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Destructive Spondyloarthropathy due to Congenital Insensitivity to Pain with Anhidrosis: A Case Report of Long-Term Follow-Up

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Congenital insensitivity to pain with anhidrosis (CIPA) is a rare autosomal-recessive hereditary neuropathy causing congenital loss of pain sensation, thermoception, and perspiration. CIPA sometimes causes destructive spondyloarthropathy, the so-called Charcot spine, because of insensitivity to pain stimuli. Herein, we report a case of CIPA with severe spinal destruction treated by multiple spinal reconstructive surgeries and over 15 years of follow-up. A 15-year-old male patient who had been diagnosed with CIPA at the age of 17 months presented to his previous spine clinic with gait disturbance due to muscle weakness in his lower extremities. Imaging studies revealed that collapsed L3 and L4 vertebral bodies involved the spinal canal, and it was treated by L3-L4 instrumented posterior fusion. Fourteen years after surgery, the patient became unable to walk again due to spinal canal stenosis at the proximal fusion segment. An L2-L3 posterior interbody fusion alleviated his gait ability for 2 years; however, he became unable to stand again because of the collapsed fusion segment that caused severe lumbar kyphosis. Subsequently, a two-staged posterior and anterior fusion surgery from the lower thoracic spine to the pelvis was performed, and spinal fusion and neurological recovery were achieved 3 years after surgery. A kyphotic deformity in patients with CIPA-associated Charcot spine could be favorably treated by a long spinal fusion in combination with a reconstruction of an anterior spinal column. This case report provides a significant lesson for a treatment of CIPA-associated Charcot spine.

Keywords: Charcot spine; congenital insensitivity to pain and anhidrosis (CIPA); destructive spondyloarthropathy; kyphotic deformity; posterior and anterior spinal fusion surgery
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Introduction

Congenital insensitivity to pain with anhidrosis (CIPA) is a rare autosomal-recessive hereditary neuropathy classified as hereditary sensory and autonomic neuropathy type IV, causing congenital loss of pain sensation, thermoception, and perspiration (Indo 2001). CIPA is known to cause major joint destruction from the early stage of patients' life because of insensitivity to joint pain stimuli, known as the so-called Charcot's joint (Kayani et al. 2017). A similar mechanism is applied to the spinal column, causing destructive spondyloarthropathy (DSA), or Charcot spine (Tsirikos et al. 2004). The spinal destruction in patients with CIPA is often very severe, resulting in spinal deformity and neurological deficits (Staudt et al. 2018). Fusion surgeries for the Charcot spine often fail due to the loss of the protective sensation and thus require revision surgeries (Vialle et al. 2005; Cassidy and Shaffer 2008; Feng et al. 2013). Herein, we report a difficult-to-treat case of CIPA with severe spinal destruction from childhood, which was treated by multiple spinal reconstructive surgeries in over 15 years.

Case Presentation

A 15-year-old male patient complained of numbness and muscle weakness in the lower extremities and walking inability. He was referred to his previous spine clinic and

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was diagnosed with CIPA at the age of 17 months based on clinical criteria. He had experienced hip dislocation and lower extremity fractures 10 times by the age of 10. A grade 3 or 4 muscle weakness was found in the iliopsoas and quadriceps femoris and a grade 2 or 3 in the tibialis anterior, toe extensors, and flexors. Deep tendon reflexes of the lower extremities were decreased. Sensations could not be evaluated because of insensitivity to pain.

A lumbar radiogram demonstrated damaged L3 and L4 vertebral bodies with a narrow L3-L4 intervertebral disc space (Fig. 1a). Magnetic resonance imaging (MRI) revealed spinal canal stenosis at L3-L4 due to the damaged and protruded vertebral and disk materials (Fig. 1b, c). Posterior decompression and instrumented fusion were performed in combination with curettage of the protruded materials in the spinal canal through a posterior approach (Fig. 1d). The patient became ambulatory and was uneventful following intervertebral fusion of L3-L4 in a kyphotic alignment (Fig. 1e).

At the age of 29, he became unable to walk again and visited the previous clinic. Lumbar radiograms in a sitting position demonstrated remarkable lumbar kyphosis (Fig. 2a). MRI revealed spinal canal stenosis at L2-L3 due to protruding intervertebral disc and thickened ligamenta flava (Fig. 2b, c), besides the preserved spinal canal at L4-L5 (Fig. 2d). Then, posterior lumbar interbody fusion (PLIF) at L2-L3 was performed after removing the original implants (Fig. 2e). Neurological improvement was achieved; however, the spinal instruments became loosened within 1 year after surgery (Fig. 2f). Subsequently, he was referred to our clinic at the age of 30.

