Author's response to reviews

Title: Primary muscular cystic hydatidosis: case report

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Author's response to reviews: see over
Responses to the reviewer

Reviewer: Nefise Cagla Tarhan

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1) First of all the English of the manuscript needs to be edited by a native English speaker who understands medical literature because, some of the sentences are too long and hard to follow. Some terms are not used as they usually appear in the medical literature.  
The text was completely revised by a native English speaker skilled in medical literature.
2) On figure 1, MRI sequence used needs to be written on figure legend for readers to follow and as they mentioned that the thin wall shows contrast enhancement, it would be better to also give the precontrast T1-weighted image from the same localization to show the enhancement.  
A precontrast image was added.
3) I think with these MRI images, hydatid cyst should be the first choice of differential diagnosis even though the patient had no hydatid cysts in liver or lungs. The authors in discussion said," MRI of the thigh were not diriment for diagnosis". Would they please explain here what they meant? I understand that although MRI and US are suggestive of hydatid cyst of muscle in this case, the initial serological tests did not confirm the diagnosis. Is this what they meant here?  
   We hope that the English revision made the text more comprehensible. MRI and US images were very suggestive of hydatid cyst but the initial serology did not allow us to confirm the hypothesis.
4) In background section, 30th line, "bicep" should be "biceps".  
We corrected the error.
Responses to the reviewer

Reviewer: Hector H. h Garcia

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

- The cysts do not grow 1 cm per mont (Background). Some people says they grow 1 cm per year, but this is a very gross estimation.

  The growth rate of hydatid cysts is variable (1-160 mm per year), although generally slow. It depends on factors in part still unknown; surely on location (liver cysts grow at a lower rate than lung cysts), and probably on strain/genotype. In our manuscript, “1 cm per month” was a typing error. We meant “1 cm per year”, as reported from Heath DD, 1973.

- There should be a clear differentiation of the ranking of hydatid disease in the differential diagnosis in endemic versus non endemic countries.

  We agree with the referee, but we find this point expressed in the text

- The initial serological tests were sub-optimal assays. This should be mentioned.

  We agree with this observation and modified the text accordingly (See “Conclusions”).

  - Not clear for this reviewer what is the help provided by the PCR (over adequate, species specific serology as the WB).

    We agree about the validity of WB assay, especially if in accordance with other clues (imaging and epidemiological context). In fact, we stressed in the text its higher sensitivity. However, we must not forget the limitations of this test although it is considered as the highest specific E. granulosus assay (possible false-positive results in subjects with other forms of echinococcosis or cysticercosis). In our case, the PCR analysis allowed us to confirm the presumptive diagnosis and to provide the strain typing, with its epidemiological value. Considering the request of the reviewer we modified the text to clarify this point.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

- Needs some polishing in the English grammar and spelling

  See the response to first reviewer, point 1.

  - Multilocular hydatidosis should be mentioned and discussed in the differential.

    Multilocular Hydatidosis was not considered in the differential diagnosis because the patient had never lived in areas at risk for the disease. In Italy, E. multilocularis worms were detected for the first time in two red foxes from an Italian Alpine area near the Austrian border (Manfredi et al., 2002). Our patient had never been there. Moreover, the primary infection in humans is almost exclusively in the liver (approximately 99% of the cases). We decided not to mention Multilocular Hydatidosis to focus better on the peculiarity of our case, in which the serological and molecular approaches were very useful in reaching a diagnosis.
Responses to the reviewer

Reviewer: FABRIZIO BRUSCHI

The Au. describe a case report of cystic echinococcosis localised in the skeletal muscle. The interest of the manuscript is mainly due to the serological and molecular approaches which help in making diagnosis. The title should be changed in Muscular cystic echinococcosis: case report. This why, since a total body CT scanner was not performed to exclude other localizations, the Au. Cannot state that the lesion observed is certainly primary. Although Chest X-ray and abdominal ultrasound had excluded the most common locations, we modified the title as suggested by the referee.

Furthermore, the fact that serum comes back to negativity after surgery might be a consequence of the elimination of the only cyst present in the host but also of the effects of albendazole treatment. That’s true. We cannot establish if the negativity of serological tests was related to surgery or to perioperative prophylaxis or both. A brief comment on higher sensitivity of immunoblot compared to that of other tests used should be done. The text was modified in accordance with the suggestion of the referee (See “Conclusions”).

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
Page 3, Line 36: Ref. 16 and not 17; We corrected the error.
Page 4, Lines 7 and 23: these References are not appropriate and should be changed with one general review on cystic echinococcosis such Ref. 1, for example. We think that the error was on page 2. We changed the references.
Responses to the reviewer

Reviewer: Enrico Brunetti

Abstract: Case presentation, line 6: “Serological tests for hydatidosis gave negative results” is at odds with “Serological tests gave positive results for hydatidosis” 6 lines down. We modified the text considering the referee’s comment.

Background: Line 24: It is debatable that most cysts are univesicular. This is not the case in referral centers or what can be learned from mass ultrasound screening in endemic areas. We agree with the referee, but several authors report that most cysts are univesicular. Anyway, we changed the sentence (see text).

Case report Images from histological specimens would be helpful to the reader. Unfortunately it was not possible to obtain images from the histological specimens.

Absence of protoscolices in a cyst with such MRI appearance does not rule out CE. Cysts may well be sterile. Further, why was Western Blot assay not performed when the first blood sample tested negative with imaging techniques highly suggestive of CE? This should be the rule as false negatives at routine tests (ELISA, IHA) are often seen, especially in extra-hepatic locations.

The first serological screening was performed in the lab of our hospital. Screening analysis is based on IHA and IFA, as still commonly used in many laboratories. The additional analyses was performed later in the lab of Dipartimento di Scienze di Sanità Pubblica, Università “La Sapienza”, Rome (Prof. G. Cancrini).

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
I doubt that definitive diagnosis could be achieved only by molecular diagnosis. This was surely helpful and strain differentiation has epidemiological value and is increasingly being performed, but the diagnosis here was made by means of imaging, pathology and Western Blot.

We considered this important point raised by the referee and modified the text accordingly. Imaging and serology made a presumptive diagnosis possible. Microscopic and histologic examinations did not allow us to confirm this hypothesis, while PCR offered the only direct and unequivocal proof for a definitive diagnosis of cystic hydatidosis.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
The entire paper should be edited by a native speaker of English