Author’s response to reviews

Title: Toxoplasma, Toxocara and Tuberculosis co-infection in a four year old child

Authors:

   Randeewari Guneratne (randeewari@yahoo.com)
   Devan Mendis (devanmendis@gmail.com)
   Tharaka Bandara (tharakabandara@hotmail.com)
   Sumadhya D Fernando (ferndee@gmail.com)

Version: 3 Date: 21 April 2011

Author's response to reviews: see over
Reviewer's report: Reviewer 1

The authors present a case report of a 4 year old child who had an association of three infectious diseases which are very common in undeveloped countries: toxocariasis, toxoplasmosis and tuberculosis. This association probably is due to the high prevalence of these diseases in Sri Lanka.

Comment

This case report does not give some details about the child, for example: the time of the initial presentation, the time of last follow up (after a TB treatment) and if the patient had been investigated for an immune deficiency. It seems that the association of these diseases was incidental.

Response

The authors agree that the three infectious diseases are common in under developed countries but there was no report of an infection of all three diseases occurring in the same person to be found in the literature.

Since the publication was sent to the BMC Paediatrics for review the reports of repeat serology and HIV profile were made available at the clinic and results of these tests have been included in the case study.
The publication wanted to highlight the diagnostic challenges that are encountered by the clinicians as lymphadenopathy and eosinophilia commonly point towards a parasitic infection. The high eosinophil count with lymphadenopathy, positive serology (at the first admission) and blood picture reports combined with a mild hepatomegaly could have limited the final diagnosis to Toxoplasma, Toxocara co-infection and the child may have been discharged following the appropriate treatment.

The first visit of the child was in September 2010 at which time blood was taken for serology. However the reports were available only when the child came back in December 2010. It is then the diagnosis of Toxoplasma and Toxocara was made. During this visit, blood was taken for HIV profile and repeat serology for Toxoplasma and Toxocara, the results which were made available in March 2011. The reports have to be collected and shown to the doctors by the patients. Thereby the case report was sent to the journal prior to these reports being presented as there was no guarantee that the patient would come back to the same Paediatric clinic.

The parents have been asked to report back to the same Paediatric clinic 6 months after completing treatment for Toxocariasis (May/June). However, once again there is no guarantee that the patient will attend. Tuberculosis treatment and follow up of the patient is being done by the National Chest clinic.

Comment

In Discussion the authors stated that they did not consider important to investigate TB in this child and enhanced the importance of performing a tuberculin skin testing (TST) and searching for a history of contact with a TB
infectious person to identify this disease in children. In fact, TST aims at the identification of latent TB infection and is an important test in sick children with chronic adenopathy who live in high burden TB areas. I do not believe it was the case in the present discussion. The case management was otherwise correct.

**Response**

*Tuberculosis is a common disease in South Asian region though Sri Lanka is found to be a low prevalence country (79 per 100000 population). Further the number of cases occurring in children less than 14 years is almost nil.*

(http://www.searo.who.int/en/Section10/Section2097/Section2100_14802.htm)

Thus TB remains low on the differential diagnosis of children presenting with lymphadenopathy and eosinophilia specially in the presence of a positive Toxocara and Toxoplasma serology.

The authors wanted to highlight the importance of ruling out TB in a country like Sri Lanka where the incidence of tuberculosis is low in the population.

This has been included in the discussion and a new reference has been added (reference 13).

**Reviewer's report: Reviewer 2**

**Comment**

Major Compulsory Revision: Although HIV infection may not be as high as in
other countries, mention of the HIV sero-status of the child is important as both
Tuberculosis and Toxoplasma gondii are considered to be opportunistic
infections in HIV infected persons.

Response
As mentioned early a blood sample was sent for HIV screening in December but reports
were not received at the time this case report was sent to the BMC and there was no
guarantee that the patient would come back with the report (due to the social stigmata
attached to the disease) we did not include it during the initial presentation of the case
study to the journal.

