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SURGICAL NEUROLOGY INTERNATIONAL
SNI: Head and Spinal Cord Transplantation a supplement to Surgical Neurology International
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Editor: Prof. Sergio Canavero, MD (US FMGEMS) and Prof. Xiaoping Ren, MD

Case Report

Accelerated recovery of sensorimotor function in a dog submitted to quasi-total transection of the cervical spinal cord and treated with PEG

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Received: 07 August 16 Accepted: 31 August 16 Published: 13 September 16

Abstract

Background: A case report on observing the recovery of sensory-motor function after cervical spinal cord transection.

Case Description: Laminectomy and transection of cervical spinal cord (C5) was performed on a male beagle weighing 3.5 kg. After applying polyethylene glycol (PEG) on the severed part, reconstruction of cervical spinal cord was confirmed by the restoration of sensorimotor function. Tetraplegia was observed immediately after operation, however, the dog showed stable respiration and survival without any complication. The dog showed fast recovery after 1 week, and recovered approximately 90% of normal sensorimotor function 3 weeks after the operation, although urinary disorder was still present. All recovery stages were recorded by video camera twice a week for behavioral analysis.

Conclusion: While current belief holds that functional recovery is impossible after a section greater than 50% at C5-6 in the canine model, this case study shows the possibility of cervical spinal cord reconstruction after near-total transection. Furthermore, this case study also confirms that PEG can truly expedite the recovery of sensorimotor function after cervical spinal cord sections in dogs.

Key Words: Cervical spinal cord transection, dog, polyethylene glycol, sensorimotor function

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Access this article online
Website: www.surgicalneurologyint.com
DOI: 10.4103/2152-7806.190476
Quick Response Code:

INTRODUCTION

It is a clinical dogma that there is no recovery from full transection of the spinal cord at whatever level as seen, for instance, after stab wounds.[5,10,11,14-16] When the transection is partial, recovery is possible; in the largest reported series, 66% of 450 patients with stab wounds could eventually walk without or with only minimal help. In another large series of 217 patients, over half returned to their former occupation, usually within 6 months of the injury.[1,13] Brown-Sequard types of lesion (i.e., a hemisection) also recovered. For instance, in a recent report, two patients with cervical hemisection

How to cite this article: Kim CY, Hwang IK, Kim H, Jang SW, Kim HS, Lee WY. Accelerated recovery of sensorimotor function in a dog submitted to quasi-total transection of the cervical spinal cord and treated with PEG. Surg Neurol Int 2016;7:S637-40.
http://surgicalneurologyint.com/Accelerated-recovery-of-sensorimotor-function-in-a-dog-submitted-to-quasi-total-transection-of-the-cervical-spinal-cord-and-treated-with-PEG/

recovered walking at 10 and 2 years.[7] Another recovered almost completely at 3 years.[6]

However, if the section is greater than 50% (of a hemisection), results are similar to a complete section. For example, in a patient, whose spinal cord was almost completely divided at C7/T1, only sensory disturbance was slightly improved at 4 months after the injury.[17]

The recently proposed GEMINI spinal cord fusion protocol[4] aims at restoring neurophysiologic conduction in a sharply transected cord. Preliminary data in rats confirm the capacity of GEMINI to restore motor function whose cord (cervical and lumbar) has been transected fully.[9,18]

In this paper, we report on a dog whose cervical spinal cord was transected >90% at visual inspection, and that showed motor recovery within 3 weeks of surgery. In patients with stab wounds to the spinal cord, there is no known method to refuse their severed cord and even in partial wounds, where recovery in many cases takes months to years.

The dog in this experiment was submitted to a sharp transection and treated with polyethylene glycol (PEG). PEG is a fusogen that has the capacity to restore the integrity of severed cell membranes[3] and is an ideal candidate for neural restoration in the clinic.[4,9,18]

CASE REPORT

The experiment was carried out in accordance with the guidelines of the animal ethics committees and approved by the Institutional Animal Care and Use Committee of the Konkuk University (Seoul, South Korea). A male Beagle (Orient Bio, Seongnam, Korea) dog weighing 3.5 kg at the time of surgery was included in the study. The dog was housed in a cage under simulated daylight conditions with alternating 12-hour light-dark cycles and had free access to food and water.

The dog was starved 12 hours prior to the operation to prepare for the paralysis of the digestive system post-operation. Anesthesia was first induced by propofol (10 mg/kg), and respiratory anesthesia (isofurane 2%) was maintained through a ventilator. Constant heart rate was maintained and monitored (electrocardiogram). After the surgical site was sterilized, an incision was made on the skin and the upper trapezius muscle in order to expose the spinous process of the 5th cervical vertebra (C5); the location was confirmed by C-arm fluoroscopy [Figure 1a]. Bipolar forceps was used to stanch bleeding during the operation.

The dorsal part of C5 was removed with a bone rongeur, and the cervical cord was isolated [Figure 1b]. The cervical cord was lifted gently and laid down with a hook to confirm the depth and size before transection; cerebrospinal fluid was released by lightly incising the dura mater and arachnoid using a surgical blade no. 11.

Finally, the surgical site was prepared by applying PEG (PEG MW 400, Sigma-Aldrich, USA) until the cord was submerged [Figure 1c]. Complete transection of the cervical cord was attempted by traversing the same area twice in opposite directions with the blade in contact with the bony floor of C5 [Figure 1d]. At visual inspection, the cord was clearly severed, save for a minimal amount of bridging tissue ventrally. This bridge was not further severed given the profuse bleeding; in addition, further damage by surgical manipulation had to be avoided since PEG needs sharply severed surfaces to act optimally.

