Reviewer’s report

Title: Haemolytic uraemic syndrome associated with non shiga toxin-producing Escherichia coli bacteraemia: a case report

Version: 1 Date: 21 Dec 2018

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?
No - there are minor issues

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?
N/A - no methodology

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?
No - there are minor issues

Statistics - Is the use of statistics in the manuscript appropriate?
N/A - there are no statistics in this study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?
No - there are major issues

OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?
Probably - with minor revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: The authors report on a case of a 58-year old man who was admitted for haemorrhoids surgery. He subsequently developed the clinical presentation of prostatitis with fever, and thereafter went into AKI with neurological symptoms. He also had developed thrombocytopenia as well as several other abnormalities compatible with HUS. Urinary and blood cultures came back positive for E Coli. Renal biopsy was compatible with HUS and ADAM-TS13 was negative. The patient had never any gastro-intestinal complaints, nor could a known E.coli typically associated with HUS or anti-LPS antibodies for several serogroups be detected. Clinical symptoms and renal function recovered without specific treatment. Finally, the
authors found a heterozygous factor H mutation (p.Val215Ile; c.643 G>A) upon gene panel analysis. The conclusion is that this patient suffered from a rare type of HUS. This is a very interesting case report that highlights the possibility of a genetic predisposition in combination with an infectious trigger (although we cannot be sure on what triggered it) that leads to the clinical picture of HUS.

REQUESTED REVISIONS:

Objective
The objective was not made clear (although I wonder if that is necessary for this type of article)

Design
N/A

Execution
- The Abstract (mainly the conclusion) and the Background sections are not so well written. For example, "Infections play a central role in the development of HUS" (Introduction) as a single sentence is not appropriate, I would consider leaving it out of the intro and discussing this more in-depth in the discussion section. This point is also partly due to the language which should be improved throughout (suggest to consult a native speaker to carefully go through the work).
- I suggest to display the most important lab results, along with the reference values, perhaps for some key time points in a table.

Interpretation
- The suggestion that the CFH mutation (p.Val215Ile; c.643 G>A) could be pathogenic based on the region (SCR4) seems a bit premature (no functional studies have been performed by the authors or others); the authors should be a bit more careful in their interpretation.
- Haptoglobin was in the normal range, could the authors comment?
- Furthermore, quite extensive complement analysis was performed, but all came back negative. Does this make the diagnosis less likely? The authors should discuss these findings in detail in the Discussion.
- I would like to see a more extensive discussion on previous studies suggesting the possibility of genetic predisposition to HUS that was "triggered" by an (infectious or other type of) event. Please also add references to support this.

Note: This reviewer report can be downloaded - see attached pdf file.

Please confirm that you have included your review in the ‘Comments to Author’ box?
As a minimum standard, please include a few sentences that outline what you think are the authors’ hypothesis/objectives, their main results, and the conclusions drawn. Your report should constructively instruct authors on how they can strengthen their paper to the point where it may be acceptable for publication, or provide detailed reasons as to why the manuscript does not
fulfill our criteria for consideration. Please supply appropriate evidence using examples from the manuscript to substantiate your comments. Please break your comments into two bulleted or numbered sections: major and minor comments.

Please note that we may not be able to use your review if no comments are provided.

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Yes

**Are the methods appropriate and well described to allow independent reproduction of experiments?**
Please state in the ‘Comments to Authors’ box below what you think are the strengths and weaknesses of the methods (study design, data collection, and data analysis), and what is required, if anything, to improve the quality of reporting.

No

**Does the work include the necessary controls?**
If not, please explain in the ‘Comments to Author’ box below.

No

**Are you able to assess the statistics?**
- Are the statistical test(s) used in this study appropriate and well described?
- Is the exact sample size (n) reported for each experimental group/condition (as a number, not a range)?
- Are the description of any error bars and probability values appropriate?
- Are all error bars defined in the corresponding figure legends?
- Has a sample size calculation been included, or a description and rationale about how sample sizes were chosen?

Please can you confirm which of the following statements apply to your statistical assessment of the manuscript (Please include details of what the authors need to address in the ‘Comments to Author’ box):

This question is not applicable to this manuscript

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in the ‘Comments to Author’ box below.
No

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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No

**Declaration of competing interests**
Please complete a declaration of competing interests, considering the following questions:

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3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

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