Reviewer’s report

**Title:** Lymphocyte apoptosis in children with central nervous system tuberculosis

**Version:** 1  **Date:** 5 September 2011

**Reviewer:** Anna Dubaniewicz

**Reviewer’s report:**

The Authors analysed spontaneous peripheral T-lymphocyte (PBT) apoptosis, related markers Fas and FasL, and the expression of the costimulatory T cell activation receptor CD28 in infants and children with central nervous system (CNS)-TB, before and after starting chemotherapy, and compared results with those of healthy children. They revealed that PBT and CD4 lymphocyte subpopulations isolated from CNS TB patients showed stronger apoptotic activity and underwent apoptosis more rapidly than in normal subjects, even after beginning specific treatment due to high levels of Fas ligand expression on lymphocyte populations. In contrast to the CD4+ apoptosis profile, they did not find any difference between the illness and healthy group with respect to CD8+ cell apoptosis. This could be the consequence of increased apoptosis of CD4 + lymphocytes through the Fas / FasL system. CD8+ CD28 + T cells were lower in the illness group, suggesting a hypoergic status in CD8 T-cells in CNS tuberculosis. The Authors concluded that CNS tuberculosis in pediatric patients increases sensitivity toward apoptosis in CD4 T-lymphocytes and causes a decrease of CD4 and CD8 activated T-lymphocytes. This could play a key role in the immune pathogenesis of this complicated form of TB and specific chemotherapy was able to normalize both apoptosis sensitivity and T-cell activation.

The manuscript is very interesting but needs some comments:

1. Regarding the Abstract section:
   - The Author should avoid words like interestingly
   - The Authors should shortly introduce in background why important is apoptosis of lymphocytes T in the etiopathogenesis of TB
   - The Authors should supplement this section with:
     - number of included patients and healthy controls
     - used methods
     - a specification of tested lymphocytes: it was percentage or number?
     - values of obtained results, in current section we see only discussion, not results

2. Regarding the Introduction section:
   - The Authors should supplement this section with some epidemiological information about occurrence of TB in Italy
• The Authors should shortly introduce in background why important is apoptosis of lymphocytes T in the etiopathogenesis of TB and why FAS and CD28 markers were tested
• In my opinion, part of general information of Fas and CD28 should be removed to this section

3. Regarding the Material and method section:
• We don’t know if tested children with CNS-TB had pulmonary TB or not?
• How many tested patients had M. tuberculosis positive CSF culture?
• What about of familiar TB?

4. Regarding the Results section:
• This section should be divided into paragraphs with particular subheadlines
• The Authors should be supplement this section with the results of analysis of blood count and information about number or percentage of tested T-cells
• The Authors should clearly state that T-cells were stimulated or not
• Why did the Authors write “p 0.019” without “=”?

5. Regarding the Discussion section:
• This section should be entirely rewritten:
  - at the beginning of this section, the Authors should be introduce their results with following discussion of obtained results with others studies and in the end, explain obtained results in the context immunological background; in current study, the Discussion section, the explanation of obtained results needs entirely more immunological knowledge;
  - the sentences were the same in both the Discussion in the Abstract/Conclusions section.

5. Regarding the English:
• The English language in current manuscript needs native speaker help

Level of interest: An article of importance in its field

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests