Author's response to reviews

Title: Tuberculosis presenting as multiple intramuscular nodules in a child: a case report

Authors:

Ajaya Kumar Dhakal (ajayakdhakal@gmail.com)
Subhash Chandra Shah (subashshah2012@gmail.com)
Devendra Shrestha (devendra.shrestha@gmail.com)
Niroj Banepali (nirojbanezali@yahoo.com)
Geetika KC (geetikakc@hotmail.com)

Version: 2
Date: 12 December 2014

Author's response to reviews: see over
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Ajaya Kumar Dhakal: (ajayakdhakal@gmail.com)
Subhash Chandra Shah: (subashshah2012@gmail.com)
Devendra Shrestha: (devendra.shrestha@gmail.com)
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Geetika KC: (geetikakc@hotmail.com)

Version: 1  Date: 12 December 2014

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Thank you for consideration of our manuscript for publication in your journal.

We have reviewed the above manuscript according to your reviewer’s comments.

The changes have been carried out in red font in the main manuscript.

Reviewer's report

Title: Tuberculosis presenting as multiple intramuscular nodules in a child: a case report

Version: 1 Date: 12 December 2014

Reviewer: Konstantinos Zorbas

Reviewer's report:

1. “The hypo-echoic space occupying lesion in the right lobe of liver maybe is a primary liver TB and maybe is the primary site of inoculation. Maybe would be more appropriate to investigate this lesion with a CT-scan and to describe the ultrasound characteristics of this lesion”

   There were well defined hyper echoic lesions (not the hypoechoic lesions as mentioned in the manuscript) in the right lobe of liver with peripheral feeding vessels suggestive of hemangioma. Therefore we did not perform CT scan abdomen in this child. This has been rectified in the main manuscript.

2.” Which was the immunologic status of the patient? Did you check the viral status of the patient (such as HIV status) and the serum immunoglobulin’s (Ig)”?

   There were no clinical features suggestive of immunodeficiency, malnutrition as well as no high risk factor for HIV infection. Therefore we did not perform HIV serological status and serum immunoglobulin level in this patient. Serum immunoglobulin is not readily available in our country and these tests are very expensive.
3. “Among the superficial palpable swellings, except cysticercosis and sarcoidosis, are filarial infections and Echinococcous infections something that should be mentioned. (Reference: A cytological study of palpable superficial nodules of parasitic origin: a study of 41 cases PMID: 24757574)”

We took those diseases (Echinococcous and Filarial infections) also into consideration. The patient was investigated however reports were negative and has been included in the revised manuscript as the following.

“Neurocysticercosis, hydatid cyst of muscles, filarial worms and sarcoidosis are common causes of multiple nodular swellings in different parts of body which were ruled out based on clinical features and histopathological finding of caseating granuloma, absence of scolex of cysticercus, absence of cyst and fragment of acellular lamellate membrane of echinococcous and absence of microfilaria including absence of eosinophils in both biopsy specimens”.
This has been mentioned in the main manuscript as reviewer indicated.

4) “In line 84, 8th word you write “live” instead of liver”
The spelling has been changed in the revised manuscript.

6) “In line 98, 2nd word you write regime instead of regimen”.
The spelling has been changed in the revised manuscript.
Reviewer's report

Title: Tuberculosis presenting as multiple intramuscular nodules in a child: a case report

Version: 1 Date: 12 December 2014

Reviewer: Lee Fairlie

Reviewer's report:

1. “My primary concern about the case is that I don't think that it convinces the reader that tuberculosis was the cause of these lesions for the following reasons:
   - There was no history of a TB contact (I appreciate that the contact may not have been identified and that she may have been infected at school etc. or this may have been reactivation of latent TB
   - She had a non-reactive PPD
   - The initial biopsy showed that there were features suggestive of parasitic cysts which suggests that neurocysticercosis or hydatid cysts were a very likely diagnosis
   - She had a positive cysticercus IgG
   - Given that there appeared to be no progression, could this have been a natural progression of neurocysticercosis? Were the lesions re-X rayed once resolved as perhaps they had calcified rather than completely resolved as would be expected from neurocysticercosis?
   - No acid fast bacilli were identified from the lesions, geneXpert was negative and TB was not cultured from the lesions.
   - The child did respond to TB treatment but as previously mentioned this could have been natural progression of neurocysticercosis?”

As the reviewer pointed out, we agree that there was no history of tuberculosis contact, non reactive PPD, no acid fast bacilli in lesions along with negative culture and negative geneXpert. We also made initial diagnosis of neurocysticercosis based on clinical feature and presence of intramuscular swelling and FNAC report as parasitic cyst however which was subsequently later to be less likely. Reasons are as below.

We would like to highlight that though the features suggestive of parasitic cysts were observed in the FNAC of the swelling but there was no evidence of cysticercus cellulosae in FNAC. Hence excisional
biopsy was performed for the confirmatory diagnosis. Histopathological examination of biopsy of swelling from interscapular region showed caseating granulomatous inflammation along with Langerhans Giant cells suggestive of tuberculous lesion and we have included histopathological slide in the manuscript (Figure 3, 4). However we failed to demonstrate AFB in the tissue biopsy slides as well as tissue culture from the biopsy for AFB was also negative. With these reports we faced a diagnostic dilemma, with one hand showing FNAC report of parasitic cysts with positive cysticercus IgG antibodies and other hand BIOPSY report showing granulomatous inflammation suggestive of tuberculosis.

Because of the diagnostic dilemma we performed second biopsy from right forearm swelling (different from initial site) to confirm diagnosis. The second histopathology also showed caseating granulomatous inflammation suggestive of tuberculosis. The histopathological slide of second biopsy is also included in the main manuscript (Figure 5, 6). Given the high prevalence tuberculosis in this part of world and along with these histopathological features of two separate biopsied intramuscular swelling from two separate sites suggesting tuberculosis, the patient was started on antitubercular treatment. The patient was kept in close follow up. There was rapid decrease in size of swelling after starting of antitubercular drugs which was also in favour of the diagnosis of tuberculosis. We have included in the discussion as follow:

“It must be highlighted that most of the patients were diagnosed as muscular tuberculosis with muscle biopsy [3, 7, 10] in previous studies and very few of these cases have Mantoux test positive. In one study with muscular tuberculosis out of 11 patients who underwent PPD (purified protein derivative) test and only one was strongly positive while 10 others were negative [10]”. These changes has been carried out in main manuscript.
2. “I think that this is an interesting case but that it should be reframed as a diagnostic dilemma as there is not clear proof that this is TB”.

   This issue has been clarified in the above statement.

3. “There are a number of grammatical errors and the manuscript would benefit from revisions and edits based on this”

   The grammatical errors have been corrected in the main manuscript.