

A Mini Review on My Study of the Spinal Cord Injury

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Abstract

Spinal cord contusion was an injury that had never been effectively treated. The general pathology of the spinal cord contusion had long been studied and published. The major point is that after spinal cord contusion there develops a secondary injury with a necrotic center, which induces gradual expansion of the injury. The logical treatment should be debridement of the necrotic center to terminate further expansion. An early neurosurgery of the spinal cord contusion was designed and practiced clinically. Basically, MRI to determine the level of spinal cord contusion, make a longitudinal incision of the dura mater to expose the injured part of spinal cord. Debride ts necrotic tissue. The operation was followed by intensive rehabilitation for three months. Thirty ASIA-A grade patients were admitted. All the patients resumed certain degree of walk ability. The best result occurred in 13 patients operated 4-14 days after injury (the optimal operation time window). Eleven of the 13 cases were able to walk with a pair of crutches or even to walk without any support.

A laboratory of cellular and molecular biology was established to study the mechanism of spinal cord injury. It has an SPF laboratory for making transgenic/knock-out mice, and SPF animal housing rooms with a maximum capacity of 8,000 mice.

In all, 103 SCI articles on spinal cord injury have been published.

Keywords: Spinal cord injury; Neurosurgery; Molecular biology; Animal experiments

Intorduction

There was a publication which estimated that there are around 39 spinal cord injured patients among a million population in North America, 16 spinal cord injured patients among a million population in Western Europe. There is also report estimating the occurrence in China, but it does not have any meaning because beside the major cities in China there is no statistic analysis at all in remote countries. The major causes of spinal cord injuries are traffic accident, fall from a height, collapse of building, and mine accident. It often occurred in the past, but the situation has been much improved, though it still happens today in China, probably in other parts of the world as well [1,2].

Since the major part of the spinal cord injured persons are young peoples and their life expectance is about the same as healthy ones. It causes long last pain of the suffered and their family, as well as a burden on the society. Therefore, study on the treatment of spinal cord injury is a major issue all over the world till today [3].

Early Neurosurgery of Spinal Cord Contusion

Request from the Clinical Centre of spinal cord injury of PLA Kunming General Hospital

They were transplanting fetal Schwann cells into the cavity of secondary injury of chronic cases of spinal cord contusion. They invited two renowned orthopedists to evaluate the effect. They came to the hospital. After listened the report of the host, they were asked to examine the patients. They simply refused and said that it was impossible. Someone suggested the chair of the Clinical Center of Spinal Cord Injury to ask my advice. My first response was also "it is impossible", but as a scientist the conclusion should not depend on what I think before I have examined the patients. So I went to the hospital and watched their operation. Their operation was perfect. The fetal Schwann cells were provided by the Institute of Zoology of the Chinese Academy of Sciences. They soaked the Schwann cells in absorbable sutures before they filled the cavity with them. It was a smart idea that the Schwann cells were transplanted in solid vehicle, thus in much larger amount. Yet I told them that although it had long been proven in animal experiments that transplantation of Schwann cells is

beneficial, but in your case there is little hope for the Schwann cells to migrate through the cavity wall into the tissue of the spinal cord. Then I examined the patients in the ward and found only one of the patients, a young lady, had a merely detectable voluntary movement of her right leg. With the help of a body support she "seemed" to be able to walk. The word "seemed" here means that the step forward was so difficult for her that she automatically swung her pelvis to help. Whenever a patient swings the pelvis, be it strongly or weakly, the orthopedists would refuse to agree that the patient can walk. I then asked her to sit on a high chair, on which her lower legs could not touch the ground. I raised her lower legs one by one and let it go. They swung like a pendulum. Then I told her try to stop it when I say "stop". It had no effect on her left leg, but her right leg swung a few times and stopped. It clearly proved that her right leg did have a mild ability to move [4-7].

The pathology of spinal cord contusion is well known (Figure 1).

The deteriorate substances of the primary injury would ooze out, causing secondary injury of the spinal cord filled with a necrotic center walled up by astrocytes. The deteriorate substances continue to ooze out and the size of the secondary injury expands gradually. The logic of treatment is clear: early debridement of the secondary injury, thereby terminates its further expansion and reduces the pressure on the rest of the cord. Therefore I suggested the head of the Clinical Center of Spinal Cord Injury to practice early neurosurgery for patients of spinal cord contusion [8-10].

