

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62643

Title: Gastrointestinal cytomegalovirus disease secondary to measles in an immunocompetent infant: A case report

Reviewer's code: 01221188

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2021-01-14

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-01-15 01:32

Reviewer performed review: 2021-01-18 00:35

Review time: 2 Days and 23 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

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

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62643

Title: Gastrointestinal cytomegalovirus disease secondary to measles in an immunocompetent infant: A case report

Reviewer's code: 03260094

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Chief Doctor

Reviewer's Country/Territory: Greece

Author's Country/Territory: China

Manuscript submission date: 2021-01-14

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2021-01-16 06:56

Reviewer performed review: 2021-01-18 17:14

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

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:

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

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

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. 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. 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. 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. 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.



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

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62643

Title: Gastrointestinal cytomegalovirus disease secondary to measles in an immunocompetent infant: A case report

Reviewer's code: 05699121

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: United States

Author's Country/Territory: China

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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SPECIFIC COMMENTS TO AUTHORS

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