Biomarkers in spinal cord compression Ethics and perspectives

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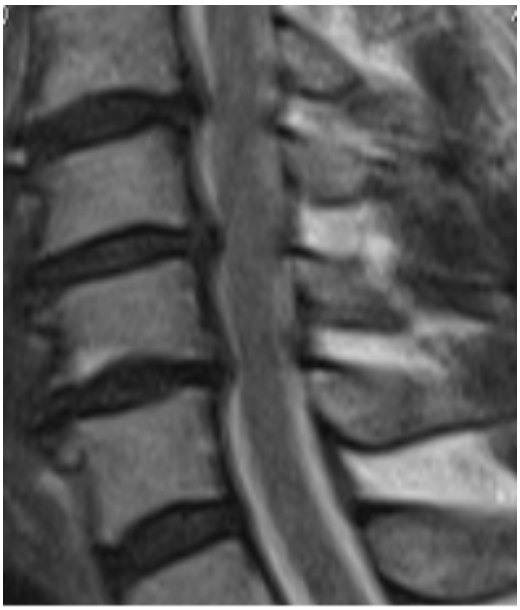
Abstract: The phosphorylated form of the high-molecular-weight neurofilament subunit NF-H (pNF-H) in serum or in cerebro-spinal fluid (CSF) is a specific lesional biomarker for spinal cord injury. The lesional biomarkers and the reaction biomarkers are both presented after several hours post-injury. The specific predictive patterns of lesional biomarkers could be used to aid clinicians with making a diagnosis and establishing a prognosis, and evaluating therapeutic interventions. Diagnosis, prognosis, and treatment guidance based on biomarker used as a predictive indicator can determine ethical difficulties by differentiated therapies in patients with spinal cord compression. At this point based on studies until today we cannot take a decision based on biomarker limiting the treatment of neurological recovery in patients with complete spinal cord injury because we do not know the complexity of the biological response to spinal cord compression.
Key words: ethics, lesional biomarkers, reaction biomarkers, spinal cord compression

Introduction

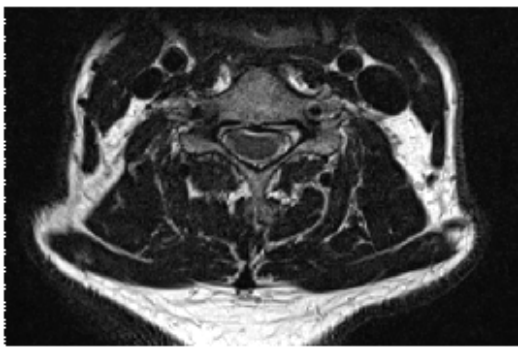
Spinal compression with radicular or spinal cord injury is caused by inflammatory diseases, disk degeneration, spinal injuries or other causes as tumors, infections etc. The phosphorylated form of the high-molecular-weight neurofilament subunit NF-H (pNF-H) in serum or in cerebro-spinal fluid (CSF) is a specific biomarker for spinal cord lesion.

In spinal cord injury the direct mechanical injuries cause axonal destruction and destruction of the neurons and their destruction releases the lesional biomarkers. The reactions of other injured cells start simultaneously and the produced substances are the reaction biomarkers. The lesional biomarkers and the reaction biomarkers are both presented after several hours post-injury. A comparison between degenerative diseases of the nervous system (amyotrophic lateral sclerosis or multiple sclerosis) and traumatic spinal cord injuries shows that the same biomarker: pNF-H can be a lesional biomarker in traumatic injuries and is a reaction biomarker in degenerative diseases, because of the different pathophysiological mechanisms: direct injury or secondary response caused by other factors.

A new proposed approach in spinal compression is based on the biomarkers as pNF-H; the heavy phosphorylated neurofilament subunit concentration can be a predictive lesional biomarker because the pattern in its values can show the reduction or stoppage of the secondary lesion in spinal cord injury with a favorable result.



A



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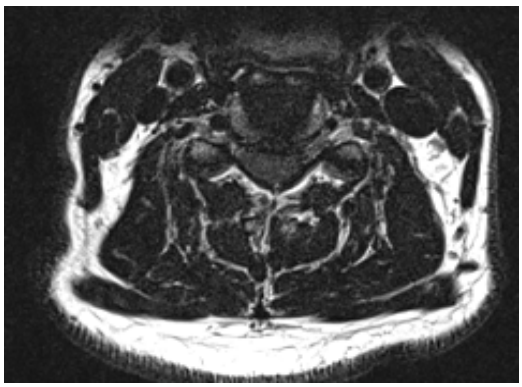

C

Figure 1 - MRI of three-level disc herniation with cervical myelopathy: **A.** sagital image; **B.** normal transversal image of cervical spinal cord; **C.** transversal image of compression of cervical spinal cord

