B Cell-Targeted Therapy with Anti-CD20 Monoclonal Antibody Reduced Secondary Tissue Damage and Enhanced Behavioral Recovery Following Experimental Spinal Cord Injury in Mice

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Spinal cord injury (SCI) is defined as an acute traumatic lesion of neural elements in the spinal canal (spinal cord and cauda equina), resulting in a change, either temporary or permanent, in normal motor, sensory, or autonomic function. SCI usually begins with a sudden, traumatic blow to the spine that causes local segmental damage to the spinal cord, which is called primary injury. The primary damage to tissue is followed by a second phase of tissue degeneration, the 'secondary injury', that can occur over weeks or even months. In secondary injury, acute inflammation can develop into a chronic process if feedback mechanisms fail to inhibit amplification of the inflammatory response. Traumatic injury to the spinal cord activates B cells, which culminates in the synthesis of autoantibodies. The functional significance of this immune response is unclear. Antibodies produced after SCI caused pathology, in part by activating intraspinal complement and cells bearing Fc receptors. These data indicate that B cells, through the production of antibodies, affect pathology in SCI. There is increasing appreciation of the important role of B cells in spinal cord trauma and consequently, increasing interest in treating these disorders through B cell-depletion therapy. The purpose of this study was to investigate the effects of anti-CD20 mAb B cell depletion therapy within the first 24 hours of SCI.
In this study, a longitudinal incision was made on the midline of the back, exposing the paravertebral muscles. These muscles were dissected away, the spinal cord was exposed via a four-level T5 to T8 laminectomy and SCI was produced by extradural compression at T6 to T7 level, using an aneurysm clip with a closing force of 24 g. Following surgery, 1.0 cm^3 of saline was administered subcutaneously in order to replace the blood volume lost during the surgery. The anti-murine CD20 IgG2a antibody (clone 18B12, 1 mg/kg) was intravenously administered starting 1 hour and 6 hours postinjury. Animals were sacrified at 24 hours. The anti-CD20 antibody treatment caused significant attenuation of leukocyte infiltration, reactive oxygen species-associated enzymes, and secondary tissue damage. Basso-Beattie-Bresnahan (BBB) scores were significantly higher in anti-CD20-treated mice than controls 10 days postinjury. Our data demonstrate an important role of B cells which could possibly lead to B cell-based strategies for the treatment of SCI.