Author's response to reviews

Title: Leishmania infantum leishmaniasis in corticosteroid - treated patients.

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Author's response to reviews: see over
Dear editor of BMC Infectious Diseases,

Please find enclosed the manuscript entitled “Leishmania infantum leishmaniasis in corticosteroid - treated patients” Manuscript number 432989538960661 revised according to the different suggestions of the two reviewers.

A point-by-point response to the concerns of the two reviewers is also included.

Thanks in advance for the consideration of our work

Rome, June 21, 2006

Emanuele Nicasri
Answer to Reviewer: Hiro Goto

Major Compulsory Revisions

a) The definition of the species of Leishmania was supposedly based on PCR using primers described in reference 3. However, PCR using these primers do not allow to define the species, unless PCR products had been submitted to sequencing. This point has to be clarified, and if sequencing was not carried out or if any other method was used to identify the species, the title of the article should be modified removing Leishmania infantum from. However, even though the definition of the species is interesting, it does not enable the publication of these observations.

Answer

The genotyping method employed to identify the *Leishmania* agent from the infected tissues (PCR-RFLP) (Minodier et al, ref. 3) allows us to discriminate between organisms of the *L. donovani* complex and the Old World dermatropic parasites *L. tropica* and *L. major*. Sequencing of the RFLP fragments has no discriminating value in this context. Within the *L. donovani* complex, *L. infantum* and *L. donovani* genotypes can also be distinguished apart from overlapping endemic settings of both parasites, such as Sudan, Ethiopia and Kenya. The epidemiological background of our patients indicates undoubtedly *L. infantum* as the agent. Based upon this epidemiological link, we decided to maintain the title of the article not removing the species, but if the referee thinks that this geno-epidemiological support does not show enough evidence to maintain it, we can definitively change the title in "Leishmaniasis in corticosteroid - treated patients".

b) In the discussion, the endemicity of leishmaniasis of the areas where the patients were coming from should be mentioned for foreigners.

Answer

The following sentence was included in Discussion: ‘Our three patients lived in rural areas of central Italy (Latium and Tuscany regions) where both visceral and cutaneous leishmaniasis are endemic. In the past 7 years, some 200 cases of visceral leishmaniasis were recorded from these regions, and in most of the patients parasites have been identified as *L. infantum* by means of isoenzyme analysis (unpublished data from Istituto Superiore di Sanità, Rome).’
c) In the discussion, an overview of clinical manifestations and laboratory findings would be desirable, not only the discussion of manifestations of each case. Mainly it would be desirable to analyze if some parameters would be of importance to suggest diagnosis of leishmaniasis.

Answer
The following sentence was included in Discussion: ‘We therefore suggest a careful clinical evaluation of patients resident in areas at risk for Leishmania such as the coasts of the Mediterranean Basin, and who are experiencing an immune suppression status related to HIV, use of drugs, or other clinical conditions. In such patients the occurrence of lymphopenia, anemia, pancytopenia or hypergammaglobulinemia with recurrent febrile episodes or of long-lasting painless ulcerative lesions should alert clinicians to include leishmaniasis in the differential diagnosis.’

Minor Essential Revisions

a) The table has been numbered and the format of the numbers standardized.

b) The references 5 and 6 have been substituted with


Answer to Reviewer: Piero L Olliario

Minor Essential Revisions

a) Section on PKDL

Answer
The following sentence: ‘The PKDL is frequently described in Sudan and in India after the visceral leishmaniasis by L. donovani. The PKDL skin lesions usually appear most prominently on the face and can develop during therapy or within few months thereafter. Commonly, PKDL recovers spontaneously within months or years, but relapse of visceral leishmaniasis during PKDL can occur [14]. Zijlstra et al. proposes to classify such skin conditions with systemic involvement as para-kala-azar dermal leishmaniasis [15].’ has been removed.

b) Section on steroids

Answer
The following sentence was included in Discussion: ‘In a murine model the prolonged use of steroids has been associated to a decreased production of IL-2, IFN-gamma, IL-4 and TNF-alfa and to a significant 3-fold increase in amastigote burden in the spleen [9].’

c) Text

Answer
The text has been revised by a native English speaker and shortened.

d) Table

Answer
The table has been adjusted.

e) Pictures

Answer
Unfortunately, we have no pictures/photos.