Reviewer's report

Title: Rapid improvement in verbal fluency and aphasia following perispinal etanercept in Alzheimer's disease and semantic dementia

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Reviewer: roger anwyl

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This paper reports a phase 2 trial on the perispinal administration of etanercept in 15 Alzheimer's patients and also gives a detailed description of two further patients treated with etanercept, one patient with Alzheimer's disease and the other with semantic dementia.

Comments

The results provide further strong evidence that TNF-alpha is a therapeutic target in Alzheimer's disease / dementia. Etanercept, a dimeric fusion protein which binds to TNF-alpha and inhibits its interaction with TNF-alpha, was administered via a novel route, perispinal administration, thus enabling etanercept to cross the blood brain barrier. While previous reports from this author and his colleagues have provided certain evidence that perispinal administration of etanercept is an effective treatment for Alzheimer’s disease, this new paper demonstrates that perispinal etanercept administration can lead to a novel rapid cognitive and behavioural improvement particularly in verbal learning and memory.

The use of perispinal injection of etanercept highlights the great advantage of using the choroid plexus to deliver agents to the brain. Moreover, the paper is extremely important for further demonstrating the success of the use of a TNF-alpha inhibitory agent in Alzheimer’s disease.

Although the trial was open-ended and not controlled and the data is limited, the reports of the patient’s improvement with etanercept provides further insight into the basic mechanisms of Alzheimer’s disease as well as emphasising the need for further research and clinical trials of perispinal etanercept administration.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.