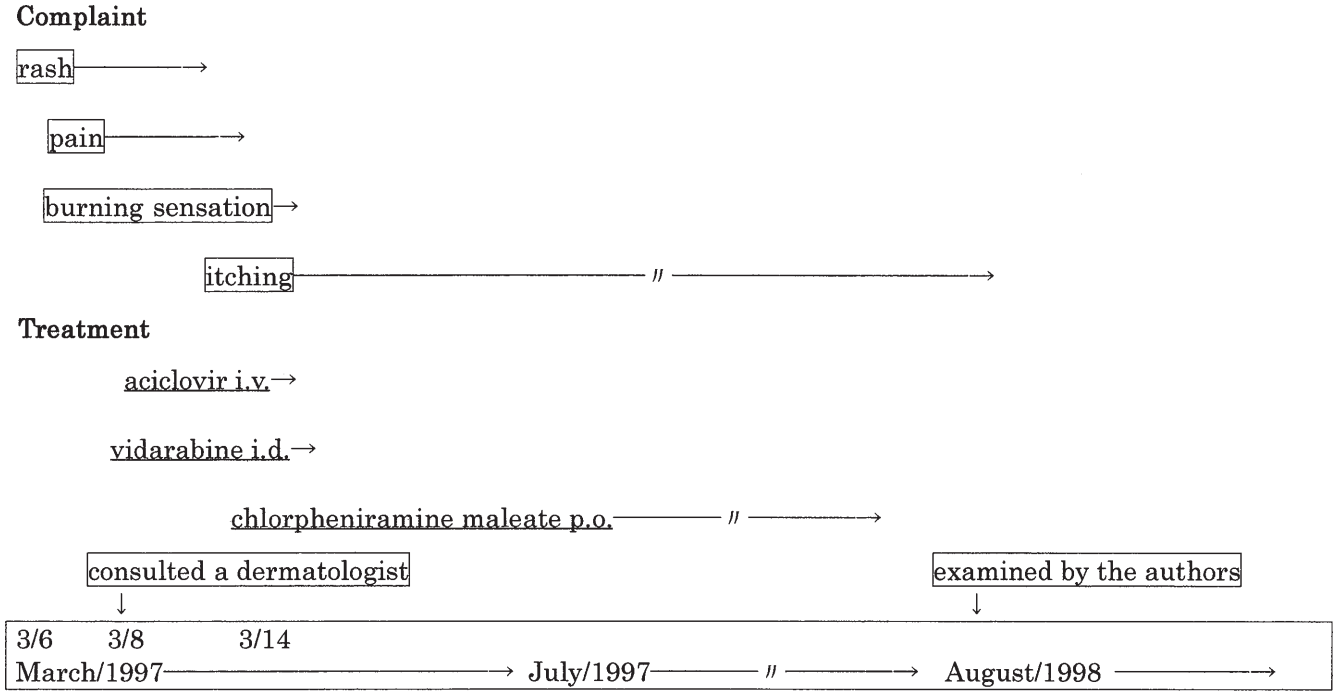

Fig. 1. Time course of patient's symptoms

Discussion

Hereditary sensory and autonomic neuropathy (HSAN) is classified into five types: I: sensory radicular neuropathy, II: congenital sensory neuropathy, III: familial dysautonomia or Riley-Day syndrome, IV: congenital insensitivity to pain with anhidrosis, and V hereditary sensory neuropathy with predominant loss of small myelinated nerve fibers. CIPA corresponds to type IV HSAN [2]. CIPA is characterized by insensitivity to pain, anhidrosis, and mental retardation. [3,4] Recently, Indo et al. [1] reported that a lack of the nerve growth factor (*NGF*) gene on chromosome 1 caused some cases of this disease. The insensitivity to pain is derived from a lack of the thin myelinated and unmyelinated nerve fibers that conduct the pain impulse. The sweat deficiency results from a lack of the peripheral sympathetic end-fibers that innervate the blood vessels surrounding the sweat glands. The case in our patient was classified as type IV HSAN from the clinical findings, such as insensitivity to pain and anhidrosis at birth, and the mental retardation shown after growing up.

Post-herpetic neuralgia is defined as persistent pain subsequent to *Herpes zoster* infection. Histologically, in this disorder, the peripheral nerves show greater damage to the thick myelinated fibers than to the thin myelinated and unmyelinated nerve fibers [2,5]. The mechanism of post-herpetic neuralgia is not known; however, both an imbalance between the peripheral excitatory or inhibitory neurons, and/or the presence of spinal deafferented neurons may play a role [6,7]. The general mechanism of itching is twofold: there is a central mechanism via opioid receptors, and a peripheral mechanism via unmyelinated nerve fibers. We speculate that the peripheral mechanism caused the itching in our patient. A pattern theory and a specific receptor theory have been advanced to explain the peripheral mechanism of itching. According to the pattern theory, an increase in C-fiber spikes causes not only itching but also pain.

Although CIPA is characterized by a marked decrease in thin myelinated and unmyelinated nerve fibers, with normal thick myelinated fibers, the *Herpes zoster* virus generally damages normal thick myelinated fibers. While the mechanism of the itching in our patient remains unclear, it is possible that the *Herpes zoster* virus damaged the normal thick myelinated nerve fibers, and the remaining few unmyelinated nerve fibers temporarily predominated, resulting in this patient experiencing itching as a symptom of post-herpetic neuralgia. In other words, this patient did not have enough unmyelinated nerve fibers to experience pain, and he therefore complained of itching.

In summary, we experienced a patient with CIPA who complained of itching as a sequela of *Herpes zoster* infection. We believe that this itching was a symptom of post-herpetic neuralgia.

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