After the transection, bleeding was controlled by applying surgifoam (Ethicon, USA), coagulated blood was suctioned out, and more PEG was added. Then, the dura mater was sutured by pulling 5 mm of each section so that the severed stumps were in contact. Coagulated blood was thoroughly removed, and additional PEG (5 ml) was applied before definitive dural closure. The surgical site was sutured by layer (muscle and then skin).

The dog was weaned from anesthesia. After voluntary respiration and consciousness were confirmed, the dog was taken to the intensive care unit (ICU) for 24 hours after the operation, and was treated with low doses of sedatives to minimize the stress from total paralysis. The dog was treated with antibiotics and sedatives for 1 week after the operation, and was supported by 5% dextrose and electrolyte solution (Halfsol, Daihan Pharm, Korea) and total parenteral nutrition.

Video files were recorded for analyzing functional recovery twice a week (Video), and behavioral functions were measured using the modified Frankel score (MFS)[8] applied on fore and hind limbs at each recording points. The MFS scoring goes from 0 (no movements) to 5 (normal movements) [Table 1].

Twenty-four hours after the surgery, tetraplegia and absence of four-limb deep pain perception were observed; involuntary shaking of the limbs was observed at 48 hours. Restoration of respiratory control was confirmed by whining. The sound stopped intermittently when the dog was unable to control respiration, however, this had improved considerably after 48 hours to the extent that the dog could make sounds at will. Tetraplegia continued for 72 hours post-operation [Figure 2a; Video], although response to tickling and deep pain was observed sporadically (MFS: 0~1). Subsequently, there was a recovery of strength in both forelimbs and hind limbs, with minimal movements. Small, uncoordinated movements, such as folding and stretching the limbs and wagging the tail, were detected after a week (MFS: 2). After 10 days, the dog had recovered to the point that it was able to balance its torso by moving its forelimbs

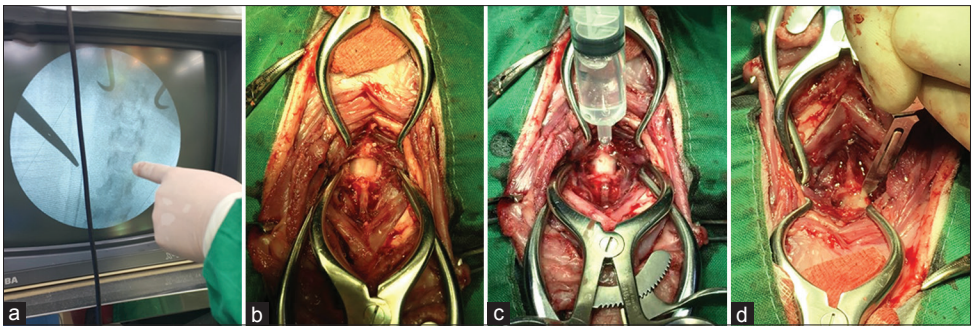

Figure 1: Operation of cervical spinal cord transection in a dog. C-arm fluoroscopy (a). Exposure of cervical cord (b). PEG application (c). Cervical cord transection using blade (d)

Figure 2: Functional recovery over 3 weeks. 72 hours (a), 10 days (b), 14 days (c), 17 days (d), 20 days, and (e) 24 days post-operation (f)

Table 1: Modified Frankel Scale (MFS) for Dogs

Grade	Neurological status
0	Para/tetraplegia with absent deep nociception
1	Para/tetraplegia with absent superficial nociception
2	Para/tetraplegia with intact nociception
3b	Non-ambulatory para/tetraparesis; inability to bear weight on the limbs without support
3a	Non-ambulatory para/tetraparesis; ability to bear weight on the limbs without support
4	Ambulatory para/tetraparesis (ataxia)
5	Normal gait with paraspinal hyperesthesia

[Figure 2b; Video]. In 2 weeks, the dog was able to drag its hind limbs by using the forelimbs and torso [Figure 2c; Video]. Digestive function recovered enough to digest and excrete soft food, and therefore intravenous support was replaced by oral nutrition. The dog began to crawl using forelimbs and hind limbs and was able to lift its head and torso halfway through the second week (MFS: 3b) [Figure 2d; Video]. Later during the week, the dog occasionally stood up and was able to support itself on its limb (MFS: 3a) [Figure 2e; Video]. During the third week, function of the limbs considerably recovered to the point that the dog was able to walk without slipping too much and even run occasionally (MFS: 4~5) [Figure 2f; Video]. At the end of the third week, the dog stopped crawling and walked normally, except for some occasional loss of balance. The dog recovered >90% of motor function, and a normal life (e.g., grabbing objects with his forelimbs, tail-wagging, etc.).

DISCUSSION

Results in the dog, although in need of confirmation in larger samples (in progress), are spectacular and, to the best of our knowledge, have never been reported in the literature. Sensory function was restored in parts of the animal's body in 48 hours, and small movement of the limbs were observed within a week. As reported, a section greater than 50% at C5-6 in the canine model leads to no recovery of respiration and death,[2] unlike what happens for hemisections,[12] thus mimicking what occurs in humans (above). This case confirms that PEG

can truly expedite the recovery of sensorimotor function after spinal cord sections in a dog, in line with what has been observed in rats.

No neurophysiologic testing was conducted and the animal was not sacrificed for histologic analysis; these tests were not part of the experimental protocol that focused on motor and sensory recovery following the use of fusogens. Similarly, there is no credible explanation for this recovery other than postulating that PEG acted according to the principles laid out in previous papers.[3,4] The goal of this study was behavioral, i.e. confirming GEMINI's clinical assumption.

If confirmed, these data open a new vista on the treatment of sectional spinal cord injury in man.

Acknowledgement

We thank Prof Canavero for assistance in writing the paper and assisting with the interpretation of the data.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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