OPEN PEER REVIEW

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- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
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- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

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Peer Review Report for "A Rare Case of *Ralstonia pickettii* Infection in a Patient Undergoing Thyroid Surgery"

Author(s): Liyan Zhou, Weijuan Qin, Zhengyi Liang, Huanhuan Wei, Xiaoning Wu

Review Timeline:

Submit Date: 13 Sep 2021
Revised Date: 17 Oct 2021
Accepted Date: 17 Oct 2021

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Rezvan Moniri: Associate Editor | Revision (0) — 25 Sep 2021

Dear EIC
The reviewer(s) have recommended publication, but also suggest some minor revisions to the manuscript. Therefore, I invite the author to respond to the reviewer(s)' comments and revise his manuscript.
Kind regards,

REFEREE: EIC | Revision (0) — 25 Sep 2021

Dear Authors,
Thank you for submitting your manuscript to JJM. I have completed the review of your manuscript and a summary is appended below (Pleases find attached files). The reviewers recommend the reconsideration of your paper following major revision. I invite you to resubmit your manuscript after addressing all reviewer comments.
1. Please answer point by point to the reviewer's comments on a separate sheet under WORD format and write your modifications in the revised version (WORD format) in colored or highlighted letters.
2. Your answers to reviewers' queries are not only for the Editorial Board but for the readers

and should be included, when appropriate, in the manuscript for improvement and a better understanding. Moreover, add line numbers for text and put suitable line numbers for each response.

3. When resubmitting your manuscript, please carefully consider all issues mentioned in the reviewers' comments, outline every change made a point by point, and provide suitable rebuttals for any comments not addressed.

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Thanks.

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Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear Reviewers:

We are grateful for your comments, which have helped us improve our manuscript. Our responses to your comments are provided.

Associate Editor 1:

Introduction

1. Describe the strategy of the literature review and provide search terms.

PubMed and Microsoft Academic Search were searched using the terms “Ralstonia pickettii” or “Ralstonia” and “Sepsis.”

2. Justify the merit of the case report by using the literature review. Introduce the patient case to the reader.

According to the literature review, we knew that *Ralstonia pickettii* could be an opportunistic pathogen that causes infection in immunocompromised patients. In our report, we described a case of *R. pickettii* infection in a woman with normal immunity. To our knowledge, this is the first report of sepsis caused by *R. pickettii* in the absence of risk factors in the literature (lines 20-23).

3. Make the introduction brief and less than three paragraphs.

We appreciate your remarks. We have shortened the Introduction.

Patient case presentation

1. Provide patient demographics (age, sex, height, weight, race, occupation).

The patient was a 36-year-old woman who was 160 cm in weight and 50 kg in weight, and she worked in an individual business (lines 26-27).

2. Describe the patient's complaint.

The patient was admitted to the hospital for thyroid nodule surgery (line 25).

3. List the patient's present illness. List the patient's medical history.

The patient had no previous medical history (lines 28–30).

4. List the patient's family history.

The patients' parents and children were in good health, and none of them had a similar medical history (lines 28–29).

5. List the patient's medication history before admission and throughout the case report.

The patient had no medication history before admission (lines 27-29).

6. Ensure that the medication history includes herbals, vaccines, depot injections, and non- prescription medications, and state that the patient was asked for this history.

When assessing the patient's medical history, she denied the use of herbals, depot injections, the 2019-nCoV vaccine, and non-prescription medications.

7. List each drug's name, strength, dosage form, route, and dates of administration.

The bacterium was sensitive to ciprofloxacin, cefoperazone/sulbactam, sulfamethoxazole, and ceftriaxone. In accordance with the drug susceptibility test results, doctors in the intensive care unit then prescribed levofloxacin. According to the inflammatory index (e.g., white blood cell count, procalcitonin level, C-reactive protein level) and the patient's body temperature, the doctor changed the antibacterial drugs several times. Because the patient had sepsis, liver function was severely compromised, and treatments such as liver protection and nutritional support were provided (lines 49-56).

Discussion

1. Compare and contrast the nuances of the case report with the literature review.

We conducted a comprehensive literature review to determine the circumstances under which *Ralstonia* was linked with bacteremia. In 33 cases, co-morbidities were reported. Most patients presented with risk factors (e.g., cancer surgery, organ transplant, chemotherapy, poor immunity, *in situ* blood vessel catheterization). Contrastingly, our patient was a 36-year-old woman with no known history of any underlying chronic disease or immunosuppression. Her thyroid surgery was considered a clear surgery according to the surgical incision classification. She had no obvious risk factors (lines 61–70).

In our report, this bacterium was only sensitive to ciprofloxacin, cefoperazone/sulbactam,

sulfamethoxazole, levofloxacin, and ceftriaxone, a finding consistent with the drug resistance characteristics reported in other studies (lines 94-97).

2. Explain or justify the similarities and differences between the case report and the literature.

According to a literature review, *Ralstonia* species can be opportunistic pathogens that cause infection in immunocompromised patients. However, our report highlights the potential of *Ralstonia* to cause sepsis in patients with normal immunity. This finding emphasized that *Ralstonia* should be considered as a cause of infection irrespective of the immune status of the patient. When the patient experienced high fever of sudden onset after surgery, her clinical signs suggested a thyroid crisis. To avoid the possibility of a missed infection, we quickly obtained blood cultures for monitoring, which enabled the causative agent of the bloodstream infection to be identified within 10 h after surgery. This proved important for the choice of antibacterial treatment and the patient's final recovery. This finding also emphasized the importance of blood culture testing when a hospitalized patient has unexplained high fever (lines 64-76).

