CYTOKINE INCREASES IN THE SPINAL CORD AND SERA OF MICE IN PASSIVE TRANSFER MODELS OF ALS

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Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by the selective loss of upper and lower motor neurons. Neuroinflammation has been implicated in the pathogenesis of the sporadic form of the disease. To investigate this, our group had previously developed immune-mediated animal models.
Presently we examined whether the previously documented ultrastructural changes and microglia accumulation induced by intraperitoneal injection of IgG isolated from sALS patients or anti-motoneuronal IgG from immunized animals (anti-MN IgG) are associated with changes in pro-(TNF-α, IL-6) and/or anti-inflammatory (IL-10) cytokines in the spinal cord ventral horns and sera of mice. The level of cytokines was measured by ELISA.
ALS IgG induced subclinical symptoms of motor neuron disease, while injection of anti-MN IgG resulted in severe respiratory dysfunction and limb paralysis 24 hours after the injections. A significant TNF-α and IL-10 increase could be detected in the spinal cords of mice injected with sALS IgG. The level of the secondary cytokine IL-6 was not elevated in the spinal cords, however a highly significant increase in IL-6 levels was noted in the sera. Anti-MN IgG induced an elevation in the levels of all three cytokines both in the spinal cords and sera of mice.
Our results proved that sALS or anti-MN IgG is sufficient to induce motor neuron damage and this pathological process is paralleled by microglia accumulation and cytokine production. Thus ALS IgG and anti-MN IgG is a crucial element in motor neuron damage both in human ALS and in its immune mediated animal models.