

Olfactory ensheathing cell transplantation for a patient with chronic sciatic nerve injury

Feng Zhang^{1,2}
Xiangzhi Meng²
Fang Lu²
Aixian Liu²
Hongyun Huang^{1,2}

¹Cell Therapy Center, Beijing Hongtianji Neuroscience Academy,
²Neurorehabilitation Center, Beijing Rehabilitation Hospital, Capital Medical University, Beijing, People's Republic of China

Objective: To observe the result of olfactory ensheathing cell (OEC) transplantation in a patient with chronic sciatic nerve injury.

Case report: A 53-year-old male patient with chronic (1 year) sciatic nerve injury on left side received OEC transplantation at the lesion site. He received follow-up assessment according to the American Spinal Injury Association standard at 10 days, 6 months, and 1 year after OEC therapy. The muscle strength of his left lower limb increased and numbness decreased during the early stage of cell therapy. His motor function improved with each evaluation. His limp walking gait recovered, and numbness sensation got nearly normal after 1 year of follow-up. There were no side effects.

Conclusion: OEC transplantation may be an option for chronic peripheral (sciatic) nerve injury.

Keywords: olfactory ensheathing cell transplantation, sciatic nerve injury, peripheral nerve injury, function improvement, neurorestoration

Introduction

The incidence of peripheral nerve injury has been increasing with increasing traffic accidents, sharps injuries, and major events such as natural disasters. Axonal regeneration of peripheral nerve after complete transection injury is far more successful than after central nervous system (CNS) injury, but sometimes the regeneration is incomplete. Generally, Schwann cells play an important role in peripheral nerve regeneration and remyelination by providing neurotrophic support, guiding axonal regeneration, and myelinating the regenerated axons.¹⁻⁴ As the patients with peripheral nerve injury do not receive timely treatment and do not recover completely, their quality of life will be affected to some extent. Some preclinical studies report that transplantation of olfactory ensheathing cells (OECs) for peripheral nerve injury in acute phase enhanced peripheral nerve restoration.⁵⁻⁹ Currently, there are no reports about clinical studies on OEC for restoring chronic peripheral nerve injury. Herein, we report the case of one patient with chronic sciatic nerve injury who received OEC therapy and showed neurological functional improvement. The results indicate that this method may be used as an alternative therapy for chronic peripheral (sciatic) nerve injury.

Case report

A 53-year-old male patient suffered from left sciatic nerve injury below the buttocks by stab wound 1 year ago and lost some sensation and movement in the left lower extremity. After initial injury, he underwent emergency surgery for sciatic nerve stump anastomosis, and then he took neurorehabilitation exercise every day and

Correspondence: Hongyun Huang
Cell Therapy Center, Beijing Hongtianji Neuroscience Academy, No. 1 Gucheng Street, Shijingshan District, Beijing, People's Republic of China
Tel +86 139 1011 6608
Email hongyunh@gmail.com

gradually recovered some sensation and motor functions. His neurological functions with the left leg numbness and weakness were stable 3 months before he received our treatment.

Examination: Proximal muscle strength of the lower left limb was grade 4, distal muscle strength was grade 2, no left foot dorsiflexion, paresthesia from left lateral ankle to the left hallux toe, and feeling disappearing in the four toes of the left foot and in the dorsolateral part of the foot. Clinical assessment according to the American Spinal Injury Association (ASIA) standard is presented in detail in Tables 1–3.

The patient received OEC therapy at Beijing Hongtianji Neuroscience Academy in conjunction with Beijing Rehabilitation Hospital affiliated Capital Medical University, in accordance with the guidelines issued by the Chinese Ministry of Health (91-006) in which functional transplantation can be done according to clinical routine rule.¹⁰ The study was approved by the research ethics committee of Beijing Hongtianji Neuroscience Academy and Beijing Rehabilitation

Hospital affiliated Capital Medical University. The patient was fully informed about the nature of the treatment, and he signed the informed consent form to undergo OEC transplantation and for use of his data in this study. OECs were isolated and cultured according to the Good Manufacturing Practice standard for laboratories, as described previously.^{11,12} Under local anesthesia, 2×10^6 OECs were slowly injected into the site of the left leg sciatic nerve anastomosis below the buttocks. Clinical assessment was done according to the ASIA standard at 10 days, 6 months, and 1 year after the cell therapy, the details of which are provided in Tables 1–3. There was an increase in the muscle strength of the lower left limb with decreasing numbness. His motor function after cell therapy improved with each evaluation. He recovered his limp walking gait and numbness sensation to be near normal after 1 year of follow-up. There were no side effects from OEC therapy.

