Author's response to reviews

Title: Brucella bacteremia in patients with acute leukemia: two case reports

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Author's response to reviews:

Letter to the reviewers

Very happy day to you.
Thank you very much for reviewing our manuscript. We did our best to answer all the questions you raised and to make all the modifications requested. Your suggestions were very sound and made the new version of our manuscript much better than the one initially submitted.

Here are the modifications made [All the changes made were highlighted]:

1- Abstract section:
(A) Background: The sentence [Brucellosis causes serious infections and bacteremias] was changed to [Brucella may cause serious infections in healthy individuals].

(B) Case presentation:
- The brucella species was mentioned in this section and throughout the manuscript.
- The phrase [which required an induction of leukemic transformation] was omitted.
- The phrase [The patient suffered of his leukemia] was also omitted.
- The spelling mistakes eg metlimicin and doxycyclin were corrected throughout the manuscript.

(C) Conclusion: The last sentence was rephrased and the good outcome was associated with early diagnosis and appropriate antimicrobial therapy given for enough duration.

2- Background:
(A) Most of the second paragraph was deleted and the patients presented were mentioned. The first sentence was kept as it gives introduction to the infection presented [brucellosis] and in order to have more than one reference in this section [background].

2- Case presentations:
(A) The species of brucella was mentioned.

(B) Regarding the duration and the relapse of brucellosis:

- Case (1): It was already mentioned in the history that the patients was unwell for one week only. A new statement was added towards the end to confirm that no relapse of brucellosis was encountered [There was no clinical or microbiological evidence of recurrence of the old brucella infection].

- Case (2): It was mentioned in his history that he had chronic relapsing brucellosis. The duration in years [15 years] was added. A new phrase was added at the end of the history [ and no further recurrence of his brucellosis was encountered ].

(C) Page 5/ Case 2: The first paragragh was made shorter.

(D) The typing mistake in Compylobacter was corrected.

3- Discussion:

(A) The discussion section was made at least one third shorter.

(B) The section on brucellosis in immunocopromised individuals was moved towards the end of the discussion and the 2 patients presented were discussed and compared to those reported in literature.

(C) The conclusion part was also made shorter.

4- Answers to other specific comments:

A- The cases presented were reported from the Riyadh Armed Forces Hospital (RAFH). The corresponding author works now at King Faisal Specialist Hospital & Research Centre. He was involved in the management of these 2 patients during his work at RAFH.

B- We never mentioned that we are the first authors to report brucellosis in acute leukemia. We mentioned in our discussion and in the letter addressed to the Editor-in-Chief that there are few case reports on brucella infection in acute leukemia. There are as well few other studies/reports on brucellosis in cancer and neutropenic patients. We did mention that cases of brucella bacteremia in acute leukemia patients are exceedingly rare and that our first case represents the first case report of brucella bacteremia in an AML patient.

C- Eser B et al reported 2 cases of brucellosis in acute lymphoblastic leukemia (ALL) [not acute myeloid leukemia- AML] patients and only one of them had positive blood cultures for brucella. Sari R et la reported three cases of brucellosis in three cancer patients [gastric and breast cancer] (ie not leukemia) having febrile neutropenia. Ozcan F ea al reported 1 case of brucellosis in a child with ALL. Two of these studies/reports were included in the references of both versions of the manuscript [ref.4 & ref.5]. Furthermore, as mentioned clearly in the title of our manuscript that we are reporting 2 cases of brucella bacteremia [not brucellosis per se ie diagnosed by serology etc] in 2 patients with acute leukemia and we are not talking about febrile neutropenic infections only.

D- The second case is fascinating because of the following reasons:
1- The recurrence of brucella infection while the patient was not severely neutropenic and when his disease was under control.

2- Presentation with acute abdomen at the time of brucella sepsis.

3- Despite his reduced immunity, the patient was able to mount a brisk immunological response in the form of high antibody titers. This was seen also in the first patient. This fact/finding has not been clearly described in other studies in immunocompromised patients.

Thank you once again for your valuable comments and suggestions.

Please accept the best regards and wishes of my co-author and myself

Khalid Al-Anazi