In our report, the bacterium was initially identified as *R. mannitolilytica* by MALDI-TOF MS. However, subsequent 16S rRNA gene sequencing identified the bacterium as *R. pickettii*. The confidence value was 2.319. Using Bruker Biotyper software to analyze blood culture specimens, the estimated sensitivity using a cut-off of ≥2.0 was 74.6% with

an estimated specificity of 88.0%. MALDI-TOF MS can improve the speed at which unusual pathogens are identified. However, MALDI-TOF MS wrongly identified the pathogen as *R. mannitolilytica*, whereas 16 rRNA typing identified the microbe as *R. pickettii*. Therefore, 16S rRNA sequencing continues to be a reliable identification system (lines 86–92).

This is the first time *R. pickettii* was identified as a bacterial cause of blood infection in our hospital. The isolated bacterium was sensitive to ciprofloxacin, cefoperazone/sulbactam, sulfamethoxazole, levofloxacin, and ceftriaxone, a finding consistent with the drug resistance characteristics reported in other studies. By reviewing the history of antimicrobial treatment (Figure 1), levofloxacin was identified as the effective drug for the patient, who was eventually discharged. This was consistent with the in vitro antibacterial drug susceptibility test results. Thus, in vitro drug susceptibility testing is useful and necessary to guide the clinical use of antibacterial drugs (lines 94-102).

3. List the limitations of the case report and describe their relevance. Confirm the accuracy of the descriptive patient case report.

One limitation of the case report was that the route by which the patient was infected by this opportunistic pathogenic was not clarified. The environment of the surgery room and the parental solutions and airway tubes were negative for infection in culture testing. The

cultures of blood, thyroid drainage fluid, and the tip of the thyroid drainage tube tested positive for *R. pickettii*, matching the result of in vitro drug susceptibility testing. Given the positive results for thyroid drainage fluid and the tip of the thyroid drainage tube and the negative results for blood culture and bacterial gene sequencing of thyroid tissue, we considered the contamination of fluid and the tube was related to bacterial contamination in blood opposed to infection of thyroid tissue (lines 77-85).

This bacterium was sensitive to ciprofloxacin, cefoperazone/sulbactam, sulfamethoxazole, levofloxacin, and ceftriaxone, a finding consistent with the drug resistance characteristics reported in other studies. The cause of its widespread resistance may be related to two variants of the class D β-lactamase-encoding gene blaOXA (blaOXA-573 and blaOXA-574). However, the mechanism should be studied in depth (lines 102-104).

4. Establish a causal relationship.

We checked the language and logic of our report.

5. Justify the uniqueness of the case.

This is the first time *R. pickettii* infection was identified in blood in our hospital. To our knowledge, this is the first report of sepsis caused by *R. pickettii* in the absence of risk factors.

Conclusion

The author should next summarize the essential features of the case report, justify why this case is unique, and draw recommendations and conclusions.

We have described a case of bloodstream infection caused by *R. pickettii* in a young woman with normal immunity, and typing of the microbe was performed in our laboratory. The patient had no obvious risk factors. This is the first report of sepsis caused by *R. pickettii* in the absence risk factors. MALDI-TOF MS was effective for rapid species identification, but accurate species classification required 16S rRNA typing. Clinicians should be aware that high fever after thyroid surgery may be caused by opportunistic pathogens. Therefore, in addition to post-surgery thyroid crisis, infection should be considered in patients with pyrexia. Finally, drug resistance in a rare bacterial species such as *R. pickettii* is possible. The mechanism of resistance should be studied in depth (lines 105-110).

The manuscript is not free of grammar, punctuation, sentence-structure and spelling errors.

We thank Joe Barber Jr., PhD, from Liwen Bianji (Edanz) (www.liwenbianji.cn/), for editing the English text of a draft of this manuscript.

Title of Table 1 must be corrected.

We corrected Table 1.

EIC Decision:

1. Please answer point by point to the reviewer's comments on a separate sheet under WORD format and write your modifications in the revised version (WORD format) in colored or highlighted letters.

Our responses to your comments are provided.

2. Your answers to reviewers' queries are not only for the Editorial Board but for the readers and should be included, when appropriate, in the manuscript for improvement and a better understanding. Moreover, add line numbers for text and put suitable line numbers for each response.

We added line numbers for each response.

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We added ORCID number.

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Revision (1)

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REFEREE: Associate Editor | **Revision** (1) 17 Oct 2021

Dear EIC
The manuscript was completely revised based on reviewers and associated editor comments and it is acceptable for publishing in JJM.
Regards

REFEREE: EIC | **Revision** (1) 17 Oct 2021

Dear Authors,
I am pleased to inform you that your manuscript has been accepted for publication in the JJM. Your accepted manuscript will now be transferred to our production department. If we need additional information from you during the production process, we will contact you directly. Please remember to always include your manuscript number, whenever inquiring about your manuscript. We will create a proof which you will be asked to check. When you receive the proof, please check all names and affiliations very carefully, as these cannot be corrected once the article is published. Moreover, please add the ORCID number to your and your collages account as soon as possible. For more details https://sites.kowsarpub.com/jjm/knowledgebase/category/tree.html#orcid.html
We appreciate you submitting your manuscript to JJM and hope you will consider us again for future submissions.
Thanks.