Reviewer’s report

Title: A bipolar disorder patient becoming asymptomatic after adjunctive anti-filariasis treatment: a case report.

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Reviewer: Rami BOU KHALIL

Reviewer’s report:

I have read with great interest the manuscript written by Hamdani N. et al. which presents a case report about a 31 years old patients suffering from a manic episode that has been successfully treated only after the adjunction of anti-filariasis treatment. Although the case is of great interest for psychiatrists, neurologists, infectiologists and physicians from other specialties and that the rationale supporting its publication is sufficient, many important aspects of the manuscript have to be addressed before its final acceptance.

Major Compulsory Revisions:

1- The introduction comes very briefly on the importance of antimicrobial agents in the treatment of patients with mood disorders. The authors only cite one reference to this subject (Bode L, Dietrich DE, Stoyloff R et al., Amantadine and human Borna disease virus in vitro and in vivo in an infected patient with bipolar depression. Lancet 1997, 349 (9046):178-9). The readers of the manuscript should bare in mind from the introduction of the manuscript, that they are reading about one aspect of the psychiatric management of patients with mood disorders that has been present ever since isoniazid had manifested antidepressant properties.

2- Authors describe very briefly some of the aspects of filariasis infection such as some epidemiologic data and modes of transmission. It is clear that the introduction of such a case report is not the best place to extensively describe the clinical manifestations of filariasis as well as its diagnosis, treatment modalities etc. but these issues should be generally overviewed and the reader should be oriented to one or two important and recent references in the domain such as: Chandy A, Thakur AS, Singh MP, Manigauha A. A review of neglected tropical diseases: filariasis. Asian Pac J Trop Med. 2011 Jul;4(7):581-6.

3- Authors state that "Usually asymptomatic, rare cases of neurological symptoms have been described" without giving further details. Are those symptoms psychiatric in nature? What do the authors think about the case of acute disseminated encephalomyelitis (ADEM) caused by filariasis described in: Paliwal VK, Goel G, Vema R, Pradhan S, Gupta RK. Acute disseminated encephalomyelitis following filarial infection. J Neurol Neurosurg Psychiatry 2012 Mar;83(3):347-9.

4- In the case presentation: Authors mention very briefly that the patient suffers from bipolar disorder. How did they confirm the diagnosis? Is he a patient with a
previous psychiatric history of bipolar I disorder or has he been diagnosed of suffering from the disorder because of the actual episode? In case the patient had already been diagnosed with bipolar type I disorder, what are the features of this diagnosis (how many years elapsed since the onset of disease? how many hospitalizations? what drugs have been given in the past? is there a history of substance abuse?)

5- In the case presentation: Authors mention briefly that the patient suffered from a manic episode with agitation and aggressive behavior and that he received benzodiazepines, FGAs, SGAs and mood stabilizers with no efficacy. Could the authors be more specific regarding the current clinical presentation of the patient? What were his symptoms? Was he delusional or not? How many weeks has he been manifesting manic symptoms before his admission? How much did he scored on the Young Mania Rating Scale (YMRS) at his admission? What are the names of the psychopharmacologic drugs he received? at what dosages and for how long? What clinical and paraclinical tests have been done on admission? Were they all normal except for the hypereosinophilia? Was it possible to make a complete neurologic examination to him? Was he compliant to his pharmacologic treatment?

6- In the case presentation: regarding the discovery of filariasis, has any test been done in order to eliminate an ADEM or any other neurologic impairement due to filariasis? Did the patient accept to take the antihelmintics without resistance? What was his YMRS estimated at after two weeks of administration of antihelmintics? Have any psychopharmacologic drug been introduced or escalated in dosage during the administration of antihelmintics?

7- In the conclusion section: It is not clear whether the final hypothesis of the authors is in favor of a certain antimanic effect of albendazole or ivermectin or that they think that an infectious state might interfer with the efficacy of mood stabilizers. As a matter of fact, authors are making some assumptions throughout the manuscript that are not clearly formulated in the conclusion section. The improvement of manic symptoms in their patient could be related, in my opinion, to four possible explanations that should better be further discussed :

a- Antihelmintics, especially ivermectin which is a semisynthetic macrolide, may have mood stabilizing properties. Authors can refer to: Bou Khalil R. Is there any place for macrolides in mood disorders? Med Hypotheses. 2012 Jan;78(1):86-7.

b- The patient is presenting a manic episode that is no more than the manifestation of an ADEM (unless the authors gave the sufficient proffs that it is not an ADEM or any neurologic manifestation related to filariasis). In the case where an ADEM is probable some references regarding neuropsychiatric manifestation of ADEM must be included such as: I- Krishnakumar P, Jayakrishnan MP, Devarajan E. Acute disseminated encephalomyelitis presenting as depressive episode. Indian J Psychiatry. 2011 Oct;53(4):367-9; II-Patel SP, Friedman RS. Neuropsychiatric features of acute disseminated encephalomyelitis: a review. J Neuropsychiatry Clin Neurosci. 1997 Fall;9(4):534-40.

c- The comorbid infection with filariasis provoked a resistance of mania because
of an inflammatory state exacerbated by the parasitic infection in a way that cytokines were influencing the CNS and mood stabilizers became inefficient. In this case authors have to present more data about what kind of cytokines are dysregulated during filariasis infection and what is the known effect of these cytokines on mood?

d- The treatment with antihelmintic was a fortuite association to the recovery from the manic episode due to causes unrelated to the parasitic infection.

8- In the conclusion section: Authors are concluding that antiparasitic drugs "could be useful as they are known to have immuno-modulatory properties (4) especially among patients native from endemic countries". It is not clear what the authors mean by this sentence because antiparasitic agents have immuno-modulatory properties not only in patients native from endemic countries.

Minor essential revisions:

9- Some sentences in the abstract especially the sentence constituting the conclusion might need some restructuring after modifying the text body.

10- More keywords such as "mood stabilizers" should better be added.

Level of interest: An article of importance in its field

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I have no conflict of interest of any kind