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Research article

A pilot study of cell-mediated gene therapy for spinal cord injury in mini pigs

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HIGHLIGHTS

- Intrathecal injection of the gene-cell constraction was used for the first time for SCI treatment in large animal mini-pig SCI model.
- Results provide evidence of feasibility and potential efficacy of proposed UCBC-based delivery of three therapeutic genes therapy.
- Observed recovery in treated animals support the positive effect of the gene-cell constriction after SCI.

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ABSTRACT

Currently, in clinical practice there is no efficient way to overcome the sequences of neurodegeneration after spinal cord traumatic injury. Using a new experimental model of spinal cord contusion injury on miniature pigs, we proposed to deliver therapeutic genes encoding vascular endothelial growth factor (VEGF), glial cell line-derived neurotrophic factor (GDNF) and neural cell adhesion molecule (NCAM) to the damaged area, using umbilical cord blood mononuclear cells (UCBC). In this study, genetically engineered UCBC (2×10^6 cells in 200 ml of saline) were injected intrathecally to mini-pigs 10 days after SCI. Control and experimental mini pigs were observed for 60 days after surgery. Histological, electrophysiological, and clinical evaluation demonstrated significant improvement in animal treated with genetically engineered UCBCs. Difference in recovery of the somatosensory evoked potentials and in histological findings in control and treated animals support the positive effect of the gene-cell constriction for recovery after spinal cord injury. Results of this study suggest that transplantation of UCBCs simultaneously transduced with three recombinant adenoviruses Ad5-VEGF, Ad5-GDNF and Ad5-NCAM represent a novel potentially successful approach for treatment of spinal cord injury.

1. Introduction

Spinal cord injury (SCI) is classified as a neurotrauma, although it is followed by disturbance in blood supply, neurodegenerative and other pathological consequences [1]. Regardless numerous animal studies and clinical trials, to this time there is no successful clinical protocol for SCI treatment. To enhance the efficacy of SCI therapy along with experiments on rodents and clinical trials, experiments

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