Author's response to reviews

Title: Use of anabolic-androgenic steroids masking the diagnosis of pleural tuberculosis: a case report.

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Use of anabolic-androgenic steroids masking the diagnosis of pleural tuberculosis: a case report. Carlos Fernandez de Larrea, Aglea Duplat, Ismar Rivera-Olivero and Jacobus H. de Waard

Subject: comments on the reviewer’s reports

Dear Sir,

Herewith my response to the concerns of the reviewers.

**Reviewer 2- Chong-Jen Yu**

This reviewer considers the case worth reporting however he states that there is a lack of a mechanism to link the steroid use with TB activation. As he writes: “A single case report can’t conclude that anabolic hormone will mask the presentation of tuberculosis. The authors should seek more evidence or raise feasible hypothesis to explain this”.

**Answer:** As we wrote in the manuscript, it has been shown that a high dose of anabolic steroids can have significant effects on immune responses significantly inhibiting IFN gamma production. This last cytokine is essential in monocyte and macrophage Th1 activation, the most effective response against intracellular pathogens like *M. tuberculosis*. In addition, IFN gamma is a potent inducer of intracellular ADA and the low level of ADA activity found in the pleural liquid just after the use of nandrolone decanoate could have been caused by the inhibitor effect of the AAS on the IFN production.

We have looked for more evidence to confirm this hypothesis but there are no other reports linking AAS with developing TB. That’s why we conclude in the manuscript “This case suggests” that patients using anabolic steroids might be susceptible to developing tuberculosis etc etc. In this scope it is interesting to mention that, although suspected to induce tuberculosis, it took more than 20 years after the introduction of corticosteroids before the first serious report appeared emphasizing the risk of developing TB in these immunosuppressed patients. See Millar JW, Horne NW. Tuberculosis in immunosuppressed patients. Lancet. 1979 2;1(8127):1176-8.

**Reviewer:** Ming-Shyan Huang

This reviewer states that “The utility of the routine measurement of ADA has not been determined and this test is not generally available”. We don’t agree with this. Searching “PubMed” for “adenosine deaminase activity” and “pleural effusion” results in more than 150 references. In addition, 4 different reviews conclude that the method (High ADA level) is a useful diagnostic tool for tuberculous pleurisy. See:


This reviewer also states that “ADA and/or skin test may reveal false negative results, especially, during patient received steroid treatment” Our answer on this comment is that as far as we know this has only been established for patients who receive glucocorticosteroids. Our case report is about the use of anabolic steroids and false negative results of the skin test or ADA after treatment with this type of steroid have never been reported nor has been investigated.

Concerning his questions:

**Question 1.** Why did not show the initial pleural effusion cell and differential counts data? Such as the differential cell counts: ?% mononuclear cells and ?% neutrophils. **Answer.** We added this information to the text: 30% eosinophils and 50% lymphocytes and 20% neutrophils.

**Question 2.** Why did not perform the pleural biopsy? As we know the pleuroscopy-guided biopsies increase the yield in pleural sampling. **Answer:** As we indicated in the manuscript, the patients didn’t show up for follow-up after the first thoracentesis. It was only during the second visit that we were able to perform the biopsy and confirm the diagnosis of TB.

**Question 3.** The using steroid masking the diagnosis of tuberculosis is not uncommon. **Answer:** This question was already answered. See above. This report is about the use of anabolic steroids and not about the use of glucocorticosteroids.

Sincerely

Jacobus H. de Waard