Author’s response to reviews

Title: Adult pneumococcal meningitis presenting with normocellular cerebrospinal fluid: two case reports

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Author’s response to reviews: see over
Dear Professor Kidd,

Thank you very much for sending the reviews and comments on our manuscript entitled “Adult pneumococcal meningitis presenting with normocellular cerebrospinal fluid: two case reports.”

We are grateful to the reviewers for their helpful and pertinent comments. We have amended our paper accordingly and have summarized the responses to the reviewers’ questions and editorial office’s suggestions on the following pages. We hope that the paper is now suitable for publication in the *Journal of Medical Case Reports*.

Thank you for your consideration of our manuscript. We look forward to hearing from you again soon.

Sincerely yours,
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To the editorial office

Thank you very much for your comments on our manuscript. Our changes are marked in red font in the revised version of the paper.

**Suggestion :** Please include the study design in your title, i.e. Case report. For example: A presenting with B in C: a case report.

**Response:** We have changed our manuscript title based on your suggestions as follows:

“Adult pneumococcal meningitis presenting with normocellular cerebrospinal fluid: two case reports”

**Suggestion:** Please include a list of abbreviations used in the manuscript and their meanings after the Conclusions section.

**Response:** We have added an abbreviation section according to your request.

**Suggestion:** Please reformat the Case presentation sub-section of the Abstract. If the Case reported is of multiple patients, please enumerate them accordingly.

**Response:** We have reformatted the Case presentation subsection of the Abstract as suggested.
Dear Dr. Mehmet Ulug,

Thank you very much for reviewing our manuscript and providing helpful comments.

**Suggestion:** In the discussion section of the study, the sensitivity of some antibiotics (especially penicillin, ceftriaxone, and others) to *S. pneumoniae* strains in the study center can be submitted.

**Response:** In Case 1, the drug susceptibilities to *S. pneumoniae* were determined by the disk dilution method and showed susceptibility to penicillin ($\geq 20$ mm), erythromycin ($\geq 21$ mm), and levofloxacin ($\geq 17$ mm). We have included these results in the Case presentation section (page 7, lines 1–3). In the microbiology report, the strain was also susceptible to ampicillin, piperacillin, cefazolin, cefotiam, cefozopran, and imipenem, but these results did not adhere to the CLSI susceptibility criteria and we did not include them in the manuscript.

In Case 2, the drug susceptibilities to *S. pneumoniae* were determined by the microdilution method with MicroScan WalkAway (Siemens Healthcare) and showed susceptibility to ampicillin ($\leq 0.5$ µg/mL), cefotaxime ($\leq 0.5$ µg/mL), and meropenem ($\leq 1$ µg/mL), but resistance to penicillin (0.12 µg/mL) and erythromycin ($\geq 2$ µg/mL). We have included these results in the revised manuscript (page 7, line 18 to page 8, line 3).
Dear Dr. Emmanuel Montassier,

Thank you much very much for reviewing our manuscript. We have revised the manuscript based on your suggestions.

**Suggestion; Family members or intimate contacts with a similar illness?**

**Response:** No contact histories were recorded in the medical charts of either patient.

**Suggestion; Please give to Glasgow Coma Scale score**

**Response:** In Case 1, the patient presented to our hospital with no assistance, and her consciousness was clear at the time of the initial presentation. She completed the medical questionnaire sheet well. However, she became progressively disoriented (GCS rating of E3V4M6) during outpatient management. We have described the change in her mental status in the Case presentation section (page 6, lines 4–6). In Case 2, there were no records of the GCS score in the medical chart.

**Suggestion; Intercurrent use of antibiotics? (especially in the case with splenectomy)**

**Response:** In Case 1, the patient had visited a clinic near her house for evaluation of fever the day before visiting our hospital, and oral cephalosporin (cefditoren pivoxil) had been prescribed with an antipyretic analgesic (loxoprofen sodium hydrate). Thus, she was receiving antimicrobial therapy at the time of the lumbar puncture. We have added this information to the revised manuscript (page 5, lines 17–19). In Case 2, the patient did not receive antimicrobial therapy before being transferred.
**Suggestion:** Appearance of the patient’s cerebrospinal fluid?

**Response:** In Case 1, the appearance of the CSF was described as “clear,” and we added this clinical information into the manuscript (page 6, line 10). In Case 2, no clinical information on the CSF appearance was recorded.

**Suggestion:** Case 1: can you describe more pyrexia?

**Response:** The patient stated that she had experienced sudden chills before developing a fever (39.7°C) two nights before visiting our hospital. The fever continued, and an antipyretic analgesic (loxoprofen sodium hydrate) was prescribed at a nearby clinic the day before admission. She was afebrile at the time of presentation to our hospital, probably secondary to the effects of the antipyretic analgesic. We have added a detailed history of the fever to the revised manuscript (page 5, lines 15–19).

**Suggestion:** Please describe more precisely delay between onset of the symptoms and the lumbar puncture.

**Response:** Thank you for your comment. We thoroughly analyzed the medical chart of the patient in Case 1. We have added a description of the onset time of nausea, headache, and loss of hearing, which involved the right ear. Although she developed a fever 2 days prior to the presentation to our hospital, she had begun to develop other symptoms such as nausea, headache, and loss of hearing on the morning of the hospital visit (a few hours before presenting to our hospital).

The outpatient management in this case can be summarized as follows:

9:40 Hospital visit (general medicine)

10:45 Intravenous catheter inserted
11:13 Lumbar puncture performed
11:24 Intravenous administration of penicillin G, 4 million units
11:50 Blood culture obtained
12:40 Intravenous administration of cefotaxime, 2 g
13:20 Hospital admission

Thus, lumbar puncture was performed 1.5 hours after presenting to our hospital. We have added the onset time of fever and neurological symptoms and the time of lumbar puncture to the Case presentation section (pages 5–6) and have described the delay between the onset of neurological symptoms and the performance of the lumbar puncture to the Discussion section (page 8, lines 9–13).

Suggestion: Realization of blood cultures? Results?
Response: In Case 1, two sets of blood samples for culture were obtained simultaneously with the start of intravenous antimicrobial therapy in the emergency department, but no bacteria were cultivated (page 6, line 18 to page 7, line 1). In Case 2, the patient (page 7, lines 17–18) died before blood culture was obtained. We have added this clinical information to the revised manuscript.

Suggestion: In the discussion please state that “results of tests on cerebrospinal fluid can be normal, especially when a lumbar puncture is done soon after the start of symptoms”
Response: Thank you for this important comment. We have inserted this information into the Discussion section (page 8, lines 11–13).