

Success with neurotropin in treating pediatric lower extremity pain induced by spinal cord injury after epidural anesthesia

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Abstract: Spinal cord injury (SCI) complicated by epidural anesthesia, though rare, can result in neuropathic pain. However, the treatment for this kind of life-altering injury remains a challenge. A 7-year-old girl was referred with dyskinesia and severe pain in her right lower extremity due to an accidental SCI following lumbar puncture. After treatment with analgesics such as gabapentin, mecobalamin, and dexamethasone/methylprednisolone for 1 week, the myodynamia had improved, but progressive pain persisted. After treatment with neurotropin, a gradual decrease in visual analog scale score from 7 to 0 was observed. We herein first describe that neurotropin produced sustained relief of pain induced by SCI. This case suggests that neurotropin might be a promising drug in treating pediatric neuropathic pain caused by SCI.

Keywords: spinal cord injury, pain, neurotropin, children

Introduction

Spinal cord injury (SCI) remains a significant problem causing great damage to physical systems and functional abilities. Although mainly caused by spine fracture or dislocation,^{1,2} SCI can also result from lumbar puncture during an epidural block.³ Because drugs such as lidocaine and its analogs can be injected into the subarachnoid space, epidural anesthesia has rare, but serious complications such as epidural or spinal subarachnoid hemorrhage and arachnoiditis, thus causing SCI with dyskinesia and chronic pain.⁴⁻⁶ Several pain treatments have been widely studied. However, neurotropin, which has been known to regulate neuronal growth, has not yet been reported to treat SCI pain caused by epidural anesthesia in children. We herein describe a case of SCI complicated by epidural anesthesia successfully treated with neurotropin.

Case report

A 7-year-old girl was hospitalized in a local hospital on April 2, 2015. Her height and weight were 130 cm and 20 kg, respectively. She was diagnosed with appendicitis and underwent emergency appendectomy with epidural anesthesia (midline approach to T12–L1 interspace) combined with propofol sedation.

Her past medical history was noncontributory. During appendectomy, her vital signs remained stable. One incident, however, occurred during the course of anesthesia. A transient involuntary movement occurred while performing the lumbar puncture with 1% lidocaine, causing the anesthetic needle to penetrate to a depth of 15 mm (a depth of ~25 mm was first measured, but 15 mm was finally confirmed by the anesthetist). Because of the possibility of SCI, the patient was treated with dexamethasone (injection, 5 mg) in

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the local hospital to reduce inflammation and eliminate local potential edema. After the end of anesthesia, the patient woke up without mental disorder or disturbance of consciousness, but then complained of pain with a visual analog scale (VAS) score of 4, pinching, fatigue and numbness in the right lower extremity, and impaired walking. Tenderness to palpation was found as hyperesthesia of the skin on the right lower leg and hyperalgesia on the right side of the above area (Figure 1). Magnetic resonance imaging (MRI) showed an increased abnormal T2 signal found in the T12–L1 level spinal cord (Figure 2). The MRI result indicated that her symptoms seemed to result from the unexpected needle puncture.

Because of the possibility of SCI, gabapentin, meclobamine, diclofenac sodium, ganglioside, and pulsed methylprednisolone were administered for analgesia and neuroprotection.

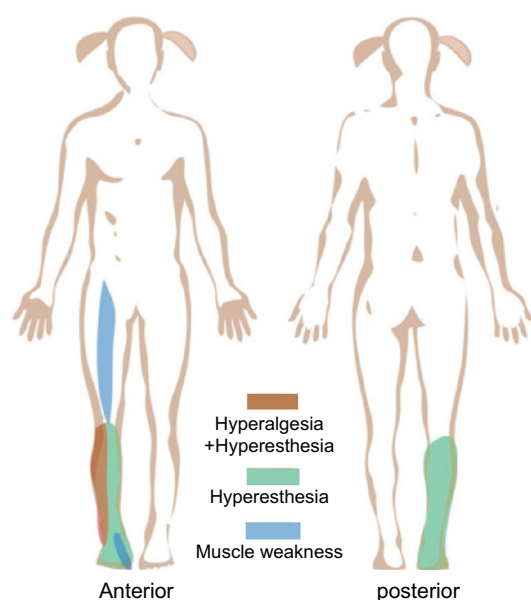


Figure 1 Images illustrating the subregion of hyperalgesia, hyperesthesia, and muscle weakness.

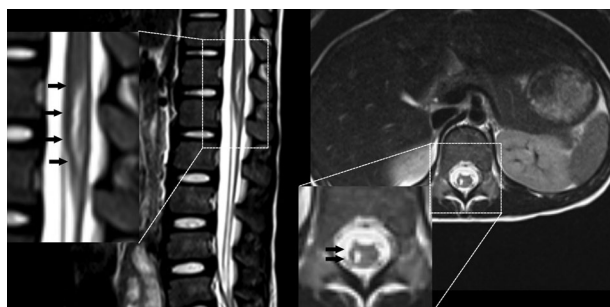


Figure 2 Emergency MRI after the girl recovered from anesthesia in the local hospital.

Note: The black arrows show the location of cord injury.

Abbreviation: MRI, magnetic resonance imaging.

The patient recovered gradually. The myodynamia, measured by the Lovett muscle strength grading scale, improved after corticosteroid treatment for 7 days. However, the patient did not achieve any pain relief, so she was then transferred from the local hospital to our department on April 11, 2015, which was the ninth postoperative day.

After transferring, she expressed more frequent and more aggravated spontaneous pain during the night, which often lasted for about an hour each time with a VAS score of 7. We then found that the area of hyperesthesia within her right leg originated in the lumbar segments L4–S1, associated with muscle atrophy or weakness involving the right quadriceps femoris, peroneus longus, and brevis. Furthermore, the Achilles reflex on the right had disappeared without any pathologic signs.