Routine MRI to examine the injured spinal column and the location and the type and severity of the injured spinal cord. If the type of the spinal cord meets the criteria of early neurosurgery, the patient is the candidate for admission [11,12].

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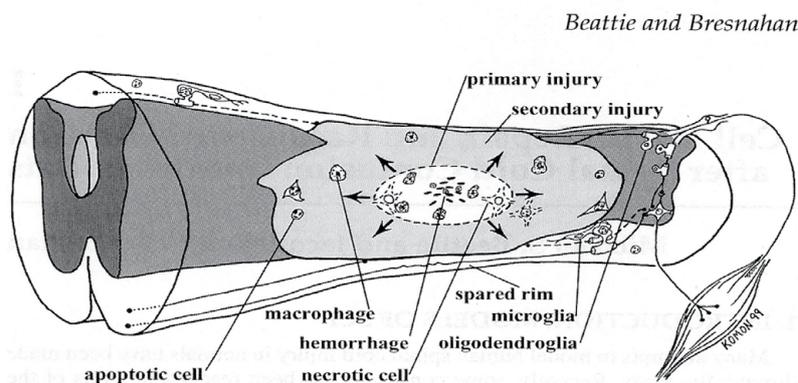


Figure 1: Pathology of spinal cord contusion (Taken from “cell death, repair, and recovery of function after spinal cord contusion injury in rats. Neurobiology of Spinal Cord Injury, R.G. Kalb and SM Strittmatter. Humanna Press, Totowa).

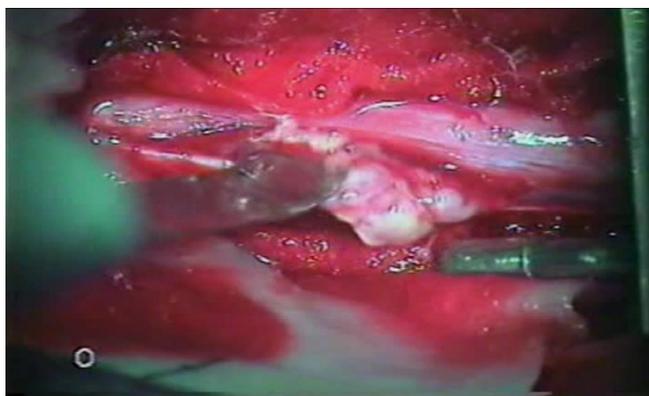


Figure 2: The blade of a scrapper is inserting into the cavity of the secondary injury to squeeze out the necrotic tissue. The horizontal suction tube is shown at the right side of the figure.

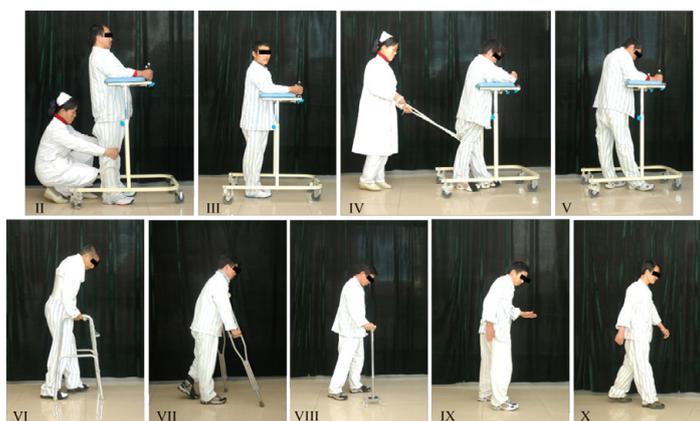


Figure 3: Roman numerals show the grades of locomotion ability.

Inclusion criteria: Routine MRI at admission.

Non-selective inclusion of all ASIA-A patients (Loss of all sensation and voluntary movement below the lesion) under age of 50 (arbitrary, senior patients recover slower than the younger ones).

Exclusion criteria: They are as follows:

1. Complete disruption of the continuity of the spinal cord, or the cord has a stab wound.

2. Brain injuries or other neurological diseases.

3. Others include pregnancy, significant medical disease or infection, significant psychiatric conditions.

To start with, only ASIA-A patients should be recruited, because all kinds of somatic sensations and voluntary movements are lost below the spinal cord injury in ASIA-A patients. Thirty patients in all met the criteria and were admitted [13-15].