The studies on biomarkers in spinal cord injuries highlight that the most important lesional biomarkers are the phosphorylated neurofilament subunits, light or heavy (pNF-L or pNF-H). The phosphorylated neurofilament subunits (pNF-L or pNF-H) are specific lesional biomarkers for spinal cord compression and they can distinguish the severity of SCI. The heavy phosphorylated neurofilament subunit (pNF-H) is a predictive lesional biomarker; its values pattern shows the reducing or stopping of the secondary lesions and the favorable outcome. There is a specific pattern of daily values of pNF-H in complete spinal cord compression patients with a favorable outcome: a sudden increase up to a maximum value then a progressive decrease to normal. Also there are two patterns in the patients with unfavorable outcome: an increase to a plateau of pNF-H values or a progressive increase up to a peak followed by a progressive decrease to quasi-normal values. These specific patterns could be used to aid clinicians with making a diagnosis and establishing a prognosis, and evaluating therapeutic interventions.

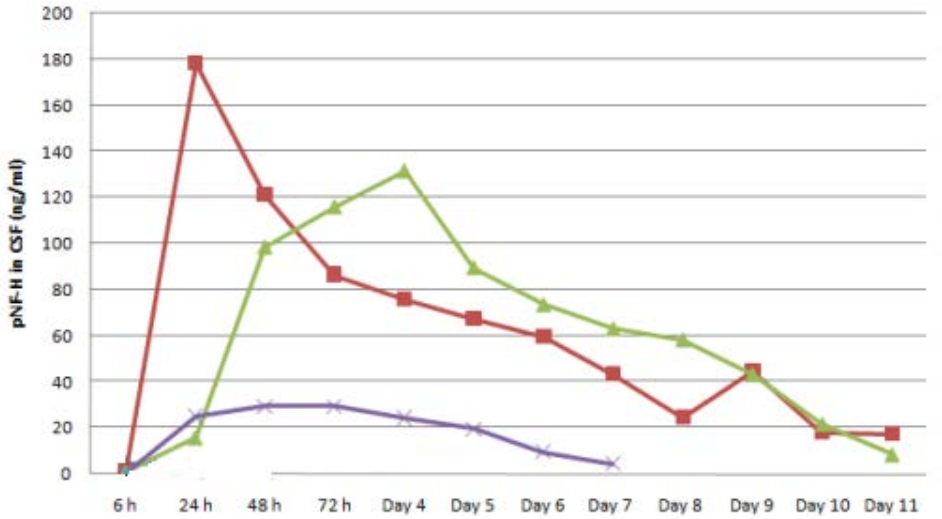

Figure 2 - The three specific and predictive pattern of daily values of pNF-H in traumatic SCI (from ref. 12)

The studies on lesional biomarkers in spinal cord compression should continue on larger groups of patients to prove the clinical usefulness. Also the studies on reaction biomarkers are very important, but obtaining cells from the site of spinal cord compression is problematic in humans.

A new approach in the management of acute traumatic spinal cord injury has been proposed that could enable obtaining cells from the site of spinal cord injury without adverse consequences for the patient. In the cases with a predictive pattern of unfavorable outcome or neurological stationary after decompression and stabilization during the first 24 hours, a new approach was proposed based on the predictive pattern of daily values of pNF-H. If the clinical neurologic evolution is unfavorable and imaging techniques (MRI) show a complete SCI and the daily values of pNF-H as lesional biomarker form predictive unfavorable pattern, a second microneurosurgery in the spinal cord injury site can create favorable conditions for functional recovery of the remaining spinal cord: opening the spinal cord in the midline and microsurgical debridement of the necrotic tissue. At the same time this second microneurosurgical approach in the spinal cord injury site could enable obtaining cells from this site without adverse consequences for the patient. The use of these cells (neurons and glial cells around the lesion) for cell culture techniques will allow the study of the changes in the spinal cord compression at the molecular and structural levels in humans.

Diagnosis, prognosis, and treatment guidance based on biomarker used as a predictive indicator can determine ethical difficulties by differentiated therapies in patients with spinal cord compression. It is difficult to stop or to limit the treatment of neurological recovery in patients with complete spinal cord injury, with paraplegia or tetraplegia, with complete spinal cord lesions on imaging techniques and unfavorable

patterns of predictive lesional biomarkers. We do not currently know the value of the lesional predictive biomarkers, and also the reaction biomarkers, for the neurological outcome several years after the injury.

At the moment, we cannot take a decision limiting the treatment of neurological recovery in patients with complete spinal cord injury because we do not know the complexity of the biological response to spinal cord injury. This requires extensive and profound research both on lesional biomarkers and on reaction biomarkers correlated with genetic and molecular response in spinal cord compression and we hope further research will deliver effective treatments.

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