He could barely stand on his own, and he had grade 3 or 4 muscle weakness of the lower extremities. Imaging studies, at the age of 30, revealed severely damaged vertebral bodies, instrument failure in L2 and L3, and spinal canal stenosis (Fig. 3a-c). His hip joints and left shoulder were also destroyed or degenerated as a Charcot change (Fig. 3d-f), whereas the knee and ankle joints were kept relatively intact (Fig. 3g). Then, a two-staged spinal fusion was performed. First, after removing the posterior instruments, posterior decompression from L1 to L4 was followed by instrumentation from T9 to the pelvis. Then, vertebral bodies were partially resected and curetted from the L1 to L2 disk space to the L4 vertebral body through an

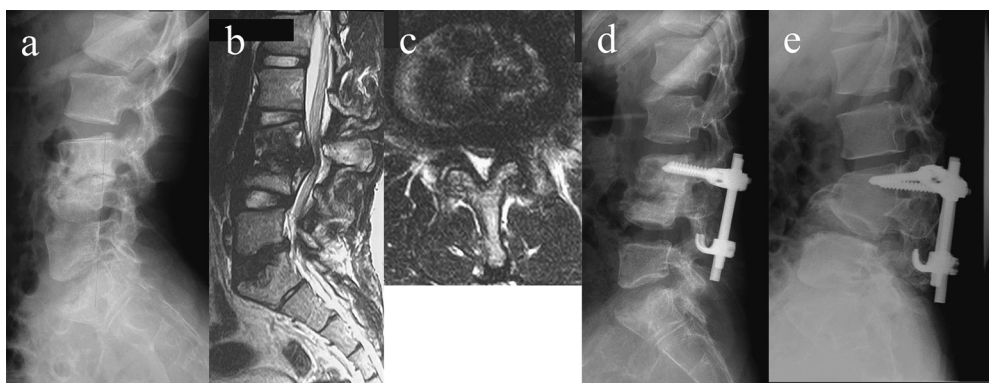

Fig. 1. Pre- and postoperative images at the age of 15.
(a) Preoperative lumbar lateral radiogram. Preoperative T2-weighted sagittal (b) and L3-L4 axial (c) sections. (d) Postoperative lumbar lateral radiogram after L3-L4 instrumented posterior fusion. (e) Lumbar lateral radiogram 5 years after L3-L4 instrumented posterior fusion.

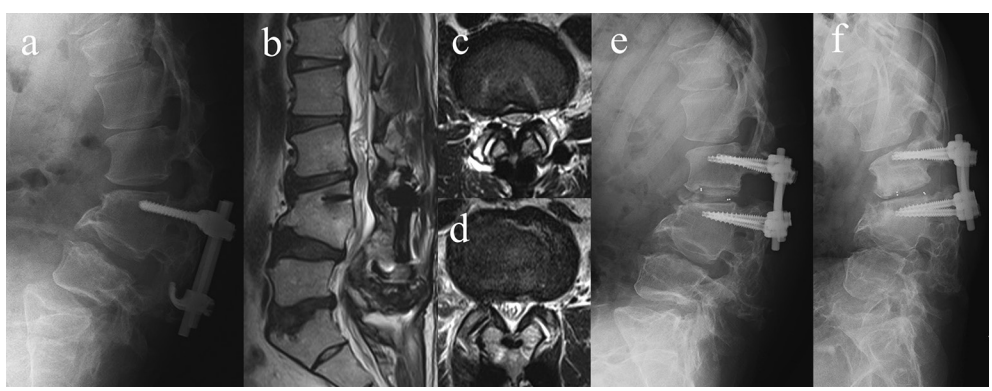

Fig. 2. Images at 14 years after L3-L4 posterior fusion surgery at the age of 29.
(a) Lumbar lateral radiogram before revision surgery. Sagittal section (b) and axial section at L2-L3 (c) and L4-L5 (d) disc levels of T2-weighted lumbar magnetic resonance imaging before revision surgery. Lumbar lateral radiogram just after (e) and 1 year after (f) revision L2-L3 posterior lumbar interbody fusion.