The surgery: Bilateral laminectomy to expose the dura mater of the

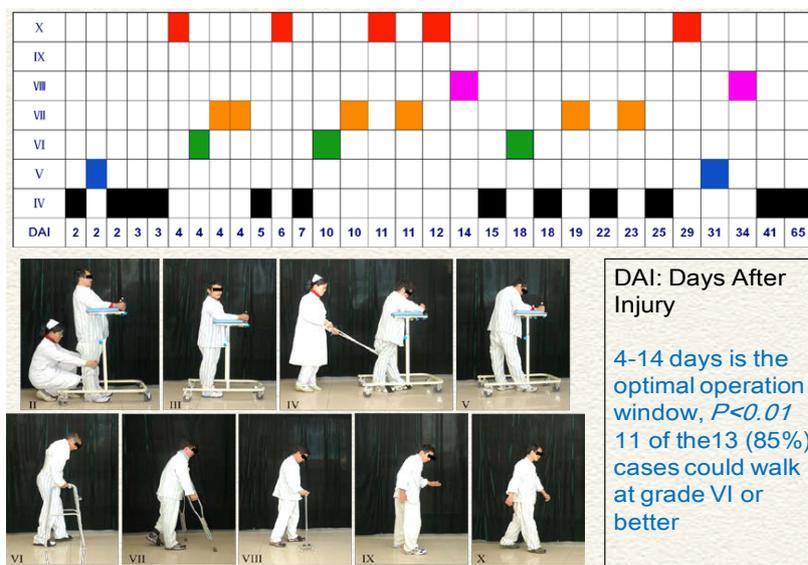


Figure 4: The grades of locomotion ability.



Figure 5: An example of a patient walking with a pair of crutches.

injured spinal cord region followed by internal fixation of the spinal column. Make a longitudinal incision of the dura mater of 2-3 mm to expose the injured spinal cord. Since the surface of the secondary injury is very thin, like a water filled balloon, it is easy to locate it by gentle touching of the exposed spinal cord. Make a sagittal cut of 2-3 mm. If the pressure is high inside, the necrotic tissue will gush out, which is sucked out. If not, the blade of a small neurosurgical scrapper is inserted to squeeze out the necrotic tissue. The cavity is further cleaned by rinsing with physical saline (Figure 2).

Post operation cares: The patients were kept in ICU for 2-3 days, after which any medication that might affect functional recovery was avoided, otherwise it would hard to determine how much of the beneficial result of the operation is due to the operation itself.

Although there are standard grading systems to evaluate walking ability, but all are too difficult for not having been well trained doctors and nurses. I then designed a system using pictures which is very clear, so much so that even the patients can identify their improvement themselves (Figure 3).

In Figure 3, Roman numerals show the grades of locomotion ability. Grade I is not shown in the chart because the patient cannot stand even with the help of the body supporter. and the nurse. Patient of Grade IV can walk, but when the patient start to walk he must shift the body weight to one leg before he can step forward, but his weight supporting leg is not strong enough and his knee joint will bend down without the help of the nurse to fix it with a band pulling form behind. Patient of Grade VI can walk with a pair of crutches, but staggeringly. Therefore he needs a light four-legs walker to help [16-19].

After three months of rehabilitation, the outcome turned out to be far beyond my boldest expectation. All of the patients were able to walk with the help of a body weight supporter. The optimal operation time window was 4 to 14 days after injury, in which 13 patients were include, among them 11 were able to walk with a pair of crutches or even free walking without any help (Figures 4-6).

What will happen if operated before 4 days? Because the necrotic cavity of the secondary injury has not formed yet. At that period the injured part of the spinal cord is just a mashed tissue mixed with blood. After cutting open the dura mater, what the surgeon can do is to remove



Figure 6: An example of a patient walking without any support. The wires attached on his legs were for electromyography.

the exposed damaged tissue. The doctor is not allowed to scrape beyond the visible region which may run the risk of destroying the normal tissue. Nevertheless, it does have a limited value in improving the walking ability as shown in Figure 3.

How to Improve the Surgery?

The best time after injury for the surgery is crucial. It should be the time that the secondary injury has been well walled up. This can be determined with MRI. On the basis of sagittal view of the spinal column, identify the level of spinal cord injury followed by condensed cross section scanning of the injured region of the spinal cord, once every certain mm (every 8 mm in our case).

