Author’s response to reviews

Title: A Migraine Variant with Abdominal Colic and Alice in Wonderland Syndrome: A Case Report and Review

Authors:

sherifa A Hamed (hamed_sherifa@yahoo.com)

Version: 3 Date: 6 September 2009

Author’s response to reviews: see over
Dear Editor

I appreciate the valuable and thoughtful reviewers’ comments which helped me to improve my manuscript to a great extent. The manuscript (MS: 2377696722882079) entitled “A Migraine Variant with Abdominal Colic and Alice in Wonderland Syndrome: A Case Report and Review” was totally revised taking into consideration all reviewers' comments.

A DETAILED POINT-TO-POINT RESPONSE TO EACH REVIEWER’S COMMENTS:

Response to Editorial requests:

Editorial requests:
- We recommend that you ask a native English speaking colleague to help you copyedit the paper.
- Ethics: Experimental research that is reported in the manuscript must have been performed with the approval of an appropriate ethics committee. Research carried out on humans must be in compliance with the Helsinki Declaration.
- Informed consent must also be documented. The manuscript should also include a statement to this effect in the 'Acknowledgements' section, in follows: "Written consent was obtained from the patient or their relative for publication of study".
- Competing interests - Please include a 'Competing interests' section between the Conclusions and Authors’ contributions.
- Abstract: Please remove the direct patient quotes from the abstract.

Author:
- Typographical errors and grammar mistakes were corrected by Naïve English language speaker.
- In the method section: we stated that this study was conducted according to the principles established in Helsinki and approved by Assiut University Hospital ethics committee. Informed written consent was obtained from the patient to publish his clinical history, laboratory and imaging data.
- I also acknowledged that I would like to thank the patient and his relatives for their cooperation and providing approval to publish the clinical, laboratory and imaging results of this case report.
- I declared that I have no competing interests.
- I removed the direct patient quotes from the abstract.

**Response to reviewer 1 comments:**

**Reviewer:**
1. This case could be helpful in highlighting some of the pathophysiologic changes in migraine if presented in a much more compact and concise form. In my opinion, your message gets lost due to the length of the paper and the excessive verbiage. Improving the report, beyond heavily editing for length and comprehensibility. In the abstract, I feel a more concise summary of the case would be beneficial to the reader, as this information, particularly the patient description, is repeated later.

**Author:**
Typographical errors and grammar mistakes were corrected by Naïve English language speaker. The report was totally re-written. I feel that now it become more concise and more comprehensible. The abstract was shortened and became more concise. Detailed information were removed.

**Reviewer:**
2. I question whether 20% of pediatric migraine patients have abdominal migraine. The reference you cite in Seminars in Pediatric Surgery would not be my usual source of information for pediatric headache epidemiology.

**Author:**
The correct reference was added.

**Reviewer:**
3. The statement “Unfortunately these cases are frequently misdiagnosed….” seems to be contradicted by the following sentence as you state that “multiple unnecessary tests” are done delaying diagnosis, however in the next sentence you state “they should be differentiated from other organic, psychiatric, or CNS diseases with similar clinical presentations”, which would be done by performing tests.

**Author:**
These statements were properly revised.
Reviewer:
4. I think the review of migraine pathophysiology could be much more concise.

Author:
I made the review of migraine pathophysiology more concise as advised.

Reviewer:
5. Perhaps the explanation of the significance of the SEPs and TMS should be left for the discussion section and be made more concise, perhaps it is not necessary to explain the technology itself, but a brief explanation of the significance of the findings may be preferable.

Author:
As advised, only a brief explanation of the significance of the findings of EPs and TMS were left.

Reviewer:
6. I’m not sure you can state that “diagnostic workup confirmed that our patient had a rare migraine variant” but rather that diagnostic workup did not reveal another cause.

Author:
The sentence was corrected into “diagnostic workup did not reveal another cause”.

Reviewer:
7. Not sure I understand what you are trying to say in the following statement “Not only the genetic load is likely to determine…” p 12

Author:
This paragraph was corrected as follow:
“Migraine phenotypes may be genetically complex disorders due to the presence of different liability loci for migrainous headache or aura, variable genetic load (multiple susceptibility genes), and various polymorphisms in the related genes [15]. In families with common migraine, migraine susceptibility genes (genetic load or gene penetrance) can be cumulative. This determines a critical attack threshold which can be modulated by external (e.g. psychosocial stress, preventive therapies …etc) and/or internal factors (e.g. hormonal status, anxiety …etc) [16]. Genetic load not only determines the severity of the migrainous disorder, but also it determines complications as chronification by medication overuse [17]”.
Reviewer:
8. p 12 “Furthermore, genetic abnormalities may also… such as reduced NM junction (?missing word?)…….”

Author:
This sentence was corrected as follow: “Furthermore, genetic abnormalities may induce incidental subclinical dysfunctions such as reduced neuromuscular junction excitability [18] or subtle cerebellar hypermetria [19].”

Reviewer:
9. “This aura of abdominal migraine….”. From your case report, it seemed that the Alice-in-Wonderland phenomenon was completely independent of the abdominal migraines.

Author:
Yes, we believe that both are independent migraine variants occur in a same patient and thus at the end of the discussion we put our suggestion as follow: “We suggest that the occurrence of two different migrainous phenomena in one patient may be the result of chronicity and the concomitant central sensitization process [35]”.

