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Correlation of Pathological Findings with MRI Imaging in Traumatic Spinal Cord Injury in Hyperacute Time Period in Non Human Primate Model

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Abstract

Traumatic Spinal Cord Injury (TSCI) remains a significant cause of human suffering. The World Health Organization estimates that there are between 250,000 to 500,000 new cases every year. Magnetic Resonance Imaging (MRI) has been an important advancement in the diagnosis and management of TSCI. Nevertheless, there is a lack of literature correlating the radiological abnormalities and histopathological findings in the first hour (*i.e.*, hyperacute period) after injury. The aim of this preliminary study is to elucidate the relationship between the MRI abnormalities and histopathological abnormalities in the hyperacute time period. In this study, a non-human primate model (NHP) primate model is used to characterize the histopathological and radiological features. Specifically, an experimental TSCI is created with an epidural catheter. This is followed by MRI imaging. The subject is then humanely euthanized and a post-mortem examination is completed. These results suggest that the noted radiological abnormalities are consistent with a combination of hemorrhage, edema as well as eosinophilic cellular matter in the central canal.

Keywords

Spinal Cord Injury, Pathology, MRI, Correlation, Radiology

1. Introduction

Traumatic Spinal Cord Injury (TSCI) remains a major cause of human suffering.

The World Health Organization estimates that there are approximately 250,000 to 500,000 new cases every year [1] [2]. Magnetic Resonance Imaging (MRI), which was first introduced into routine clinical practice in the 1980s, has been a spectacular advancement in the management of TSCI [2] [3].

From a pathophysiological perspective, spinal cord injury can be conceptualized as primary and secondary injury. Primary or immediate injury relates to mechanical disruption of the spinal cord. Secondary injury encompasses a number of subsequent phenomena including hemorrhage, edema, demyelination as well as cytoxicity [2] [4].

Nevertheless, there is a lack of literature correlating the radiological abnormalities and histopathological findings in the hyperacute period (*i.e.*, within one hour post injury). This information is particularly important because decisions related to treatment are based, in part, on the radiological abnormalities [5]. This includes determination of the necessity of surgical treatment as well as the type and extent of proposed operative procedures.

Studying TSCI in humans is challenging because the time period between injury and transport to the hospital is typically one hour or more. The normal sequence of events includes an assessment in the emergency room and management of any concomitant injuries. Only after these clinical events can an MRI study be completed. As such, an MRI study is the very early time period is not readily available. Additionally, very few patients who arrive alive at the hospital die in the emergency room limiting the number of TSCI patients who would have undergone a postmortem examination.

In this context, non-human primate (NHP) models of TSCI can provide insights into these important scientific questions. The following is a preliminary report on the radiological and pathological abnormalities associated with TSCI in the hyperacute time period.

2. Materials & Methods

The subject was one adult male rhesus macaque (*Macaca mulatta*). Surgical procedures were completed under general anesthesia with sterile technique. The protocol was approved by the University of Wisconsin-Madison IACUC. Sedation was achieved with ketamine (10 - 20 mg/kg intramuscularly) and midazolam (0.1 - 0.3 mg/kg intramuscularly) and induction was with propofol (1 - 5 mg/kg intravenously). The subject was intubated and maintained on isoflurane and fentanyl (2 - 5 mcg/kg/h intravenously) anesthesia.

Baseline MRI studies of the sacral, lumbar and thoracic spine were obtained with and without contrast. The scanner was a GE 3 Tesla Discovery device. Subsequently, a small laminotomy was performed at the level of the fifth lumbar vertebra. An epidural balloon catheter was inserted and advanced approximately 10 cm cranial, to the level of the lower thoracic spinal cord. The balloon was inflated rapidly. The balloon remained inflated for 1 hour.

The balloon was then deflated. The catheter was removed, and the surgical in-

cision was closed. Additional details regarding the method of lesion creation are noted elsewhere. MRI imaging was obtained over the next hour with and without contrast.

