Peer Review File

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Reviewer A

Comment 1: My first impression was "Is this really CD?". The clinical findings of this case are not typical for CD. Gastrointestinal (GI) tract involvement of CD is not obvious in this case, and instead there are many extraintestinal manifestations; skin purpura, arthritis, and pulmonary involvement. It is sure that the clinical manifestations in this case was caused by an autoinflammatory mechanism, but is it enough to diagnosis this case with CD, mostly based on the pathology findings of the pulmonary lesions?

Reply 1: Although the patient has no gastrointestinal symptoms, it can be found that he has gastrointestinal lesions based on the patient's gastrointestinal endoscopy. This patient has a variety of extraintestinal manifestations, which is also very common in Crohn's disease. The pathology of the pulmonary nodules in the child showed non-caseating granulomatous lesions, combined with the child's medical history and examination results, it also ruled out common diseases that cause pulmonary nodules, such as infection, drug-induced, sarcoidosis, chronic granulomatous diseases, and Wegener's granulation. His pulmonary function also showed restrictive pulmonary ventilation dysfunction that is common in Crohn's disease. After treatment with glucocorticoid, his clinical manifestations, laboratory investigations, pulmonary function and radiological manifestations have improved significantly, so the final diagnosis was concluded as Crohn's disease.

Changes in the text: we have modified our text as advised (see Page 6, line 6-17, Section: Case presentation, Paragraph 4).

Comment 2: CD is diagnosed comprehensively based on clinical symptoms and signs, laboratory results, endoscopy findings, pathology, radiologic findings. Among these findings, ileocolonoscopy findings are crucial because most of CD will involve either the terminal ileum or colon as ulcers. In this case, the authors report that colonoscopy showed mucosal erosion and inflammation of the ileocecal region. Although there were no ulcers reported on colonoscopy, the authors should still provide colonoscopy images, because it is crucial for the diagnosis of CD.

Reply 2: We particularly agree with your opinion.

Changes in the text: We added this patient's colonoscopy images (see Page 5, line 10, Section: Case presentation, Paragraph 3. Figure 1B)

Comment 3: The authors have reported a bamboo joint-like appearance in the gastric body, and have discussed about this finding citing Reference #29. However, Figure 1B does not look like the bamboo joint-like appearance shown in the figure in reference #29, but instead looks like scars or pseudopolypoid lesions that result after healing of ulcers or severe inflammation. Moreover, because these lesions

you show are also observed in eosinophilic gastritis, a description on the number of eosinophilic infiltrations/HPF on pathology is required in order to rule out eosinophilic gastritis. H. pylori infection should also be ruled out, because it can also cause IDA.
Reply 3: The gastroduodenoscopy of this patient showed longitudinal inflammatory hyperplasia of the fundus and body of the stomach. The location and appearance are similar to those in the reference #29. The mechanism of occurrence may be result after healing of ulcers or severe inflammation as you mentioned. Moreover, eosinophilic gastritis and H. pylori infection also be ruled out.
Changes in the text: we have modified our text as advised (see Page 5, line 11-12, Section: Case presentation, Paragraph 3).

Comment 4: At initial evaluation of CD, a whole evaluation of the entire GI tract is required. If conducted, include the results of examinations conducted for the evaluation of small bowel involvement of CD (MRE, CTE, capsule endoscopy, abdominal U/S, small bowel follow-through, etc.) If not conducted, this would be a limitation of this case report, and should be discussed in the discussion.
Reply 4: In this case, MRI of the small bowel was perfected at the first admission, indicating that terminal ileal was thickened and inflammation.
Changes in the text: we have modified our text as advised (see Page 5, line 12-14, Section: Case presentation, Paragraph 3).

Comment 5: ASCA is the well-known autoimmune antibody associated with CD. Wasn't ASCA conducted, while so many other auto-immune antibodies were? If conducted, provide the results. Otherwise, this would also be a limitation, and should be discussed in the discussion.
Reply 5: ASCA has not been widely promoted in China. Considering that ASCA is not required in the guidelines for diagnosis and treatment of Crohn's disease, this case has not been tested for ASCA, which is indeed regrettable.
Changes in the text: we have modified our text as advised (see Page 11, line 1-3, Section: Discussion and conclusions, Paragraph 5).

Comment 6: What about fecal calprotectin? Again, if conducted, provide the results. Otherwise, this would also be a limitation, and should be discussed in the discussion.
Reply 6: Fecal calprotectin test was carried out in our hospital in the past two years, so this case was not tested at that time, it is indeed very regrettable.
Changes in the text: we have modified our text as advised (see Page 11, line 1-3, Section: Discussion and conclusions, Paragraph 5).

Comment 7: What about tuberculin skin test and/or TB interferon-gamma release assay? Were they not conducted?
Reply 7: We performed TB interferon-gamma release assay and the result was

negative.
Changes in the text: we have modified our text as advised (see Page 6, line 4-5, Section: Case presentation, Paragraph 3).

