Author's response to reviews

Title: Cerebral neurocysticercosis mimicking or comorbid with episodic migraine?

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Author's response to reviews: see over
Subject: Manuscript revisions prior to publication

Dear Sir,

We thank you and your reviewers for these relevant comments to improve the quality of our paper. Find below responses to some concerns and comments raised by the reviewers

Referee 1:

Reviewer's report:

This is an interesting case report that allows some pathophysiological discussion. Unfortunately the crucial information that would support the discussion is missing: follow-up of the patient after treatment for the cysticercosis to see whether the migraine improved.

At the time of diagnosis the patient was presenting 5 to 7 episodes of migraine-like headaches per month. Two months after treatment (the period we wrote the report), the frequency dropped to 2 episodes per months. Six months after treatment of neurocysticercosis, the patient is still presenting 1 to 2 episodes per month, easily relieved by ibuprofen intake, with no interference in his daily activities. It is probable that our patient has
a genetic predisposition for migraine without aura and that the fortuitous association of neurocysticercosis is simply an aggravating factor of his migraine.

These recent follow-up informations are added in the manuscript.

Referee 2

Major Compulsory Revisions

History p4: The authors state that the patient ‘had no previous history or family history of headaches or migraine’. This is crucial and should be described in more detail in a revision:

Who took the history? A neurologist? A neurologist with experience in headache? How detailed was the history? What about headache with fever, after alcohol, with dehydration?

This is one of the crucial statements guiding into the direction - migraine caused or migraine aggravated by neurocysticercosis (NCC). Further, treatment of NCC resulted a reduction of headache frequency over the two months period – and not a complete cessation suggesting that the patient continued to have migraine attacks despite successful treatment of the NCC.

This is further supported by the patient’s age (24 years) meaning that it is also likely that he might have experienced migraine without aura in the future anyway.

History was taken by a neurologist with experience in the field of headache disorders. When taking history, the patient did not reported any first degree relative with a history of migraine.

In the second and third degree relatives he knows, there was also no history of migraine.

Migraine expression results from the combination of hereditary (multifactorial) and environmental factors. The possibility of false paternity can also contribute to the lack or paucity of family history of migraine in patients’ relatives.

There was not a context of dehydration, fever or alcohol intake related to his headaches.
- Minor Essential Revisions

p7 last paragraph: Here it should be discussed that secondary headaches typically mimick primary headaches. It has often been suggested in the past that some secondary headaches might be more likely triggered primary headaches, as for instance shown for brain tumor-headache, post-ictal headache, GTN-induced headache and others. Again, this makes it more likely that the headache in this patient is a secondary headache in a patient with predisposition to migrainous headaches.

We will include this point in the discussion

Referee 3

Discretionary Revisions

1: The headache reported by the patient is well described (first paragraph in case presentation). Were all attacks as described or very similar, or were there any variation?

The headache characteristics described were the most frequently presented by the patient. There was some variability concerning location (bilateral frontal and/or temporal), duration (12 to 60 hours) and severity (moderate to severe) of headache episodes. All attacks fulfilled criteria for migraine without aura (ICHD-3 beta 1.1) except for criterion E. These details are added in the manuscript.
2: The authors state in the abstract that there was a significant reduction in headache frequency and severity. Does the authors suggest that there was a statistically significant reduction? If so, please present p-values and 95% CI, and add a relevant statistical paragraph to methods.

We use the term ‘significant reduction’ in headache frequency and severity because attacks frequency dropped by more than 50% (treatment goal in migraine prevention) and the patient did not experienced again severe attacks. We could not write ‘statistically significant’ because no particular statistical analysis was done.

3: Given the CT findings and the knowledge that cerebral neurocysticercosis may increase the intracranial pressure (resulting in headache, nausea and vomiting) did the authors perform a lumbar puncture? I can not find any mentions of this in the manuscript.

A lumbar puncture was not performed.

4: The frequency of the patients’ headaches increased up until the patient was seen and treated by the authors. As always in small uncontrolled reports, is is likely that rather than beeing the effect of the treatment, this treatment result was simply a regression toward the mean. This is supported by the fact that the migraine did not disappear completely after successful correct treatment of the suggested causing agent. The presented case does not necessarily support the claim in the first paragraph on p 6 (in the discussion) that this is in fact a neurocysticercosis-induced migraine. As noted by the authors, on p 7, the lack of follow-up data on headache frequency/severity makes is difficult to make robust conclusions based on this report.
Six months after treatment of neurocysticercosis, the patient is still presenting 1 to 2 episodes per month, easily relieved by ibuprofen intake, with no interference in his daily activities. It is probable that our patient has a genetic predisposition for migraine without aura and that the fortuitous association of neurocysticercosis is simply an aggravating factor of his migraine.

On behalf of all the contributors I will act and guarantor and will correspond with the journal from this point onward.

Prior publication: nil

Support: nil

Conflicts of interest: nil

Permissions: nil

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Thanking you,

Yours’ sincerely.