

Rapid Improvement of Chronic Stroke Deficits after Perispinal Etanercept

Three Consecutive Cases

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Abstract

Background: Thrombolytic therapy reduces stroke size and disability by reperfusion and salvage of ischaemic penumbra. Emerging evidence suggests that retrieved penumbra may be the site of ongoing inflammatory pathology that includes extensive microglial activation. Microglial activation may be associated with excessive levels of tumour necrosis factor (TNF) and resultant neurotoxicity. Etanercept, a potent biologic TNF antagonist, reduces microglial activation in experimental models and has been therapeutically effective in models of brain and neuronal injury. Perispinal administration of etanercept, previously reported to be beneficial for the treatment of Alzheimer's disease, may facilitate delivery of etanercept into the brain.

Objective: The objective of this report is to document the initial clinical response to perispinal etanercept in the first chronic stroke cohort so treated.

Methods: Three consecutive patients with stable and persistent chronic neurological deficits due to strokes that had failed to resolve despite previous treatment and rehabilitation were evaluated at an outpatient clinic. They were treated off-label with perispinal etanercept as part of the clinic's practice of medicine.

Results: All three patients had chronic hemiparesis, in addition to other stroke deficits. Their stroke distributions were right middle cerebral artery (MCA), brainstem (medulla) and left MCA. The two patients with MCA strokes had both received acute thrombolytic therapy. Each of the three patients was treated with an initial dose of perispinal etanercept 13, 35 and 36 months following their acute stroke, respectively. Significant clinical improvement following perispinal etanercept administration was observed in all patients. Onset of clinical response was evident within 10 minutes of perispinal injection in all patients. Improvements in hemiparesis, gait, hand function, hemi-sensory deficits, spatial perception, speech, cognition and behaviour were noted among the patients treated. Each patient received a second perispinal etanercept dose at 22–26 days after the first dose that was followed by additional clinical improvement.

Conclusions: Open-label administration of perispinal etanercept resulted in rapid neurological improvement in three consecutive patients with chronic neurological dysfunction due to strokes occurring 13–36 months earlier.