Reviewer’s report

Title: Clinical and laboratory profiles of patients with early spontaneous healing in cutaneous localized leishmaniasis: A historical cohort study

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Reviewer: Camila Indiani

Reviewer's report:

The authors address an important finding in the field of leishmaniasis which is that of spontaneous healing. The study could have benefited from a more thorough investigation of the immune mechanisms associated with the spontaneous healing, although this was not the main focus of the study. Below are listed some issues that need addressing and that would certainly improve the manuscript:

1) Abstract:

Background: ACL patients were divided into ESH and CL-treated patients. If all were CL patients, perhaps it would be clearer to name them ESH and non ESH.

Results: ESH had a scar on initial examination. This is a recurring point in the text. It is not clear if ESH is a presence of a scar at the time of patient recruitment or if it is a fast-resolving lesion for which treatment is not required.

Conclusion: The results suggest lower parasite load in ESH cases. This is highly speculative. The results suggest that ESH patients may have cleared the parasites more effectively, for various reasons, including a lower parasite load.

The treatment of cases which progress to ESH is controversial. The key point would be to differentiate a ESH case from a non-ESH. How do authors propose this could be done in the field, in order to make the decision no to treat?

2) Background: Line 14: How long does it take, in the present setting, between diagnosis and start of treatment? Is that long enough for the lesion to show signs of healing? It does seem that way but authors should give a time frame for the reader.
3) Methods

Line 14 Did inclusion criteria include presence of a scar?

Line 15 - Patients were divided in ESH and CL patients with typical CL requiring treatment. This goes back to the point raised earlier: it would be more accurate to classify patients as ESH and non-ESH. Otherwise, it seems that CL treatment is optional.

Line 18 - again, how long between a positive exam and the expected date for the start of specific treatment?

Page 6 - please include the PCR assay used (Reference), please explain what is immunohistochemistry with fragments of cutaneous lesion. Is that a tissue section from a biopsy? Were the tests performed on biopsy samples IFA, imprint, PCR? From which sample were Leishmania parasites cultivated?

4) Results

Authors state that 445 patients were evaluated (Page 8) but in 9 cases, scars were observed in the initial clinical examination. Were these scars from a previous CL so these patients had a scar and ongoing active lesion? 432 patients were treated for ACL while 13 showed spontaneous healing. In these 13, were the 9 presenting a scar included? This is shown in Table 1. I disagree that an individual presenting a scar at the time of enrollment (not in the inclusion criteria) can be considered an ESH case, especially because this patient was not evaluated at the time of lesion appearance. Na ESH case is a case that had a lesion that healed before the onset of treatment (according to authors) and presence of a scar is history of previous CL. Also, in the CL patients, 5 had scars. Were these previous CL as well?

Also, in the ESH, how is it that 7 had ulcer and 6 did not whereas 4 had scar and 9 did not? What is the clinical sign if not the presence of an ulcer? A papule?

5) Table 1:

One individual in the ESH group had 2 or more lesions. Did both heal spontaneously and at the same time? Or both developing at the same “rate”?

Why is it that for the 13 ESH cases, results were not shown for IFA, culture, ELISA, imprint and PCR?
Table 2:

Please indicate which tests were positive for ESH and CL. The authors could try to evaluate the agreement of the techniques used, especially given the diversity of reports in the literature regarding efficacy. This would also strengthen the assumptions regarding the "lower number of parasites" in ESH cases. Also, if ESH cases had only a scar and not an active ulcer (if correctly understood), where were samples obtained for culture, PCR, imprint, etc.

Please check if Fig 1 was mentioned.

6) Discussion

Page 12 - Line 10 - "Therefore we may question the need to propose specific treatment is cases with evidence to ESH". I think this is a tough point to make. This implies a lag time between diagnosis and onset of treatment and long enough for lesions to show signs of healing. This certainly varies in different clinical settings and certainly involves some kind of risk, just as using antimonials do. The question of spontaneous healing certainly is interesting, though.

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.

Yes

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

No

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