Recent clinical and basic studies verified the effectiveness of neurotrophin on analgesia and neuroprotection while treating neuropathic pain as well as primary headache.^{7–12} Meanwhile, one Japanese report established the safety of neurotrophin when used in childhood. To achieve sustained pain relief, we obtained informed consent from the patient's parents and approval from the Medical Research Ethics Committee of the First Affiliated Hospital of Nanchang University. We then treated the patient with neurotrophin (3.6 units/day, intravenously guttae, purchased from Nippon Zoki Pharmaceutical Co. Ltd.) combined with gabapentin (200 mg, per os, three times per day).

During the next few days, the patient's clinical symptoms of neuropathic pain and motor disorder started to improve, but the repeat MRI result (Figure 3A) did not reveal any healing, still indicating the myelomalacia of SCI and spinal cord swelling. On the fifth day after the described treatment, the patient's thermal hyperalgesia disappeared. After another week of treatment, her myodynamia was fully recovered (from grade III to grade IV+), while the pain was significantly alleviated

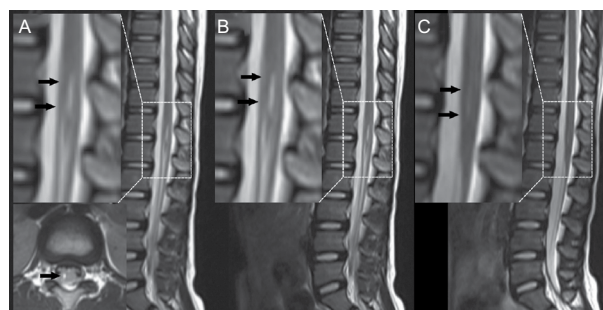


Figure 3 Repeat MRI after the administration of neurotrophin.

Notes: (A and B) Sagittal MRI shows the cord injury after the 14th and 30th days of continual treatment, respectively; (C) the myelomalacia of SCI nearly disappeared after about 15 months after continual treatment. The black arrows show the location of cord injury.

Abbreviations: MRI, magnetic resonance imaging; SCI, spinal cord injury.

and the VAS score decreased from 7 to 4. The patient was then discharged from our hospital after assessment that her condition did not affect her daily life. After leaving the hospital, she continued to take neurotrophin orally. Several days later, the patient's cutaneous superficial sensation gradually improved, and her Achilles reflex fully recovered. One month later, none of her neurologic symptoms persisted, while the MRI result indicated the recovery of SCI as well (Figure 3B). Fifteen months later, the MRI result (Figure 3C) confirmed that the myelomalacia of SCI had nearly disappeared. Ultimately, this young patient went back to school as a recovering child.

When we finished the treatment, the patient's parents provided written informed consent for publication of the case details.

Discussion

Epidural anesthesia is fundamental to pain relief for children when operating in the lower extremity and hypogastrium.¹³ It is generally safe but can be associated with complications, especially for pediatric patients due to their immature mentality, which can make them uncooperative. In this case, physical injury induced by excessive probing predominantly accounted for the patient's suffering.

In fact, neuralgia after epidural anesthesia is rare, but it may induce severe pain, which should be taken seriously. Several other factors can also result in neurologic injury. For example, anesthetics at high local concentration exert neurotoxic effects, while epinephrine, a vasoconstrictor, increases the duration and quality of anesthesia, but theoretically induces tissue ischemia.¹⁴ Furthermore, neurotoxic medications mistakenly administered and patient's pre-existing pathology, such as coagulopathy, causing an epidural hematoma directly causing neuralgia, can also be risk factors.¹⁵ Appropriate and timely medication administration is crucial for the treatment of SCI. In this case, the initial treatment followed the generally accepted strategy of administering glucocorticoids, dehydrants, analgesics, anticonvulsants, and antidepressants to treat the neuropathic pain induced by SCI complicated by epidural anesthesia,^{16,17} but no pain relief was achieved within the first week. Specific to this case, our patient received a total of 3.6 units/day of neurotrophin for pain treatment. Neurotrophin, a small nonprotein substance with pharmacologic activities, is extracted and then purified from the inflamed tissue of vaccinated rabbits.^{10,18} It has been shown to have a potential analgesic effect and is now mainly used to treat chronic pain, especially neuropathic pain.^{7,19} In this case, we first chose neurotrophin as an adjuvant treatment and obtained satisfactory beneficial effects. After treatment

with neurotrophin, the patient's neuropathic pain resolved gradually, accompanied by recovery of sensory and motor function.

Effective neuroprotection offered by neurotrophin has been confirmed in several types of experimental models.^{12,18,20} Neurotrophin could function as an antinociceptive and neuroprotective agent by activating the descending pain inhibitory system¹⁰ and by inhibiting different neurotransmitters or cytokines such as substance P, nerve growth factor, brain-derived neurotrophic factor, and even axonal transport.^{8,11,21} Neurotrophin may be effective for children with neuropathic pain, but this drug is rarely used in children. It has been demonstrated that neurotrophin has significant effects on juvenile headache.⁹ This case study first revealed its beneficial effect on SCI pain after epidural anesthesia. Thus, we consider neurotrophin a promising drug for pain relief in childhood.

Conclusion

In summary, the present case is the first direct evidence that neurotrophin may have the clinical potential for treating neuropathy caused by an epidural block in children. To fully determine the effect of neurotrophin on pain relief, more studies elucidating the underlying mechanisms and clinical benefits are needed.

Disclosure

The authors report no conflicts of interest in this work.

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