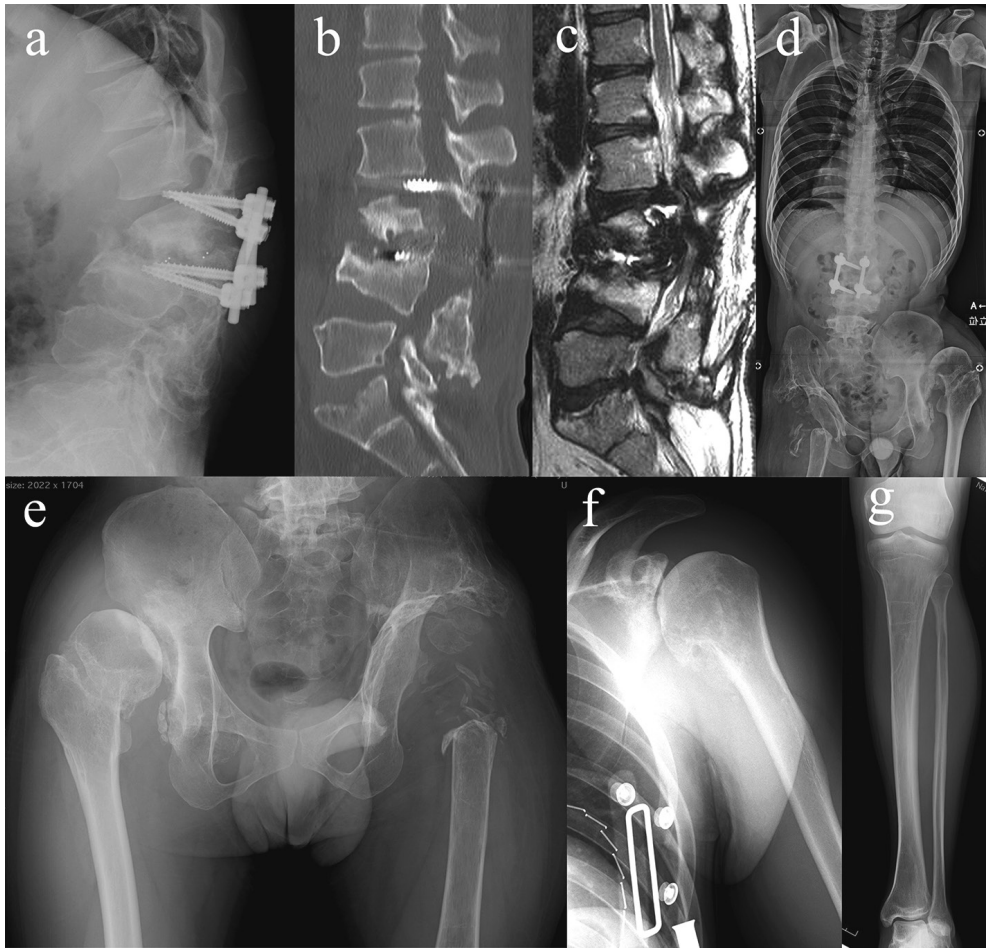

Fig. 3. Images at approximately 2 years after L2-L3 posterior lumbar interbody fusion at the age of 30.
(a) Lumbar lateral radiogram. Sagittal section of lumbar computed tomography (b) and magnetic resonance imaging (c). Anteroposterior radiograms of the whole spine (d), hips (e), left shoulder (f), and left knee and ankle (g).

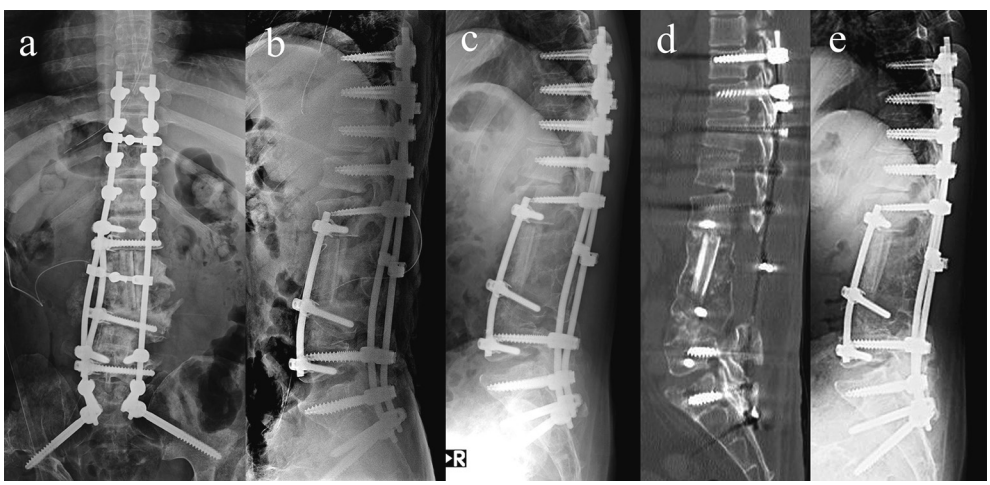

Fig. 4. Thoracolumbar images after a posterior long-fusion and anterior fusion with autologous bone grafts.
Anteroposterior (a) and lateral (b) radiograms just after the surgery at the age of 31. Lateral radiogram (c) and sagittal section of computed tomography image (d) at 1.5 years after surgery at the age of 32. (e) Lateral radiogram at 2.5 years after surgery at the age of 34.

