

Reviewer #1

Dear Authors, Please find attached your manuscript with my comments and edits. I provided suggestions to organize the content of the manuscript in order to allow a reader to follow the text much easier. In Case Report section, my suggestion is to follow the order anamnesis-physical exam-laboratory results-other results. In addition, the text in the section Discussion could be organized in a more logical way; few suggestions are provided. This is a very interesting case, and my recommendation is to accept your manuscript after the revision. Sincerely, Katarina Ilic

Response: We appreciate Katarina Ilic's constructive and helpful comments and suggestions. We revise the manuscript based on your comments.

Reviewer #2:

This is a very interesting combination of a typical measles-virus infection followed by CMV gastroenteritis in an immunocompetent infant. According to my pubmed search, I could not find such a previous combination. However, there are some very important issues for authors to resolve or clarify. Suggested considerations:

Response: Thank you for your positive comments.

Introduction

1. “intracellular pathogens” is a term that refers to microbes and parasites mostly (*Rickettsia*, *Coxiella burnetii*, *Chlamydia*, bacteria (*Mycobacterium tuberculosis*, *M. leprae*, *Listeria monocytogenes*, *Brucella spp.*), fungi (*Cryptococcus neoformans*) or protozoa (*Leishmania*, *Trypanosoma*, *Exoplasma*), that parasitize macrophages and other cells. [Orfila J. Definition of intracellular pathogens. Clin Microbiol Infect. 1996]. “Given its origins in bacteriology the intracellular pathogen concept focused primarily on prokaryotic and eukaryotic microbes but did not encompass viruses, which paradoxically are the quintessential intracellular pathogens as they are universally dependent on host cells for replication” [Casadevall A, Fang FC. The intracellular pathogen concept. *Mol Microbiol.* 2020].

Response: Thank you, we replace the “intracellular pathogens” with “other infections”.

2. “Cytomegalovirus is one of the intracellular viruses”. This is not quite accurate. All viruses are intracellular and when not, they are named virions.

Response: Thank you, we correct it in the revised manuscript.

3. “mimicking many other infectious causes, such as inflammatory bowel disease”. As far as i know IBD is not an infectious disease. This could be corrected.

Response: Thank you, we remove the sentence “such as inflammatory bowel disease”.

Case-report

1. “C-reactive protein was 39.7 mg/L” the reference of the specific number at that point of the manuscript is not helpful especially when there is a table with the laboratory findings.

Response: Thank you, we revise it.

2. “generalized coarse erythra”. I am not sure if this expression is correct.

Response: Thank you, we correct it.

3. “Blood CMV-DNA was 9.26E+3 copies/mL” i am not sure what does that mean. Plus, it could be reported only in the laboratory tables and in the text instead something like: high titres of CMV DNA in the PCR blood assay.

Response: Thank you, we revise it.

Discussion

1. Page 6, the second paragraph is not pretty much helpful for the main scope of the article. The differential diagnosis of microbes causing diarrhoea in infants could be only referred in a table. The main question of the article is if there can be a plausible explanation of how measles can make an individual susceptible to CMV infection and not the workout on how common microorganisms were excluded. In my opinion, if authors want to refer to differential diagnosis of infectious within the text, *clostridium difficile* (due to recent antibiotic treatment) and TB which is always hard to exclude, should be referred to.

Response: We appreciate you for the constructive suggestions, we revise it according to your comments.

2. Page 8: “Besides broad clinical presentations and signs, confirmation of the virus via laboratory methods is indispensable in diagnosing CMV disease. In this patient, the CMV-IgM was negative and CMV-IgG was positive.” Was CMV-IgG avidity tested to confirm recent or old IgG production? Were IgG tested after 4 weeks (convalescent phase) to document a possible alteration of their titres? Authors should comment these questions within the text.

Response: Thank you for your suggestion, we add it in the revised manuscript. The IgG titre on hospital day 36 was 82.2 U/mL which was more than 4 folds of the titre on hospital day 16 (18.3 U/mL).

2. Page 8: “Nevertheless, the false negative IgM can be obtained in immunocompromised patients and infants^[21]. Due to immunocompromised status secondary to measles infection, as in this patient, the negative IgM significantly limits its clinical application in early diagnosis of CMV infection which may delay diagnosis and treatment^[22].” If false negative IgM can be obtained in infants, then how measles-virus IgM antibody was detected? Authors should comment on this discrepancy.

Response: Thank you, we add some comments in the revised manuscript.

3. Page 9 first paragraph: “CMV DNA copies decreased to the normal range”. There is no “normal” range despite the highest laboratory cut-off given for negativity because viruses normally are negative in blood PCR.