The subject was then humanely euthanized with the administration of sodium pentobarbital (at least 50 mg/kg intravenously). A postmortem examination was conducted. For histopathology, tissue blocks were dissected from the epicenter of the lesion and sites caudal and cephalad. These blocks were fixed in 10% neutral buffered formalin for 7 d, embedded in paraffin, and cut at 5 μm. Standard hematoxylin and eosin staining was done on sections from all blocks. In addition, sample sections were stained with Luxol fast blue to highlight myelin changes.

3. Results

3.1. Radiological Findings

The sagittal images of the thoracic spine demonstrate increased signal intensity at the site of the experimental lesion. The axial images demonstrate increased signal intensity at the central canal at the site of lesion. This is consistent with edema and/or hemorrhage (Figure 1).

3.2. Pathological Findings

Histology of coronal sections of spinal cord (Figure 2), at the level of experimental injury, reveal focally extensive disruption of the grey matter and central canal with marked grey matter hemorrhage, acute necrosis, and mild multifocal white matter hemorrhage (Figure 2). Adjacent sections of spinal cord, up to 2 cm

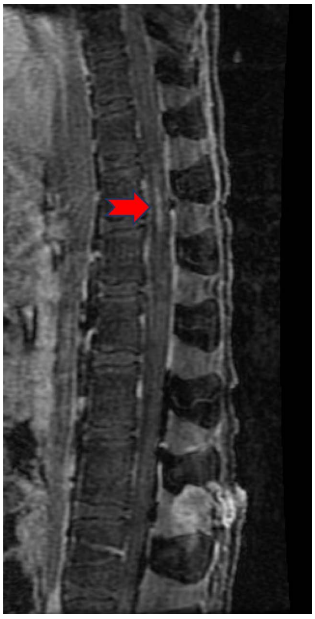

Figure 1. Sagittal Disco Image of thoracic spine post contrast. Arrow highlights area of enhancement at site of experimental spinal cord injury lesion.