Discussion

Peripheral nerve injury is one of the common clinical diseases which affects patients' daily activities to a certain extent. Main reasons for the injury include squeezing, pulling, cutting peripheral nerve, and physical and chemical reactions, which lead to nerve tissue structure or function impairment and discontinuity. Generally, patients with peripheral nerve injury could be treated for structural and functional restoration through microsurgical reconnection with or without tissue graft or biomaterial if there was a nerve defect in acute phase. Then they can receive neurostimulation or neuromodulation therapies, and neurorehabilitation for functional recovery.¹³ Clinical studies have been done on the use of cell therapy for peripheral nerve injury in acute phase, but results are awaited for long-term outcomes.^{14,15} The ability to recover from a peripheral nerve injury depends on certain factors, such as environment at the site of the nerve repair, compression from an integument that is too tight, or muscle balance.¹⁶ If patients with peripheral nerve injury did not recover well, they would have the problem of dysfunction in chronic phase even if the injured nerve exhibited good anatomic reconnection. One of the main reasons is that endogenous Schwann cells may undergo atrophy and no longer play a role in supporting, guiding axon regeneration, and myelinating regenerating axons in chronic stage of peripheral nerve injury.¹

Why did we use ASIA scale to evaluate this patient with sciatic nerve injury? ASIA scale is an evaluation tool for spinal cord injury (SCI); it can also reflect the motor and sensory functions of each nerve segment resulting from other injuries. When the patient injured his sciatic nerve,

Table 1 ASIA motor score in left leg before cell therapy and follow-up

Muscles	Before	Ten days after	Six months after	One year after
L2 – hip flexors	4	5	5	5
L3 – knee extensors	4	4	4	4
L4 – ankle dorsiflexors	1	3	4	4
L5 – long toe extensors	0	3	3	3
S1 – ankle plantar flexors	1	3	3	4

Abbreviation: ASIA, American Spinal Injury Association.

Table 2 Left leg ASIA light touch score before cell therapy and follow-up

Sensory	Before	Ten days after	Six months after	One year after
L3	2	2	2	2
L4	1	2	2	2
L5	0	1	1	1
S1	0	1	1	1
S2	2	2	2	2
S3	2	2	2	2

Abbreviation: ASIA, American Spinal Injury Association.

Table 3 Left leg ASIA pin prick score before cell therapy and follow-up

Sensory	Before	Ten days after	Six months after	One year after
L3	2	2	2	2
L4	1	1	1	1
L5	0	1	1	1
S1	0	1	1	1
S2	2	2	2	2
S3	2	2	2	2

Abbreviation: ASIA, American Spinal Injury Association.

he showed defect or dysfunction in at the level of nerve segment. Thus, ASIA scale is an appropriate tool to evaluate the dysfunction of each nerve segment resulting from sciatic nerve injury.

OECs are a special type of glial cells and display unique properties; they share many common properties of astrocytes (GFAP expression), Schwann cells (p75), and oligodendrocytes (O4). OEC is the only cell with the ability in its life span, to help olfactory nerves extend from olfactory epithelium into brain across the boundary between peripheral nervous system and CNS. After being transplanted, they can restore, promote, and maintain the integrity of impaired or lost neuronal functions and/or structures through mechanisms of neuroprotection, supporting axonal regeneration, remyelination, neurorepair, neuroplasticity, neuromodulation, neurogenesis, angiogenesis, anti-inflammatory response, etc.^{17,18} Following OEC transplantation, patients with complete chronic SCI, amyotrophic lateral sclerosis, chronic stroke, cerebral palsy, multiple system atrophy, Alzheimer's disease, etc could benefit from the restoration of some neurological functions and their quality of life could be improved.^{19–25}

During the period of recovery after acute phase, Schwann cells play an important role in peripheral nerve axonal regeneration and remyelination through providing neurotrophic support, guiding axonal regeneration, and myelinating the regenerated axons.^{5–9} However, in chronic phase, endogenous Schwann cells may lose their abilities because of cellular atrophy and can no longer perform the functions of supporting, guiding axon regeneration, and myelinating; at that time, OEC transplantation may replace Schwann cells to play those roles.^{26,27} How was this patient able to recover some functions in the early stage? We observed this phenomenon 15 years ago. At that time, we performed OEC transplantation in patients with chronic complete SCI, and they recovered their functions in a few days after treatment. Our explanation was that patients with chronic complete SCI might have some anatomical nerve connections before OEC therapy, but that those axons were not in good functional state or were in quiescent state. The neurorestorative mechanisms mainly involved unmasking the quiescent axons or neuromodulation, but not neuroregeneration for early function recovery because environment at the injured area had been changed by the secretions of OECs.²⁸ The similar mechanism of explanation after cell therapy was for patients with chronic stroke recently.²⁹ This recovery of patient's functions after cell therapy is possibly similar in patients suffering from chronic complete SCI or chronic stroke, which may explain the reason how OECs can help a patient with chronic sciatic nerve injury to improve his/her neurological functions in an early stage.

Conclusion

The therapeutic results of this case report indicate that OEC transplantation may be an optional or alternative therapy for chronic peripheral (sciatic) nerve injury. Thus, further studies of more cases are warranted to assess the benefits and risks of this intervention strategy.

Disclosure

The authors report no conflicts of interest in this work.

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