Comment
Minor Essential Revisions: No mention of the child ever receiving BCG
vaccination is made. This could influence the interpretation of mantoux test.

Response
The child has been vaccinated according to the expanded immunization programe of Sri
Lanka which included BCG vaccination at birth. Although Prior vaccination with BCG
may result in a false-positive results of mantoux for many years afterwards it is not
contraindicated to perform it in such patient (http://en.wikipedia.org/wiki/Mantoux_test).
However in this case the diagnosis was supported by histological findings. As the
diagnosis was supported by histological findings the authors have not included the
receipt of BCG vaccine at birth in the case report.
Comment

I was unable for some reasons to verify the statement "Approximately 250,000 children worldwide develop tuberculosis--------" when I visited the site quoted. Any clarification?

Response

Please check the link

http://www.searo.who.int/en/Section10/Section2097/Section2106_10681.htm

It is stated in this WHO fact sheet that over over 250,000 children develop TB and 100,000 children will continue to die each year from TB.

REVIEWER 3

Toxoplasmosis is not very common infectious causes of lymphadenitis in children

Blood picture indicated an eosinophilia with a query of reactive changes. In tropical country with costal area like Sri Lanka there are other common causes of eosinophilia and lymphadenopathy. The blood sample was sent for the detection of Toxoplasma and Toxocara antibodies. This needs justifications
**Response**

_In Sri Lanka the presence of lymphadenopathy and eosinophilia in a child will always prompt the diagnosis of a parasitic infection. Due to the large number of stray dogs and cats toxoplasmosis and toxocariasis is considered as common parasitic diseases with high incidence being reported in community based studies. References 14, 15 and 16 have now been added to justify this._

**Comment**

The presence of antibodies to toxoplasma and toxocara could either be crossreacting antibodies.

The presence of mere antibodies is only suggestive and not confirmatory.

The confirmation of Toxocara infection was possible if lymph node fluid or biopsy of involved region had shown either the larve of toxocara or an eosinophilic infiltrate.

The presence of acute Toxoplasma infection if suspected could have been confirmed by doing other serological tests like IgA, IgG avidity and a repeat IgG antibodies since IgG should have been positive if patient actually had toxoplasma infection. Moreover toxoplasma infection has no relevance except in specific groups like pregnant women or HIV patients.

**Response**

_Diagnosis of Toxocariasis is based on indirect measures i.e. detection of Toxocara specific antibodies in serum as done in this study. Larvae can be diagnosed in biopsy_
material but in general, biopsy is regarded as unrewarding due to the small numbers of larvae present and the difficult in finding them (Glickman et al., 1986; Taylor and Holland 2001). Further, there are no resources to perform biopsies for diagnosis of Toxocariasis at the state hospitals of Sri Lanka.

Toxocara specific ELISA titres will normally confirm diagnosis. As the reports of the repeat serological assays were received following the submission of this manuscript, they have been now included in the case history. The test taken three months after the previous test indicates that IgG and IgM antibodies are both positive for Toxoplasma (as compared to the previous result where only IgM was positive) and Anti Toxocara antibody levels showed a four fold increase in IgG levels.

Sri Lanka doesnot have the facilities to carry out serological tests like IgA or IgG avidity tests for Toxoplasmosis. As the reviewer has indicated as Toxoplasma infection in this age group causes a self-limiting infection the child was not treated. This has now been included in the discussion.

EDITORS COMMENTS

Editorial requests:

1) Please clarify (and state in the manuscript) that the consent was obtained from the parents/guardians of the patient.

The authors have acknowledged the parents of this child for giving consent to write up the case as a manuscript

2) Please include a title page and abstract in your manuscript. Manuscript sections should include (in the following order): Abstract; Background; Case Presentation; Conclusions; Abbreviations (if any);
Competing interests; Authors' contributions; Acknowledgements; References; Figure legends (if any); Tables (if any); Description of Additional files (if any).

*This has been done.*