Successful Management of Gait and Balance Disorder in Hereditary Spastic Paraparesis with an Intrathecal Baclofen Infusion: Case Report

Herediter Spastik Paraparezide Yürüme ve Denge Bozukluğunun İntratekal Baklofen İnfüzyonu ile Başarılı Tedavisi

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ABSTRACT Hereditary spastic paraparesis (HSP) is a genetic disorder that causes a gait disorder with spasticity and weakness of the lower extremities. HSP causes marked disability and substantial socioeconomic losses. The treatment goal is symptomatic: to improve the spasticity and gait disorder and to increase the patient's quality of life. For the symptomatic treatment of HSP, oral antispastic medications, botulinum toxin injections, physical therapy, and surgery can be useful, but there is no consensus on the ideal therapy. This report shares a case that was unresponsive to various antispastic treatments, but showed marked improvement in the gait disorder with a reduced fall risk after administering an intrathecal baclofen infusion with a pump.

Keywords: Hereditary spastic paraparesis; baclofen pump; rehabilitation

ÖZET Herediter spastik paraparezi, alt ekstremitelerde spastisite ve güçsüzlüğe neden olan genetik bir bozukluktur. Önemli oranda dizabiliteye ve sosyoekonomik kayıplara neden olmaktadır. Tedavinin hedefi; spastisiteyi azaltmak, yürüme bozukluğunu düzeltmek ve hastanın yaşam kalitesini artırmaktır. HSP'nin semptomatik tedavisinde oral antispastik medikasyonlar, botulinum toksin enjeksiyonu, fizik tedavi ve cerrahi faydalı olabilmektedir, ancak tedavisi üzerinde hâlen konsensüs sağlanamamıştır. Bu çalışmada; çeşitli antispastik tedavilere yanıt vermeyen, ancak intratekal baklofen pompası uygulamasından sonra yürüme bozukluğunda ve düşme riskinde anlamlı iyileşme olan bir olgunun sunulması amaçlanmıştır.

Anahtar Kelimeler: Herediter spastik paraparezi; baklofen pompası; rehabilitasyon

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Hereditary spastic paraparesis (HSP) is a heterogeneous group of genetic disorders.[1,2] Their inheritance can be autosomal dominant, autosomal recessive, or X-linked.[3] Clinically, HSP is divided into two groups: pure HSP and complicated HSP.[4,5] Pure HSP includes corticospinal tract findings, such as slowly progressive lower extremity spasticity and muscle weakness, and a positive Babinski's sign.[3,6] Urinary disturbances and a mild reduction in proprioception and vibration sensation in the lower extremities can be seen along with the corticospinal tract findings. Complicated HSP includes additional findings, such as peripheral neuropathy, epilepsy, ataxia, optic atrophy, retinopathy, dementia, ichthyosis, cognitive impairment, and deafness.[3] In Europe, the prevalence of HSP is approximately 3~10/100.000.[1,7] The age of onset

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ranges from infancy to the eighth decade.[2,8] In the majority of HSP subtypes, the cause of spasticity is progressive axonopathy in the corticospinal and dorsal column tracts to the lower extremity. The main problem is progressive spastic paraparesis with concomitant gait disturbance. The axonopathy is caused by defects in genes involved in myelination, mitochondrial function, and membrane transport.[1]

There is no treatment to prevent, halt, or reverse the disease process.[9] For the symptomatic treatment of HSP, oral antispastic medications, botulinum toxin injections, and intrathecal baclofen infusion with a pump or surgery can be useful, but there is no consensus on the ideal therapy.[5] We want to share a case that was unresponsive to various antispastic medications, physical therapy, and botulinum toxin injection, but showed marked improvement in the gait disorder and a reduction in fall risk after administering intrathecal baclofen with a pump.

CASE REPORT

A 29-year-old man was referred to our clinic with frequent falling, a gait disorder, and an inability to run. The patient stated that his complaints had begun at birth, and for many years, he had been followed with HSP, although he did not remember when the HSP had been diagnosed. When he was 7 years old, he underwent a tendon release operation for the hamstrings and Achilles tendon. He had no other neurological disorders, such as cerebral palsy, multiple sclerosis, Parkinson's syndrome, spinal cord injury, or cerebrovascular attack. He was not taking any medicine for his problems.

