Author's response to reviews

Title: A Fatal Case of Bupropion (Zyban) Hepatotoxicity with Autoimmune Features

Authors:

Fawwaz Humayun (humayuf@hotmail.com)
Thomas M Shehab (shehabt@trinity-health.org)
Joseph A Tworek (itworek@yahoo.com)
Robert J Fontana (rfontana@med.umich.edu)

Version: 5 Date: 21 June 2007

Author's response to reviews: see over
June 21, 2007

Michael Kidd, MD
Editor-In-Chief
Journal of Medical Case Reports

Dear Dr. Kidd:

We are honored to have the opportunity to submit our revised manuscript, “A Fatal Case of Bupropion (Zyban) Hepatotoxicity with Autoimmune Features,” to the Journal of Medical Case Reports. We appreciate the insightful comments of the two expert reviewers. We have carefully responded to and addressed the points raised by the reviewers. We have provided a point-by-point list of the changes.

We hope that addressing the reviewers concerns make this manuscript acceptable for publication in this fine journal.

Sincerely,

Thomas M. Shehab, M.D.
Director of Clinical Research
Department of Internal Medicine
St. Joseph Mercy Health System
Reviewer 1 (JGS)

1. Please clarify the duration of bupropion therapy in the second paragraph – Response: done - Please see page 4, paragraph 2, line 19

2. After his initial discharge what, if any, outpatient drugs were restarted – Response: done - Please see page 6, paragraph 1, line 5

3. Page 8, second paragraph – The sentence “This finding was recently validated…” needs a citation. Response: done – Please see page 8, paragraph 2, line 22

4. Also, regarding the use of Hy’s rule or Hy’s law you should be consistent. Response: done – Please see page 9, paragraph 1, line 3

5. Page 9, 1st paragraph – The sentence “There is anecdotal evidence that…” needs a citation. Response: done - please see page 9, paragraph 2, line 9

Reviewer 2 (SS)

1. The PT course in the case is not given beyond the initial value, somewhat confounded by the anticoagulant used. One needs to know how the PT INR responded to steroids and what it was during the second admission. Response: PT INR response to steroids and PT INR value for second admission were added to the manuscript – please see page 5, paragraph 1, line 2 and paragraph 2, line 4.

At the time of the second admission to the hospital the patient was off coumadin. His INR was 1.76. The patient developed progressive coagulopathy as his clinical status deteriorated. This information has been added to the case presentation.

2. No CBC data are given Response: done - please see page 4, paragraph 1, line 4

3. Why was the second liver biopsy done and what are the findings Response: Patient was admitted with the intention of doing a liver biopsy. However, the decision was made to restart the patient on prednisone without repeating the biopsy. The text has been changed to reflect this - please see page 6, paragraph 1, line 7.

4. I am frankly surprised that the patient was apparently not receiving antibacterial and antifungal coverage. With a 30% incidence of sepsis with
liver failure, without steroids, such a possibility would be magnified with steroid use. We need to know more about the autopsy. How extensive was the sepsis? Did he die of it?
Response: The autopsy findings have been expanded in the case presentation section.

We agree with the reviewer on the risk of infectious complications in a patient with this clinical presentation. We have clarified when antibiotics were used during the second hospitalization. We acknowledge the lack of anti-fungal therapy – please see page 6, paragraph 1, line 12 and 18.

General comments raised by reviewers: Reviewers raised the issue of bupropion vs. paroxetine as the etiologic agent. We have added additional discussion in the conclusion section (page 7, paragraph 1, line 12).

We have also discussed the patient’s response to prednisone per the reviewer recommendations (page 9, paragraph, line 9).