Comment 8: Why do the authors express the granuloma as mere "granuloma" instead of "non-caseating granuloma" if there was no evidence of caseating necrosis on pathology?
Reply 8: No evidence of caseating necrosis was found in the pathology of this case. The pathology of this child was non-caseating granuloma. The expression in the text is inappropriate and has been modified.
Changes in the text: we have modified our text as advised (see Page 5, line 21, Section: Case presentation, Paragraph 3)

Comment 9: The authors state that the patient had IDA, which implies that the patient had occult GI bleeding considering the findings of a positive stool occult blood test. Where is the site of bleeding in this case? Scars and pseudopolyps in the stomach and mucosal erosion and inflammation of the ileocecal region is subtle and insufficient to explain this long-lasting anemia. Moreover, anemia in CD is usually a mixed form of IDA and anemia of chronic disease, which can be suspected by the combination of serum iron, TIBC, and ferritin levels. Again, H. pylori infection should also be ruled out, because it can also cause IDA. Actually, the mechanism of IDA in H. pylori infection can be caused by a different mechanism aside of GI bleeding.
Reply 9: As you said anemia in CD is usually a mixed form of IDA and anemia of chronic disease. This case had a two-year medical history, and the ileocecal mucosa had erosions and inflammations, and stool occult blood test was positive. Combined with laboratory investigations, it was considered that the anemia in this case was caused by chronic minor bleeding in the gastrointestinal tract and intestinal inflammation leading to iron absorption disorders and chronic diseases caused together. In this case, H. pylori infection had been ruled out, so IDA did not caused by H. pylori infection.
Changes in the text: we have modified our text as advised (see Page 4, line 19-21, Section: Case presentation, Paragraph 3).

Comment 10: CD phenotype at diagnosis should also be reported according to the Paris classification.
Reply 10: we have modified our text as advised.
Changes in the text: we have modified our text as advised (see Page 6, line 16, Section: Case presentation, Paragraph 4)

Comment 11: PCDAI scores at diagnosis and during follow up should also be reported.
Reply 11: we have modified our text as advised.
Changes in the text: we have modified our text as advised (see Page 6, line 17, and

Page 7, line 10, Section: Case presentation, Paragraph 4,5)

Comment 12: Albumin levels should also be reported, along with WBC, Hb, Platelet, ESR, and CRP levels.
Reply 12: we have modified our text as advised.
Changes in the text: we have modified our text as advised (see Page 5, line 1, and Table 1, Section: Case presentation, Paragraph 3)

Comment 13: Why was a chest CT conducted in the absence of pulmonary symptoms?
Reply 13: Because the child has a long history of anemia, on the one hand, chest CT was performed to rule out pulmonary hemosiderinosis. On the other hand, the incidence of tuberculosis infection in China is high, routine chest CT examinations before hormone therapy to exclude tuberculosis.
Changes in the text: Not Applicable.

Comment 14: CRP levels at 2 months show an increase, which seems to be a result of steroid cessation implying that the patient is likely steroid-dependent. How did the patient's symptoms change after steroid cessation? If symptoms relapsed, how was the medication changed to control his disease?
Reply 14: We particularly agree with your opinion. The patient had already started taking azathioprine when the prednisone was reduced. We know that azathioprine has a slow onset of action. After the treatment, the child's symptoms are relieved.
Changes in the text: we have modified our text as advised (see Page 7, line 4-6, and line10-12, Section: Case presentation, Paragraph 5)

Comment 15: Considering the rarity of this manifestation, there is a logical leap to recommend the following sentence in the conclusion.
"Even children with no manifestations of typical CD need to consider the possibility of CD if they have lung nodules."
Reply 15: What I understand is that you think there is an illogical leap in this conclusion. So we made a modification.
Changes in the text: we have modified our text as advised (see Page 11, line 1-4, Section: Discussion and conclusions, Paragraph 7).

Comment 16: There are many awkward expressions in this manuscript. The tense is wrongly used in some parts and there are sentences expressed in spoken language rather than written language. English proofreading is definitely required.
Reply 16: As non-native English speakers, we had submitted this manuscript that is inaccurate in some expressions. I am very sorry for the inconvenience caused to you. This manuscript is being proofread by a native English expert with a scientific background, and we will upload the proofread manuscript later.
Changes in the text: This manuscript is being proofread by a native English expert

with a scientific background, and we will upload the proofread manuscript later.

Reviewer B

Major point

Comment 1: Detailed treatment progress is needed as a rare case report. How long was the patient administered methylprednisolone intravenously?

Reply 1: This patient was given methylprednisolone 40mg/d intravenously for 2 weeks alone with exclusive enteral nutrition. After discharge, the patient took prednisone (30mg/d) and azathioprine (75mg/d) orally and exclusive enteral nutrition, and the prednisone was gradually reduced to stop within 1.5 months. After stopping prednisone, azathioprine was continued been given orally.

Changes in the text: we have modified our text as advised (see Page 6, line 20-21, and Page 7, line4-6, Section: Case presentation, Paragraph 5).

Comment 2: Is there a recommendation about what kind of corticosteroid and how much of that should be used?

Reply 2: According to the past experience in the treatment of Crohn's disease, intravenous methylprednisolone or oral prednisone 1-2mg/kg/d can be used for 2-3 months.

Changes in the text: we have modified our text as advised (see Page 11, line 12-14, Section: Discussion and conclusions, Paragraph 6).

Minor point

Comment 3: Figure 1 legend; A and B are reversed.

Reply 3: You are correct, I am very sorry to have made such a mistake, we have modified our text. Because another picture has been added, the order of the pictures has been adjusted.

Changes in the text: we have modified our text as advised (see Page xx, line xx, Section: Figure Legends).