Physical examination showed normal lumbar and hip passive ranges of motion. He could walk independently. He had a spastic gait pattern (scissor-like walking with leg adduction). Using the modified Ashworth scale, the spasticity of the bilateral gastrocnemius medial and lateral heads and soleus muscles was grade 3, and was grade 1 for the hip adductor muscles. He had extensor plantar reflexes and the deep tendon reflexes were hyperactive. Neurological examination of the upper extremities was normal. Cranial and thoracic magnetic resonance imaging (MRI) were normal. Discopathy at several cervical and lumbar levels was seen on MRI, but there was no nerve root compression. Assessing balance with the Biodex Balance System, the patient's fall risk assessment score was 2.90±2.03 (mean±standard deviation), and his postural stability scores were 2.9±1.98 overall, 1.9±1.76 anteroposteriorly, and 1.7±1.56 mediolaterally. For the spasticity, 8 mg of oral tizanidine was tried initially, but there was no significant improvement. Botulinum toxin was injected in both gastrocnemius and soleus muscles. After the injection, we planned intensive physical therapy, including stretching and strengthening of the lower extremities, electrostimulation, balance and coordination exercises, and balance exercises with the Biodex Balance System. However, there was no significant improvement. A second botulinum toxin injection 3 months after the first produced no significant improvement. A trial intrathecal injection of baclofen was performed. A favorable response was obtained, so a pump for intrathecal baclofen administration was implanted. After 7 weeks, with a baclofen dose of 75 μg, he could walk independently without scissoring, the frequency of falling had decreased, and his balance was better, although he could not run. The spasticity of the bilateral gastrocnemius/soleus muscles was grade 1+ on the modified Ashworth scale, and there was no spasticity of the hip adductor muscles. Assessing his balance with the Biodex Balance System, his fall risk score was 1.90±2.10, and stability scores were 1.5±0.90 overall, 1.1±0.95 anteroposteriorly, and 0.9± 0.61 mediolaterally. The patient's treatment is ongoing and he is still using the pump.

DISCUSSION

Hereditary spastic paraparesis is a genetic disorder that causes a gait disorder with lower extremity spasticity and weakness. Consequently, the patient's quality of life declines. The treatment target is symptomatic improvement of the spasticity and

gait disorder and to increase the patient's quality of life. Symptomatic treatment includes oral antispastic medications such as baclofen, tizanidine, dantrolene, and benzodiazepines, physical therapy, botulinum toxin injection, intrathecal baclofen infusion with a pump, and surgical tendon release.[2,10,11,13] The effectiveness of oral antispastic medications is limited due to absorption problems and elimination of the drugs. Tizanidine, baclofen, and benzodiazepines act on the central nervous system, while dantrolene acts on muscles directly. We tried tizanidine in our patient, but there was no significant improvement. Botulinum toxin injection reduces spasticity in patients with stroke, paraparesis related to spinal cord injury, and multiple sclerosis, while little is known of its effect in HSP (11). We tried two botulinum toxin injections 3 months apart, but there was no significant improvement. Surgery, such as the release of contractures and tenotomies, may be required in some cases.[5]

Physical therapy can be useful, such as stretching for 10 minutes twice a day and daily lower extremity strengthening exercises.[10] It is necessary to prevent complications such as joint contractures and to preserve the existing functional status.[2] For balance training, devices such as the Biodex Balance System can be useful. A short communication reported that repetitive transcranial magnetic stimulation was ineffective in two HSP patients.[12]

The selective GABA-B receptor agonist baclofen can be used orally or intrathecally with an infusion pump.[1] Intrathecal baclofen is becoming a standard treatment for the spasticity arising from medulla spinalis.[13] The pump is implanted in the subcutaneous tissue and baclofen is infused intrathecally with a catheter that is inserted in the subarachnoid space of the spine. Dan *et al.* and Margetis *et al.* found that an intrathecal baclofen pump was effective for spasticity and walking performance.[1,13] In our patient, we tried an intrathecal baclofen pump because the response to oral antispastic medications, botulinum toxin injection, and physical therapy was insufficient. With an intrathecal baclofen infusion, we can bypass the absorption problems and elimination of the drug from the body, and obtain a favorable response on spasticity. There are some disadvantages of an intrathecal baclofen pump. It is an electronical device, therefore its battery needs recharging and should be refilled with baclofen periodically. Catheter fracture can also occur.[9]

We believe that an intrathecal baclofen pump is a good choice when there is no favorable response with oral antispastic medications and botulinum toxin injections. After implantation of a baclofen pump, physical therapy might prevent the need for orthopedic surgery, such as contracture release and tenotomies. These patients can take part in social life more easily than before.

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