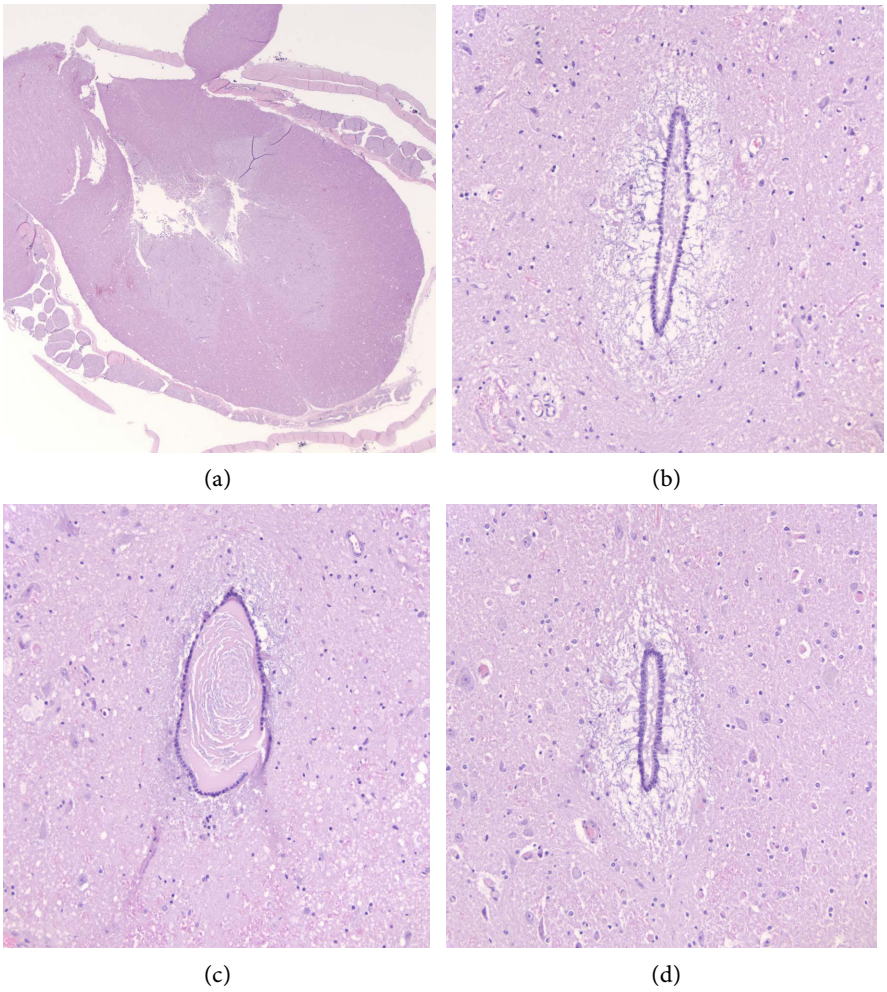

Figure 2. (a) At level of experimental lesion shows extensive disruption of the grey matter and central canal with marked grey matter hemorrhage, acute necrosis, and mild multifocal white matter hemorrhage. HE, 2× magnification. (b) Immediately adjacent to site of experimental lesion. This section shows moderate edema surrounding the central canal which is minimally distended with eosinophilic acellular material. The edema surrounding the central canal is indicated by the large white "holes" or vacuoles in the pink neuropil surrounding the dark purple ependymal cells lining the central canal. HE, 20× magnification. (c) 1 cm caudal to the area of maximal spinal cord disruption (*i.e.*, compression, hemorrhage, and necrosis). There is little to no edema surrounding the central canal which is markedly distended with eosinophilic acellular fluid and granular basophilic material. HE, 20× magnification. (d) 7 cm cranial to site of experimental injury. The central canal is not distended but there is mild to moderate edema surrounding the central canal causing separation of the cells and cellular processes of the neuropil creating white space or vacuolization. HE, 20× magnification.

caudal to the lesion, have expansion of the central canal with eosinophilic material and erythrocytes (Figure 2). At the conus, 4 cm distal to the lesion the central canal is unremarkable with mild edema of the surrounding neuropil. Multiple spinal cord sections, cranial to the lesion, have mild edema surrounding the central canal with diminution of changes at 13 cm cranial to the site of injury (Figure 2).

4. Discussion

Conceptually, the method of lesion creation corresponds to human TSCI. In human TSCI, there is a rapid transfer of energy; in this NHP model, this corresponds to the initial rapid balloon inflation. In human injury, this is followed by residual displacement of tissues such as disk material, bony fragments, or hematoma; in this experiment, this corresponds to the continued balloon inflation [6] [7] [8] [9].

The lesions in the macaques were created without compromising the dura, consistent with most human TSCI. Specifically, the model has no tearing or laceration of the dura, with no leakage of cerebral spinal fluid [7] [8] [9] [10]. As previously reported, lesions created by this method have the same histopathologic features of human spinal cord injury during the acute phase [7] [8] [9] [10].

The MRI abnormalities were striking in the hyperacute time frame. The increased signal intensity noted on the contrast-enhanced MRI images correlates to the histopathological findings; specifically, there is hemorrhage in the grey and white matter as well as the central canal. Additionally, the increased signal intensity is related to the histopathological findings of edema around the central canal and as well as cellular debris in the central canal. Of note, although the radiological abnormalities were primarily in the thoracic spinal cord, subtle histopathological abnormalities were evident throughout the spinal cord.

As noted previously, we have not able to find any studies correlating the MRI abnormalities with the histopathological abnormalities (*i.e.*, post mortem) in the hyperacute period. This is clearly a gap in the contemporary literature. There are two studies that are relevant to the discussion [11] [12]. Martin *et al.*, in 1991, reported a single case of human acute TSCI where the MRI and postmortem exam were obtained. In this particular case, the patient had a cervical injury secondary to a motor vehicle collision. The MRI study was completed 30 hours post injury and died 60 hours after injury. The T2 images demonstrated increased signal intensity in the central cervical spinal cord with T2 weighted images. The histopathological findings included severe axonal swelling and edema [10]. Quencer *et al.*, in 1991, reported the MRI findings and histopathological abnormalities in three subjects with central cord syndrome. The postmortem exams were completed 3 days to 3 months subsequent to date of injury. Of particular note, none of the three patients subject to post mortem exam had hemorrhage in the spinal cord [12]. This may reflect the difference in mechanism between central cord syndrome and TSCI associated with high velocity trauma such as a motor vehicle collision.