Table 1. Comprehensive timeline of the patient's history.

Age	Events
17 mo	Diagnosed with CIPA based on clinical criteria
-10 yo	Hip dislocation and lower extremity fractures (> 10 times)
15 yo	Leg weakness with L3-L4 vertebral body / disc destruction (Fig. 1a-c)
	L3-L4 posterior instrumentation with anterior decompression (Fig. 1d)
	Spinal fusion in local kyphotic alignment at L3-L4 (Fig. 1e)
	Able to walk after surgery
29 yo	Unable to walk due to spinal canal stenosis at L2-L3 (Fig. 2a-d)
	L2-L3 PLIF with implant removal of L3-L4 (Fig. 2e)
	Able to walk after surgery
30-31 yo	Loosening of the instruments at L2-L3 (Fig. 2f)
	Muscle weakness of the lower extremities due to severe L2-L3 destruction (Fig. 3a-d)
	Combined posterior (T9-pelvis) and anterior (L1-L4) instrumented fusion (Fig. 4a, b)
	Able to walk after surgery
32 yo	Interbody fusion confirmed (Fig. 4c, d)
34 yo	Spinal alignment well-preserved (Fig. 4e)

CIPA, congenital insensitivity to pain with anhidrosis; mo, months old; yo, years old; L, lumbar spine; T, thoracic spine; PLIF, posterior lumbar interbody fusion. *Italic letters* indicate spinal surgeries performed.

anterior approach. Then, autologous iliac and fibular bone grafts were transplanted and fixed with instruments (Fig. 4a, b; at 31 years old). The patient became ambulatory again after surgery. Interbody fusion in a preferable spinal alignment was achieved at 15 months after surgery (Fig. 4c, d; at 32 years old) and well-preserved for more than 2 years after surgery (Fig. 4e; at 34 years old). The patient's condition was uneventful for more than 3 years. A comprehensive timeline of the patient's history is shown in Table 1.

Discussion

CIPA is a rare disease first reported by Swanson (1963). Later, CIPA was revealed to be caused by an abnormal sequence of the *neurotrophic receptor tyrosine kinase (NTRK) 1* gene, a gene encoding the receptor tyrosine kinase for nerve growth factor (Indo 1993, 2001, 2002, 2012). Pain insensitivity impairs protective muscle contractions, destroying the musculoskeletal system, which is the so-called Charcot joint and spine (Harrison et al. 1991). In patients with neuroarthropathy, the spinal column is affected in 6%-21% of the cases, especially in the lower thoracic spine, thoracolumbar junction, and lumbar spine (Kapila and Lines 1987; Park et al. 1994; Staudt et al. 2018).

Staudt et al. (2018) reviewed 12 cases of spondyloarthropathy with congenital insensitivity to pain reported in 11 articles. Most of the patients developed Charcot spine mainly in the lower thoracic to the lumbar spine before the age of 30 years and had combined anterior and posterior fusion surgery, as in our case. In previous reports, patients had preferable short-term outcomes for up to 2 years, with and without neurological deficits to some extent (Staudt et al. 2018). Instead, of a risk of progressive Charcot spine in CIPA, we have not found a report with follow-up longer than 5 years. To the best of our knowledge, this report is the first to demonstrate a treatment course longer than 15 years. The present case required multiple surgeries after the failure of simple posterior instrumentation because of progressive spinal destruction over 14 years, which subsequently require long spinal fusion combined with anterior and posterior approaches.

Regarding surgery for CIPA-associated Charcot spine, implant failure is highly expected because of the loss of self-protection due to pain insensitivity (Feng et al. 2013; Staudt et al. 2018). To avoid implant failures, a 360° spinal fusion by combined anterior and posterior surgery is recommended for Charcot spine (Vialle et al. 2005; Cassidy and Shaffer 2008; Feng et al. 2013). For CIPA-associated Charcot spine, Cassidy and Shaffer (2008) and Feng et al. (2013) have reported cases of failed short-segment anterior and posterior fusion that was successfully salvaged by subsequent posterior long-fusion surgery. The common points in their cases were that the patients had a local kyphotic alignment at the upper to the middle lumbar spine due to collapsed vertebral bodies preoperatively. In our case, despite achieving spinal fusion after the first short-segment posterior fusion surgery, adjacent segment disorder with severe lumbar kyphosis became apparent with long-term follow-up. Considering the severe lumbar kyphosis, a posterior long-fusion surgery could have been better than PLIF at L2-L3 at the time point. Even after successful posterior long-fusion surgery, periodic follow-up is necessary considering the destructive nature of bones in a patient with CIPA.

Conflict of Interest

The authors declare no conflict of interest.

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