Reviewer:
10. From the current understanding of the role of cortical spreading depression in migraine aura pathophysiology, I would disagree with the statement “The altered body perceptions described in AIWS are usually caused by migrainous ischemia…”

Author:
Yes, I accept. I also disagree with this statement. I deleted this statement from the test and only I left a suggestion that: the occurrence of two different migrainous phenomena in one patient may be the result of chronicity and the concomitant central sensitization process.

Reviewer:
11. You take pains to differentiate between aura and hallucination in your discussion yet you describe flashes of light seen with the patient’s migraine headache as “hallucinations”.

Author:
No, I did not take pain to differentiate between aura and hallucination in my discussion. I analyzed the clinical and neurobiological characteristics of patient’s symptoms as follow: I related the autonomic phenomena of abdominal colic, abdominal flushing, nausea, pallor,
diarrhea, tachycardia and fear or anxiety, which simulate of temporal lobe epilepsy, to a possible generator in the amygdale, hypothalamus and medullary cranial nerve nuclei. While for manifestations of AWLS, multifocal or cortical hyperexcitability (parietal, occipital, temporal lobules in both hemispheres) are the possible causation of patient’s manifestations (complex visual aura, auditory illusions and primary visual hallucinations). I told that the abdominal migraine and AWLS are completely independent MVs occur in the same patients and I suggested chronicity and concomitant central sensitization as causes of such association.

**Reviewer:**
12. I would consider the above suggestions to be Major Compulsory revisions in addition to editing for conciseness

**Author:**
Typographical errors and grammar mistakes were corrected by Naïve English language speaker.

**Response to reviewer 2 comments:**

**Reviewer:**
1. To be very frank, it should be a much, much shorter report. The introduction should be only a few short sentences about abdominal migraine and Alice in Wonderland, and how they have not been described in the same patient. The case can be greatly shortened. The discussion can also be greatly shortened.

**Author:**
The report was totally re-written. I deleted redundant information. Now, I feel that this report become more concise and more comprehensible.

**Reviewer:**
2. The amplitude of the evoked potentials is not known to be abnormal except when studied over time when there is augmentation. Phosphene thresholds are reported to be low but there are no standard cutoffs for normal and abnormal. Motor thresholds are not generally accepted as abnormal in migraine -- the data is considered ambiguous. Essentially if you want to make the case that these tests are abnormal and help with the diagnosis of migraine, or are dramatically abnormal even for migraine, you need to tell us more about the controls.
Author:
Even in the first version, I put control values in the tables. I agree with the author, that Phosphene and motor thresholds have not to be included among the follow up parameters. I deleted information related to these thresholds from the methods, results and discussion sections.

Reviewer:
3. In these times case reports are generally very short. May I suggest you look at a few recently published neurological case reports in excellent journals as examples of how concise these reports need to be.

Author:
I saw hundreds of case reports, their presentations are variables. I made this report more concise but as you see from its title, it also includes a review of literature, by which I have to include some information to explain the results. I formatted my article in a manner which I see that it will be just enough and if more shortened, the message from it will be lost and will not be understood by wide range of readers. For example: I think readership of BMC Neurology is not only limited for neurologists but may include Pediatricians, Internists, Family Medicine Physicians, Medical Students, …etc).

Response to reviewer 3 comments:

Reviewer:
Nevertheless, even for a journal professing no restrictions of space I think the submitted text is far too long; the author gets bogged down in much too much elementary detail. I recommend the editor suggests he resubmits no more than 4 typewritten pages, concentrating on the patients subjective symptoms.

Author:
The title of this manuscript is: A Migraine Variant with Abdominal Colic and Alice in Wonderland Syndrome: A Case Report and Review. As advised by all reviewers, I deleted redundancies and the too much elementary details. The revised manuscript is ~ 8 pages shorter than the old one, and references were reduced from 51 to 38. The only following information are concisely and informatively included:
- Brief introduction including the definition of migraine variants and exemplified by abdominal migraine and Alice in Wonderland syndrome.
- A full description of the case report: clinical, neuroimaging and neurophysiological data.
- Discussion which include: the complex genetics of migraine variants, the anatomical localization of patient’s manifestations, differential diagnosis (i.e. mimics or other causes of AWLS) and the pathophysiology of this migraine variants (i.e. neurotransmitters, ion channels, complex genetics, neuronal hyperexcitability, mechanism of drug prophylactic for migraine e.g. VPA).

I feel that the above information are just enough for a title of a case report and review:

I certify that this manuscript (MS: 2377696722882079) entitled “A Migraine Variant with Abdominal Colic and Alice in Wonderland Syndrome: A Case Report and Review” has not been published and is not being submitted for publication, in whole or part elsewhere.

Again I appreciate the reviewer’s valuable revision to my manuscript.

Sincerely yours,
Sherifa

Sherifa Ahmed Hamed, MBBch., MSc., M.D.
Consultant Neurologist
Associate Professor, Department of Neurology and Psychiatry, Assiut University Hospital, Assiut, Egypt
P.O.Box 71516
Telephone: +2 088 2371820
Fax : +2 088 2333327
+2 088 2332278
email: hamed_sherifa@yahoo.com