The medical and surgical management of acute TSCI relies on clinical assessment with is supplemented by investigations including an MRI. The preliminary article provides some insights related to correlating the pathological and radiological features utilizing a NHP model.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] World Health Organization (2023) Spinal Cord Injury. https://www.who.int/news-room/fact-sheets/detail/spinal-cord-injury

[2] Meyrers, A., Graham, A. and Stacey, P. (2013) Epidemiology of Spinal Cord Injury. In: Nesathurai, S., Ed., *The Rehabilitation of People with Spinal Cord Injury*. 3*rd Edition*, AAP Publishing, Whitinsville, 9-13.

[3] APS News (2006) This Month in Physics History: MRI Uses Fundamental Physics for Clinical Diagnosis. https://www.aps.org/publications/apsnews/200607/history.cfm

[4] David, G., Mohammadi, S., Martin, A.R., *et al*. (2019) Traumatic and Nontraumatic Spinal Cord Injury: Pathological Insights from Neuroimaging. *Nature Reviews Neurology*, **15**, 718-731. https://doi.org/10.1038/s41582-019-0270-5

[5] Zhang, Y., Al Mamun, A., Yuan, Y., Lu, Q., Xiong, J., Yang, S., Wu, C., Wu, Y. and Wang, J. (2021) Acute Spinal Cord Injury: Pathophysiology and Pharmacological Intervention (Review). *Molecular Medicine Reports*, **23**, Article No. 417. https://doi.org/10.3892/mmr.2021.12056

[6] Eli, I., Lerner, D.P. and Ghogawala, Z. (2021) Acute Traumatic Spinal Cord Injury. *Neurologic Clinics*, **39**, 471-488. https://doi.org/10.1016/j.ncl.2021.02.004

[7] Miller, A.D., Westmoreland, S.V., Evangelous, N.R., Graham, A., Sledge, J. and Nesathurai, S. (2012) Acute Traumatic Spinal Cord Injury Induces Glial Activation in the Cynomolgus Macaque (*Macaca fascicularis*). *Journal of Medical Primatology*, **41**, 202-209. https://doi.org/10.1111/j.1600-0684.2012.00542.x

[8] Nesathurai, S., Graham, W.A., Mansfield, K., Magill, D., Sehgal, P., Westmoreland, S.V., *et al*. (2006) Model of Traumatic Spinal Cord Injury in *Macaca fascicularis*: Similarity of Experimental Lesions Created by Epidural Catheter to Human Spinal Cord Injury. *Journal of Medical Primatology*, **35**, 401-404. https://doi.org/10.1111/j.1600-0684.2006.00162.x

[9] Seth, N., Simmons, H., Masood, F., Graham, W.A., Rosene, D.L., Westmoreland, S., *et al*. (2018) Evidence from a Non-Human primate Model of Traumatic Spinal Cord Injury in Cynomolgus Macaques (*Macaca fasicularis*) to Evaluate for the Efficacy of a Combination Pharmacological Treatments. *Comparative Medicine*, **68**, 63-73.

[10] Sledge, J., Graham, A.W., Westmoreland, S., Sejdic, E., Miller, A., Hoggatt, A., *et al*. (2013) Spinal Cord Injury Models in Non Human Primates: Are Lesions Created by Sharp Instruments Relevant to Human Injuries? *Medical Hypotheses*, **81**, 747-748. https://doi.org/10.1016/j.mehy.2013.07.040

[11] Martin, D., Schoenen, J., Lenelle, J., Reznik, M. and Moonen, G. (1992) MRI-Pathological Correlations in Acute Traumatic Central Cord Syndrome: Case Report.

Neuroradiology, **34**, 262-266. https://doi.org/10.1007/BF00588177

[12] Quencer, R.M., Bunge, R.P., Egnor, M., Green, B.A., Puckett, W., Naidich, T.P., *et al*. (1992) Acute Traumatic Central Cord Syndrome: MRI-Pathological Correlations. *Neuroradiology*, **34**, 85-94. https://doi.org/10.1007/BF00588148