Reply to Reviewers

1. Title: Please revise - the patient had also gastritis and colitis. Therefore, the title should mention it, not just enteropathy (in fact, it was enteritis).

The patient was previously diagnosed as ulcerative colitis at different medical center, then the patient was diagnosed CVID, then CTLA-4 deficiency and immune mediated enteropathy.

2. Abstract: CASE SUMMARY: Please mention whether it was IBD per se, since the patient was treated for IBD when abatacept was administered OR it was CVID-associated digestive inflammation, four years prior to this report

First the diagnosis was ulcerative colitis, then CVID diagnosis was made. After that, genetic studies revealed CTLA-4 deficiency.Abatacept treatment was started after diagnosis of CTLA-4 deficiency.

3. Chief Complaint: The authors mentioned “Four years prior to this report” (line 116), but in the Abstract it is written “A 25-year-old female patient, who was visibly cachetic, visited our clinic over the course of five years” (lines 38-39). Please revise and clarify.

“Five years” timeline was corrected in both abstract and case presentation. (line 135)

4. History of present illness: Could you please mention what immunosuppressive agents the patients received before? The Abstract mentions “various immunosuppressive treatments”, but here there is nothing.

Steroid therapy was conducted and implemented in article

5. Biochemical examinations: a. I suggest to insert the tests’ results and normal ranges in a table (all, not just biochemical). b. Line 143 – I do not see any abnormal result in bold. Please revise. c. Please mention also mean corpuscular hemoglobin concentration and mean corpuscular volume - values, in order to be suggestive for the type of anemia. d. What was the ferritin level, please? I am aware that inflammatory markers are increased, but it would be helpful to have it. Hepcidin? e. “radiological images of the pituitary and adrenal glands” do not belong to “biochemical analyses”.

The tables were prepared and inserted to article where appropiate. MCV, MCHC and ferrtin levels were included. Unfortunately hepcidin level was not measured. Radiological images information was transferred. (line 226)

6. Immunological examinations: a. Lines 164-166: The authors wrote: “The serum levels of the IgG subgroups were below the normal limits: IgG1: 3.05 g/L (2-11), IgG2: 1.73 g/L (1-5,5), IgG3: 0.62 g/L (0,15-1,2) and IgG4: 0.17 g/L (0-1,25).”. However, they appear ALL NORMAL. Please correct. b. Line 178: Please note that in the presence of Ig A and Ig G deficiency, no matter what you use - anti-tissue transglutaminase, anti-endomysial, anti-gliadin – Ig A or Ig G or both, they can be negative. c. Did you test AAN?

Table regarding to immunglobulin levels and immunglobulin subgroup levels was designed and put in article.

7.Microbiological examinations: a. What antibiotic was given, please? b. “fecal calprotectin level was >1800 µg/g stool (<50).” – please revise, this test does not belong to microbiological exams.

Oral levofloxacin therapy was given to the patient and this information was added. (line 216)

8.Histopathological examinations: a. Please mention how many intraepithelial lymphocytes/epithelial cells. b. Line 210: “These histopathological features indicated immune-mediated enteropathy”. However, in the Abstract, it is mentioned “Histopathological findings supported the presence of inflammatory bowel disease.” Please decide.

Again the same situation. The patient was first diagnosed as ulcerative colitis, then CVID, after that; CTLA-4 deficiency and immune mediated enteropathy.

9.Treatment: The authors wrote – lines 229-231: “Peroral and rectal immunosuppressive agents (i.e., methylprednisolone and mesalamine) were administered to treat the inflammatory bowel disease.” – First, mesalamine is not an immunosuppressive agent. Second – now, again it is inflammatory bowel disease. Please decide.

First the patient was diagnosed in other medical centers as inflammatory bowel disease, then the final diagnosis was revised as immune mediated enteropathy.

10.Discussion: The authors wrote – lines 258-259: “with a 25% increase in weight within six months”. However, clinical exam did not mention weight, height, and BMI, just the fact that the patient was cachectic. Please add.

Patients weight, height and BMI value were inserted as appropiate. (line153-154)

11.Figures could be enlarged, so that details are seen better.

Figures were added as the largest version.

12.English language: please correct typos (e.g. line 36 – please correct “cachetic” to “cachectic”.)

The word typos were corrected.

13. References that could be added: a. Fevang B. Treatment of inflammatory complications in common variable immunodeficiency (CVID): current concepts and future perspectives. Expert Rev Clin Immunol. 2023 Jun;19(6):627-638. b. Olfe L, et al. CTLA-4 Insufficiency due to a Novel CTLA-4 Deletion, Identified through Copy Number Variation Analysis. Int Arch Allergy Immunol. 2023;184(1):76-84. c. Egg D, et al. Therapeutic options for CTLA-4 insufficiency. J Allergy Clin Immunol. 2022 Feb;149(2):736-746.