Response: Thank you, we correct it.

4. Page 9 2nd paragraph: I think that the “Conclusion” paragraph is very well stated but it is not strictly fitted to the main idea and scope of this report. Authors very correctly entitled the manuscript “**Extensive gastrointestinal CMV disease secondary to measles in an immunocompetent infant**” and this is a very intriguing title because it is rarely or never reported before. When someone claims that something is secondary to something else this means that there is a direct causal relationship between the former and the latter. Like saying “my finger started bleeding secondary to a knife cut”. Authors reported in the beginning of their introduction section that “The Th2 response during convalescence might inhibit Th1 responses, increasing susceptibility to intracellular pathogens in children with measles^[3].” This sentence is on the target of the main scope of the manuscript but unfortunately authors did not provided a furthermore explanation about it in the Discussion section. Authors must provide at least a paragraph in the Discussion section with unsubstantiated arguments based on literature data to strongly support their hypothesis that the CMV infection maybe be triggered by the transient immunity of measles infection in an immunocompetent. And to make

myself clear, they should carefully address which of the measles-induced immunosuppression deficits could make an individual susceptible to viral infections, and from the other side, which immune defects (innate or adaptive) either of cellular (Th2 and Th1) or humoral would make an individual susceptible to be infected by CMV. This is the most important topic of the manuscript that should be addressed.

Response: Thank you so much, we include this in the revised manuscript.

Highlights

Related reports

“Gastrointestinal cytomegalovirus disease is well documented in immunocompromised or immunodeficient patients...” I think that the words “immunocompromised” and “immunodeficient” are synonyms.

Response: Thanks. We revise it.

Reviewer #3:

This article reported a case of an infant with CMV enteritis secondary measles. Measles was confirmed by serology (serum IgM positive). CMV enteritis was confirmed by immunohistochemistry. However, major revisions are needed for acceptance.

Response: We appreciate you for your valuable comments.

1) It is difficult to precisely follow the clinical course of this case. I was very confused. The date of occurrence and disappearance of sign and symptoms is unclear. In addition, the date of treatment is unclear. Did fever and diarrhea occur simultaneously? High-fever or low-fever? When was the infant positive for measles anti-IgM? The description of the clinical course should be revised on the date of disease.

Response: Thank you. This manuscript has been revised according to your comments.

As shown, he suffered watery and bloody diarrhea 5 days after fever.

2) Discussion is too long. For instance, the sentences before measles seem to be unnecessary.

Response: Thank you for the advice. Some paragraphs are removed in the revised manuscript.

3) Figure 1, 2 and 3 are not specific findings. They should be removed. 4) Immunohistochemistry is important for the diagnosis of CMV enteritis. The information of immunohistochemistry should be briefly shown.

Response: Thanks. Figure 2 and 3 are removed.

EDITORIAL OFFICE' S COMMENTS

Authors must revise the manuscript according to the Editorial Office' s comments and suggestions, which are listed below:

(1) Science editor: 1 Scientific quality: The manuscript describes a case report of the extensive gastrointestinal CMV disease secondary to measles in an immunocompetent infant. The topic is within the scope of the WJCC. (1) Classification: Two Grades B and Grade C; (2) Summary of the Peer-Review Report: This is a very interesting combination of a typical measles-virus infection followed by CMV gastroenteritis in an immunocompetent infant. The questions raised by the reviewers should be answered; and (3) Format: There are 3 tables and 6 figures. A total of 34 references are cited, including 3 references published in the last 3 years. There are no self-citations. 2 Language evaluation: Classification: Three Grades B. A language editing certificate issued by Gorden Frameword was provided. 3 Academic norms and rules: The authors provided the written informed consent. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The study was supported by Shenzhen Innovation and Technology Committee. The topic has not previously been published in the WJCC. 5 Issues raised: (1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval

document(s); (2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (3) The "Case Presentation" section was not written according to the Guidelines for Manuscript Preparation. Please re-write the "Case Presentation" section, and add the "FINAL DIAGNOSIS", "TREATMENT", and "OUTCOME AND FOLLOW-UP" sections to the main text, according to the Guidelines and Requirements for Manuscript Revision; and (4) Authors should always cite references that are relevant to their study. Please check and remove any references that not relevant to this study.

6 Recommendation: Conditional acceptance.

Response: Thank you. We provide the files you required and revised the manuscript according to the Guidelines. We also remove some references based on your comments.

(2) Editorial office director:

(3) Company editor-in-chief: I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office' s comments and the Criteria for Manuscript Revision by Authors. However, the quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, the author(s) must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

Response: Thank you. We reviewed this manuscript again and sent it to American

Journal Expert for language editing.