Author's response to reviews

Title: Sustained remission of rheumatoid arthritis with SSRI antidepressant: a case report

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Author's response to reviews: see over
Sub: Submission of the revised manuscript “Sustained remission of rheumatoid arthritis with SSRI antidepressant: a case report” for consideration of publication.

Thank you for your valuable comments on the manuscript. Please find below the point-by-point responses to each comment. We have addressed them and made relevant changes to the manuscript. Changes to the manuscript have been highlighted by “underlining” them. I can confirm that the article has been formatted according to the journal guidelines using endnote.

Comments and responses:

1. The authors refer to a bi-directional link between mood disorders and inflammation. Are the authors suggesting that depression is able to induce inflammation? This statement should be rewritten or alternatively a reference to support this concept would need to be included.
The statement has been rewritten to include the term “biological substrates of mood disorders”. The bidirectional link between the serotonin system and inflammation has been discussed in the Discussion section.

2. The patient at one point received simvastatin, the duration of the treatment with simvastatin and the dose should be included. Was the simvastatin stopped before administering an SSRI? Simvastatin has also been reported to have anti-inflammatory effect not linked to its primary mode of action.

The points have been clarified in the manuscript. The below statement has been added.

The patient was receiving simvastatin at 40 mg dosage. No, the simvastatin was not stopped before the administration of the ssri. The patient was on the combination of aspirin 75mg and simvastatin 40mg for almost 5 years before he was commenced on the psychotropic medications. There was no perceived improvement in arthritis during this period. There was a clear temporal association between the start of escitalopram and improvement in his arthritis. Further, his arthritis relapsed when his escitalopram was stopped, and improved when it was restarted. Therefore the improvement in the patient’s inflammatory condition could be attributed to the psychotropic medication rather than the aspirin or the simvastatin.

3. The dose and frequency of escitalopram on recommencing treatment should be included in the manuscript.

This has been included in the manuscript. The dose on recommencement was 10mg.

4. The authors state that 'Inflammation is thought to have a direct impact on biological substrates'. What substrates? More detail is needed, do the authors mean cytokines?
The following statement has been added to the manuscript.

There seems to be a bidirectional relationship between biological substrates of mood disorders and inflammation. For e.g. inflammatory mediators like proinflammatory cytokines are thought to have a direct impact on biological substrates implicated in the patho-physiology of mood, particularly the serotonergic system and conversely, serotonergic pathways are thought to be important in mediating both inflammation and mood.

5. The full name should be given on the first mention of CRP and CIA

This has been done in the manuscript.

6. Toll-like receptors respond to both pathogens and to endogenous molecules found at sites of inflammation and tissue damage. They respond to molecular pattern that include nucleic acids (RNA and DNA) not just proteins.

This has been corrected.

7. In the conclusion the authors have suggest that antidepressants mediate their effect by agonistic actions on 5ht2a receptors or on toll-like receptors. The way this is written is misleading as SSRIs are shown in the reference in the discussion in the manuscript to inhibit toll-like receptors.

This has been rewritten, as below.

Postulated mechanisms through which antidepressants mediate this effect include their agonistic action on 5HT2A receptors or by inhibiting the signalling of toll like receptors that are responsible for mediating innate immunity.

Thanking you
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