Up to today, the early neurosurgery of spinal cord contusion is still the only in the world. I have presented this practice both in meetings, or been invited to give a talk in quite a few countries abroad, with appraisal each time. There is no need for approval in all countries. But till today I have no information if any doctor has practiced it [20-25].

Our studies on the mechanism of the pathology of spinal cord injury

I have established a cellular and molecular laboratory with a floor space of 1,000 m², including a SPF room for producing transgenic/knock-out mice we need and SPF animal rooms with a maximum capacity of 8,000 mice.

The following is a list of the major aspects we have studied: Neural stem cell, M1 and P1 types of macro-glia, autophagy, microRNA, the multi-facet role of astrocyte, therapeutic effect of several clinical drugs and traditional Chinese herbal drugs [26-28].

Early hemostasis after spinal cord injury

Bleed occurs after any injury on the spinal cord, which causes destruction of the spinal cord tissue. The logic tells that early hemostasis should be helpful. This had been proved in our animal experiments, both in spinal cord contusion and stab wound of the cord. This is a simple experiment with great clinical significance. Since there is no harm done if the hemostatic drug is carefully chosen, the first thing to do in handling spinal cord injury accident should be an immediate injection of hemostatic drug, which is particularly important in cases of massive accidents [29,30].

Conclusion

In all, we have published 37 SCI articles on spinal cord injury.

References

- Lang B, Liu HL, Liu R, Feng GD, Jiao XY, et al. (2004) Astrocytes in injured adult rat spinal cord may acquire the potential of neural stem cells. *Neuroscience* 128: 775-783.
- Hou B, You SW, Wu MM, Kuang F, Liu HL, et al. (2004) Neuroprotective effect of inosine on axotomized retinal ganglion cells in adult rats. *Invest Ophthalmol Vis Sci* 45: 662-667.
- Liu F, You SW, Yao LP, Liu HL, Jiao XY, et al. (2006) Secondary degeneration reduced by inosine after spinal cord injury in rats. *Spinal Cord* 44: 421-426.
- Zhang Q, Qin HY, Lang B, Liu HL, Han H, et al. (2005) Different regions of the mouse nestin enhancer may function differentially in nestin expression in an NSC-like cell line and astrocytes. *Neurosci Lett* 379: 90-95.
- Yang H, Liang Z, Li J, Cheng X, Luo N, et al. (2006) Optimized and efficient preparation of astrocyte cultures from rat spinal cord. *Cytotechnology* 52: 87-97.
- Xu Z, Wang BR, Wang X, Kuang F, Duan XL, et al. (2006) ERK1/2 and p38 mitogen-activated protein kinase mediate iNOS-induced spinal neuron degeneration after acute traumatic spinal cord injury. *Life Sci* 79: 1895-1905.
- Zhao XH, Jin WL, Ju G (2007) An in vitro study on the involvement of LINGO-1 and Rho GTPases in Nogo-A regulated differentiation of oligodendrocyte precursor cells. *Mol Cell Neurosci* 36: 260-269.
- Chen A, Wang H, Zhang J, Wu X, Liao J, et al. (2008) BYHWD rescues axotomized neurons and promotes functional recovery after spinal cord injury in rats. *J Ethnopharmacol* 117: 451-456.
- Zhu H, Feng YP, Young W, You SW, Shen XF, et al. (2008) Early neurosurgical intervention of spinal cord contusion: an analysis of 30 cases. *Chin Med J (Engl)* 121: 2473-2478.
- Yang H, Cheng XP, Yao Q, Li JW, Ju G (2008) The promotive effects of thymosin β_4 on neuronal survival and neurite outgrowth by upregulating L1 expression. *Neurochem Res* 33: 2269-2280.
- Shen XF, Zhao Y, Zhang YK, Jia LY, Ju G (2009) A modified ferric tannate method for visualizing a blood vessel and its usage in the study of spinal cord injury. *Spinal Cord* 47: 852-856.
- Yang H, Cheng XP, Jin WL, Yao Q, Ju G (2009) De-differentiation response of cultured astrocytes to injury induced by scratch or conditioned culture medium of scratch-insulted astrocytes. *Cell Mol Neurobiol* 29: 455-473.
- Gao F, Zhang Q, Zheng MH, Liu HL, Hu YY, et al. (2009) Transcription factor RBP-J-mediated signaling represses the differentiation of neural stem cells into intermediate neural progenitors. *Mol Cell Neurosci* 40: 442-450.
- Guo J, Yu C, Li H, Liu F, Feng R, et al. (2010) Impaired neural stem/progenitor cell proliferation in streptozotocin-induced and spontaneous diabetic mice. *Neurosci Res* 68: 329-336.
- Shao Z, Luo Q, Liu D, Mi Y, Zhang P, et al. (2011) Induced differentiation of neural stem cells of astrocytic origin to motor neurons in the rat. *Stem Cells Dev* 20: 1163-1170.

