Author's response to reviews

Title: Topiramate induced psychosis in a family with essential tremor: a case report

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Author's response to reviews: see over
Dear Editor,

We are grateful for the comments from the reviewers and have used their useful comments to improve our manuscript. We hope that after reviewing our manuscript you will now be able to consider it for publication in the Journal of Medical Case Reports.

Response to reviewer 1: Debra Kahn

1. The authors have presented an interesting case of a rare familial side effect of a medication. This case invites investigation into genetic factors contributing to the reported medication side effect. My criticism of the report is largely one of editing and writing style.

- We feel that our case report will highlight to the readers the importance of a family history when using topiramate as not only the diseases treated with topiramate have a higher prevalence in certain families but the side effects of this drug do too. Regarding the editing and writing style of the report we have done our best to improve it by making changes to the manuscript.

2. The case report would be more persuasive if the case itself was presented in a more linear/convincing fashion- ie including duration of psychotic symptoms, clarification of medication dosage and timecourse, re-working of statement "driven him to alcohol abuse," more details about medical investigation into psychotic symptoms.

- We have edited the manuscript to improve its readability and addressed the above concerns. We have made the following more clear within our manuscript:
  - duration of the psychotic symptoms
  - dosage of the medication (titration regime)
  - medical investigations performed during the work-up

The statement “driven him to alcohol abuse” has been removed from the manuscript and the replaced with “had in the past been drinking 8 units of alcohol per day to help control his tremor”.

3. I would also recommend a clarification of PADS findings- ie clarifying the basal rate of psychosis in a population, the rate in patients with epilepsy, and the rate in those on topiramate.

- In our manuscript we mention that the rate of psychosis in patients with epilepsy is 6 to 12 higher than in the general population and that the rate of topiramate induced psychosis in patients with epilepsy was 1.5% in the PADS findings. We did not find in the PADS findings the rate of psychosis in the general population as they only looked at patients with epilepsy.

4. Should there be a citation after the statement that "past psychiatric history is the strongest predictor for psychiatric adverse events?"
- We have now added the citation to this statement that we missed in our initial manuscript.

Response to reviewer 2: Martin Punter

1. When introducing topiramate the authors should initially present the licensed indications (generalised and focal onset epilepsies, and migraine) and then list the use as 'off-label' indications including that in essential tremor. This is important as a learning point in cases of drug induced side effects due to medicolegal implications.

- We have now indicated in our manuscript which of the indications for the use of topiramate are licensed indications and those which are “off-label”.

2. Within the body of the case presentation, paragraph 2, sentence 3 - more detail should be given (if available) on the dose titration of topiramate, although "standard dose and titration" is mentioned in the discussion. Sentence 4 - clarification of which period is meant by "during this time..." would be helpful.

- We have now mentioned more detail on the titration of topiramate used. The sentence “during this time” has been removed from the manuscript and throughout the manuscript we have made the time frame of events more clear.

3. Other points useful to mention would be to specify that neither the index case nor his sister had previously suffered with psychiatric symptoms if this is the case, and also to list any first line medications that had been used for the essential tremor in the index case (e.g. beta blockers)

- We have mentioned in our manuscript in two different paragraphs that neither the index case or his sister had a past history of psychotic symptoms. The medications used in the treatment of his essential tremor prior to the topiramate were propranolol and labetalol and we have now mentioned it in our manuscript.