Reviewer’s report

Title: Imported loiasis in France: a retrospective analysis of 167 cases with comparison between sub-Saharan and non sub-Saharan African patients.

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Reviewer: Michel Boussinesq

Reviewer’s report:

The paper submitted by Bouchaud et al. is interesting because the number of cases included in the series is fairly high. In addition, it provide interesting and new information on the performance (sensitivity) of the serologic tests used to diagnose loiasis in Parisian hospitals. The differences in the clinical and biological and presentation found between Africans and expatriates were already described in other series, but it is interesting to have a new confirmation. The paper certainly deserves publication in BMC ID but some clarification is needed on the following points:

Selection of the cases: one may wonder why the authors excluded from their series those patients who presented clinical signs very suggestive of loiasis (Calabar, eyeworm), but were found amicrofilaremic and seronegative at lab examinations. It is well known that many loiasis patients have an occult infection (without blood mf) and that the serological tests are not perfect in terms of sensitivity (as shown in the paper). It would be interesting to get an idea of the number of these excluded patients.

Other minor comments.
Line 59: reference 13 corresponds to a series of 186 subjects in the US, not in the UK or Italy
Line 62: replace "dyethylcarbamazine" by "diethylcarbamazine (DEC)"; and use the abbreviation DEC throughout the text
Line 64: are these encephalopathies really due to "parasite lysis"? See Wanji et al., PLoS Negl Trop Dis. 2017 Jul 7;11(7):e0005576.
Line 71: why were the cases restricted to this period, as we are now in 2019?
Line 74: were there cases with a microfilaraemia <1/mL?
Line 94: What volume of blood was used to prepare the blood smear? In case of negative blood smear, were concentration techniques applied?
Lines 97-102: could the authors add numbers, or (i), (ii), (iii) etc. to better explain the two techniques used in a given parasitology department?
Line 103: were all the techniques really "home-made" techniques? What is the ELISA mentioned at line 99?
Line 104: the various techniques should be described in a supplementary information file; and the number of subjects tested with each of them should be presented.
Line 105: "undetermined when it was not negative but under the threshold of positivity for each technique" is not very clear. Definitions of positivity and negativity should be clarified.
Line 114: replace diehtylcarbamazine by "diethylcarbamazine" or "DEC"; was DEC given at the same dose to all patients? Was the starting dose adapted to the microfilarial density? What was the duration of a standard course (say this here, even if the information is given below Table 4)? Was DEC systematically given with antihistamines or corticosteroids?
Lines 115 and 116: as some patients were asymptomatic from the beginning, the authors could consider the possibility to replace "disappearance" by "absence"? and "and/or" by "and"?
Line 117: what "biological changes" refers to? microfilaremia? Post-treatment serologic tests?
Eosinophilia? Replace by "when signs and symptoms persisted and microfilarial levels did not change significantly"?

Line 118: "Post-treatment parasitic lysis reaction" is probably incorrect. See comment above.

Line 136: can the authors confirm that both the median and the lower interquartile values are 3 months? Spell out "IQR" in the text.

In Table 1, replace "Republic of Central Africa" by "Central African Republic".

Line 144: are Ivory Coast, Mali and Rwanda endemic for loiasis? Were there other possible "countries of acquisition" for these subjects?

Line 150: clarify "symptoms of loiasis". The sentence suggests that pruritus is not a symptom of loiasis.

Line 156: in the Methods section, the authors distinguish Calabar oedemas ("recurrent and short-lasting (less than one week) painless oedema of the extremities") and other oedemas ("subcutaneous oedema with a different location or more prolonged duration"). Do the 29 patients with "subcutaneous migratory oedema" correspond to the latter (definitions are not the same)?

Lines 160-161: the unit is probably not mm3, but millilitre.

Line 161: were some of these 53 subjects microfilaraemic? Or were they all amicrofilaraemic? What does "microfilaraemia < 1/mm3" mean?

Lines 162-163: how many subjects were tested by immunoelectrophoresis?

Line 165: what does "prior history of loiasis" mean?

In Table 2, clarify that the mean microfilaraemias are arithmetic means, and that they were calculated on those subjects who were microfilaraemic.

Line 198: how many patients received 1, 2, 3 etc. single doses of ivermectin? What was the interval between the doses?

In Table 4, could the number of microfilaraemic and amicrofilaraemic subjects (and the range of microfilarial densities) be given for each drug regimen?

Line 212: what microfilarial density was reached after filariopheresis, just before starting DEC treatment?

Lines 217 and 223-228: the authors suggest that the distribution of loiasis goes further west of the presently-admitted limit of South-East Benin. This is very interesting (and might be possible) but needs to be much more strongly supported. More information should be presented in the paper on possible travels into endemic areas of those 3 subjects supposed to have been infected in Mali, Ivory Coast or Rwanda (i.e. can such a travel history be definitely excluded?). The clinical and biological features of these cases should also be given. At line 228, the authors mention a paper presenting a trial conducted in Benin; but Klion et al. do not suggest in this paper that "it is likely that a low level of transmission still remains in remote forested areas".

In the discussion, the authors should certainly mention that new tests are being developed to diagnose infection with Loa loa. A rapid antibody-detection test, whose performance in terms of sensitivity and specificity has still to be evaluated, has been developed (Pedram et al., PLoS Negl Trop Dis. 2017 Jul 27;11(7):e0005741). Should the first encouraging results be confirmed, this new tool would certainly be most useful to diagnose loiasis, and particularly occult (=amicrofilaraemic) loiasis.

**Are the methods appropriate and well described?**

If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**

If not, please specify which controls are required in your comments to the authors.
Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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