Reviewer's report

Title: Etanercept may induce neurosarcoidosis in a patient treated for rheumatoid arthritis

Version: 3
Date: 29 October 2013
Reviewer: Raffaele D'Amelio

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Major Compulsory Revision:

1) Results of laboratory data must be reported: cytolisis, cholestasis, glucose and proteins in cerebral fluid (CF), lymphocyte numbers and CD4/CD8 ratio in CF and in bronchoalveolar lavage (BAL), should be detailed, if Known.

2) Have an US scan or CT of abdomen (cytolisis and cholestasis were detected) or a gallium scan been performed to exhaustively assess extraneurological involvement?

3) Which was the CS dosage administered in bolus and how long?

4) MTX was stopped in 2008 for hepatic cytolisis; when MTX was restarted which was the liver enzyme value at the beginning and did it remain in the normal range or not?

5) The conclusions should include a brief comment about Anti-TNF# agents usefulness in cases of refractory sarcoidosis, its rationale and the "paradoxical" occurrence of sarcoidosis in a limited number of patients receiving such drugs. Recently Tong et al. summarized the development of sarcoid-like granulomatous disease in 37 patients in treatment with all three TNF-# blocker, suggesting a "class effect" rather than a drug specific phenomenon [Tong D, Manolios N et al (2012) New-onset sarcoid-like granulomatosis developing during anti-TNF therapy: an under-recognized complication. Intern Med J 42(1):89–94]

6) In the 2 previous cases of neurosarcoidosis occurred during Anti-TNF# use reported in the literature, infliximab and adalimumab were used and the presented case was the first in which etanercept was involved. Indeed, the conclusions would benefit from some discussion about the differences between etanercept and infliximab/adalimumab; infact etanercept partially preserve the mechanisms leading to granuloma formation, and this aspect could explain its lack of efficacy in granulomatous disorders like Crohn’s disease and in refractory sarcoidosis.

7) No mention was made about the diagnostic issue between probable or possible neurosarcoidosis, that should be debated in presence of the negative histology for noncaseating epitheloid granulomas in peripheral tissue. Diagnostic criteria for neurosarcooidosis have been more recently revised (Marangoni S,

•Minor Essential Revisions

1) The wide range of neurological conditions, associated with TNF-# blocker therapy, other than neurosarcoidosis, including multiple sclerosis, polycranial neuritis, and chronic inflammatory axonal polyradiculoneuropathy, should be debated.

2) Some language corrections are needed. In particular:

in the abstract 40 year old instead of 40 years old

in the case presentation eye dryness instead of eyes dryness, Human Immunodeficiency Virus instead of Human Immunodeficient Virus, meningitis instead of meningitides, lymphocytic instead of lymphocytes, steroid boluses instead of steroids boluses

In the conclusions arguments may be replaced by evidences, did not relapse instead of did not relapsed, sarcoidotic instead of sarcoidosic patients

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests