Author's response to reviews

Title: Coagulopathy as initial manifestation of concomitant celiac disease and cystic fibrosis

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Author's response to reviews: see over
Dear Editor,

I would like to thank You and the reviewers for your time and effort to review the manuscript. I would also like to thank the reviewers for their valuable comments and suggestions.

Additionally, I would like to apologize for the time it took us to revise the manuscript.

Below you will find the answers to the reviewer’s comments one by one.
Also all the changes that we’ve made in the manuscript are highlighted with red color.

Thank you for

Sincerely,

Prof. Aco Kostovski

Reviewer 2 – Prof. Billy Bourk

Comments to authors:

This is an interesting report of a child with both CF and coeliac disease who developed a severe vitamin K

Major Points

1. Sweat Chlorides can be abnormal in malnutrition. It would have been useful to have the sweat test checked when the patient was well or CF corroborated using some other method (even stool elastase), especially as the common mutations were not present and the patient did not necessarily have other typical features of CF.

Answer: The sweat test was positive again while the child was in a good condition and on a home treatment. Two months after establishing the diagnosis on a regularly ambulatory control the sweat test was performed and the chloride concentration were elevated again
with value of 72 mmol/l. This additional fact has been added in the revised manuscript. According to the criteria for the diagnosing CF our patient had both pancreatic and respiratory manifestations of the disease confirmed with the CFTR dysfunction – elevated chloride concentration (including the last one made ambulatory). Thus he fulfilled the criteria for diagnosing CF. In our center measurement of the faecal elastase is not available.

2. The coagulopathy is not well-defined in terms of the coagulation factor levels. Presumably it was vitamin K deficiency rather than liver failure.

**Answer:** Since the coagulation abnormalities were normalized after vitamin K administration, it’s more likely that coagulopathy was a consequence of vitamin K deficiency due to malnutrition. Also some authors suggest that parenteral vitamin K replacement corrects coagulopathy related to biliary obstruction, bacterial overgrowth, or malnutrition but Vitamin K is less effective for coagulopathy caused by severe parenchymal liver injury.  


3. It is a little unusual that there were no other fat-soluble vitamin deficiencies. Were they sought?

**Answer:** We don’t have a possibility to measure the serum concentrations of other fat-soluble vitamins. Our patient does not have any clinical signs of other fat-soluble vitamin deficiencies.

4. The boy does not have CF liver disease as his tests normalized on a GFD.

**Answer:** After introducing gluten-free diet and treatment with ursodeoxycholic acid the liver tests normalized completely. In this moment our patient does not have CF liver disease.

**Minor points**

1. The discussion section could be shortened considerably

**Answer:** The discussion is shortened in the revised manuscript.

2. There are a few minor errors of syntax

**Answer:** Changes made in the revised manuscript.

3. Pg 4 ‘IgG was 922.6 IU/ml’ does this refer to anti gliadin IgG or total serum IgG?

**Answer:** The IgG of 922.6 IU/ml refers to anti gliadin IgG.
4. Pg 5 ‘the disease results from immune system dysregulation etc’ this is a rather a sweeping statement. Also on this page can the authors cite a report of CD presenting with a proven liver related coagulopathy?

**Answer:** Most of the described patients with celiac disease develop coagulopathy due to malabsorption and vitamin K deficiency. However, literature review showed several described cases of acute liver failure and coagulopathy in children with celiac disease. During a 12 year period of time at Karolinska University Children’s Hospital in Stockholm, Sweden only six children with celiac disease developed severe liver damage and two of them had to be liver transplanted. The citation added in the revised manuscript.

5. Pg 6 ‘CF and CD were for many years recognized etc’ citation needed

**Answer:** Citation added in the revised manuscript.

6. Pg 7 CF as risk factor for CD – are other food allergies increased in CF or other pancreatic insufficient patients?

**Answer:** During a literature search we’ve found some published articles that investigate food allergy in cystic fibrosis patients. Lucarelli et al. in their study find out statistically significant difference in measurements of specific antibodies for cow milk and egg proteins (IgG and IgA for casein, beta-lactoglobulin and ovalbumin) between the CF patients and control group of healthy child. So, they suggest considering food allergy and immunological investigations in all CF patients in whom intestinal symptoms do not improve with conventional treatment- adequate diet and enzyme treatment.  


**Reviewer 1 - Udo Rolle**

**Comments to authors:**

This is a well documented case report dealing with a rare combination of celiac disease and cystic fibrosis. The report is well written and concise. The discussion is well balanced and takes much of the recent literature into account.

**Answer:** Thank You very much for your time for the revision and for the positive appraisal of our manuscript.