16. Zhao X, Wu J, Kuang F, Wang J, Ju G (2011) Silencing of Nogo-A in rat oligodendrocyte cultures enhances process branching. *Neurosci Lett* 499: 32-36.
17. Jia LY, Yao AH, Kuang F, Zhang YK, Shen XF, et al. (2011) Beneficial effect of the traditional chinese drug shu-xue-tong on recovery of spinal cord injury in the rat. *Evid Based Complement Alternat Med*.
18. Liu L, Qian XH, Feng GD, Wu MM, Yang AA, et al. (2012) Different neuro-protection and therapeutic time windows by two specific diazepam regimens on retinal ganglion cells after optic nerve transection in adult rats. *Restor Neurol Neurosci* 30: 335-343.
19. Zhao X, Wu J, Zheng M, Gao F, Ju G (2012) Specification and maintenance of oligodendrocyte precursor cells from neural progenitor cells: involvement of microRNA-7a. *Mol Biol Cell* 23: 2867-2878.
20. Fan H, Liu X, Tang HB, Xiao P, Wang YZ, et al. (2013) Protective effects of Batroxobin on spinal cord injury in rats. *Neurosci Bull* 29: 501-508.
21. Zhang YK, Wang J, Liu L, Chang RC, So KF, et al. (2013) The effect of *Lycium barbarum* on spinal cord injury, particularly its relationship with M1 and M2 macrophage in rats. *BMC Complement Altern Med* 13: 67.
22. Ju G, Wang J, Wang Y, Zhao X (2014) Spinal cord contusion. *Neural Regen Res* 9: 789-794.
23. Cheng P, Kuang F, Zhang H, Ju G, Wang J (2014) Beneficial effects of thymosin β 4 on spinal cord injury in the rat. *Neuropharmacology* 85: 408-416.
24. Yao A, Liu F, Chen K, Tang L, Liu L, et al. (2014) Programmed death 1 deficiency induces the polarization of macrophages/microglia to the M1 phenotype after spinal cord injury in mice. *Neurotherapeutics*. 11: 636-650.
25. Fan H, Tan HB, Sha L, Kan JJ, Keqing ZH, et al. (2015) Involvement of endoplasmic reticulum stress in the necrotosis of microglia/ macrophages after spinal cord injury. *Neuroscience* 311: 362-373.
26. Zhao Y, Zhang H, Zhang D, Yu CY, Zhao XH, et al. (2015) Loss of microRNA-124 expression in neurons in the peri-lesion area in mice with spinal cord injury. *Neural Regen Res* 10: 1147-1152.
27. Zhang K, Zheng J, Bian G, Liu L, Xue Q, et al. (2015) Polarized macrophages have distinct role in the differentiation and migration of embryonic spinal-cord-derived neural stem cells after grafting to injured sites of spinal cord. *Mol Ther*. 23:1077-1091.
28. Fan H, Kun C, Duan L, Wang YZ, Ju G (2016) Beneficial effects of early hemostasis on spinal cord injury in the rat. *Spinal Cord* 54: 1058.
29. Fan H, Zhang K, Shan L, Kuang F, Chen K, et al. (2016) Reactive astrocytes undergo M1 Microphage/macrophage-induced necroptosis in spinal cord injury. *Molecular Neuro-degeneration* 11:14-30.
30. Zhang Q, Bian GL, Chen P, Liu L, Yu CY, et al. (2016) Aldose reductase regulates microglia/macrophages polarization through cAMP-responsive binding element after spinal cord injury in mouse. *Mol Neurobiol* 53: 662-676.