

Dear Editor,

Please find enclosed the edited manuscript in Word format (File name: ESPS Manuscript NO: 7124-edited).

Title: Successful treatment of liver abscess secondary to foreign body penetration of the alimentary tract: A case report and literature review

Author: Lee-Won Chong, Cheuk-Kwan Sun, Chin-Chu Wu, Cheuk-Kay Sun

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 7124

The manuscript has been improved based on the suggestions of the reviewers:

1. Format has been updated. Please also kindly note that the original title **“Successful treatment of liver abscess secondary to toothpick penetration of stomach: A case report and literature review”** has been changed to **“Successful treatment of liver abscess secondary to foreign body penetration of the alimentary tract: A case report and literature review”** to more accurately reflect the scope of the review.

2. Revision has been made according to the suggestions of the reviewers as follows:

Responses to comments of Reviewer 1 (Corresponding changes have been marked in “pink” in the revised manuscript):

Major comment: Although, as a case report, this manuscript is of limited scientific or innovative value, it offers an interesting synopsis of this topic (and illustrative pictures, too).

Response: Thanks for the Reviewer’s appreciation.

Minor comments:

Comment 1: Section “Demography and Clinical Manifestations”, last sentence: “As in our case, the patient did not recall any episode of foreign body ingestion...” – which patient is meant here? Please rephrase this statement in order to clarify it. (You probably wanted to say that also in your case the patient did not recall...). There is a similar problem in the section “Treatment Strategy and Hospital Course” (third paragraph, last sentence): “Indeed, as in our patient, liver abscess...”

Response 1: In compliance with the Reviewer’s insightful comments, the two sentences have been rewritten as “In addition, in our case,” and “Indeed, a liver abscess up to seven cm was resolved after antibiotics treatment in our patient”, respectively, in the revised manuscript (Page 7, first paragraph and Page 12, second paragraph, highlighted in pink).

Comment 2: Please correct/complete reference 40

Response 2: In accordance with the Reviewer’s comment, reference 40 has been corrected (Page 21, highlighted in pink).

Comment 3: Figure 1B: Figure legend: “Coronal...” - this is not a “coronal” view.

Response 3: We apologize for the incorrect description. The word “coronal” in the legend for Figure 1B has been changed to “sagittal” to correctly describe the actual body position on examination in the revised manuscript (Page 26, highlighted in pink).

Comment 4: Table 2: Entorobacter cloacae >> Enterobacter cloacae

Response 4: The Reviewer’s keen observation is highly appreciated. The term has been corrected accordingly in Table 2 of the revised manuscript (Page 28, highlighted in pink).

Responses to comments of Reviewer 2 (Corresponding changes have been marked in “green” in the revised manuscript):

General comment: This manuscript describes a comprehensive literature of review and useful for clinicians.

Response: We would like to express our appreciation for the Reviewer’s encouraging comment.

Specific comments:

Comment 1: I want to know how to decide the duration of treatment of antibiotics for this case without drainage.

Response 1: There are no standard treatment guidelines regarding the duration of antibiotic treatment for liver abscesses without drainage. In our case, the duration of antibiotics treatment was mainly decided based on the clinical symptoms (e.g. fever curve, severity of abdominal pain) and results of laboratory parameters (e.g. white blood cell count, CRP level) of the patient. The antibiotic is usually given till WBC count and CRP level returned to the normal limits. Our patient did not have fever during hospitalization, and he was symptom-free after discharge with his CRP level normalized at the first week of his outpatient clinic follow-up. This is based on our usual practice of following the level of serum CRP once a week during oral antibiotic treatment at outpatient clinic follow-up. If the serum CRP level is within normal limits (i.e. same as the patient in our report), one more week of oral antibiotic will be given. Therefore, oral antibiotic was given for two weeks after discharge. Besides, after discharge, the patient underwent serial abdominal ultrasonographic examinations every two weeks for one month and then monthly to evaluate the resolution of the liver abscess. In our case, the size of the abscess decreased gradually and complete resolution of the abscess was noted six months after discharge. Although ultrasonographic follow-up was recommended to evaluate the character of the liver abscess (size, degree of liquefaction), we seldom use ultrasonography to determine the duration of antibiotics treatment, as complete resolution of the abscess may require a prolonged period of time. To address the Reviewer’s concern and clarify the actual situation of our patient, the above information has been added to our revised manuscript (Page 5-6, highlighted in green).

Comment 2: In the review of literature, drug-resistant organisms cause liver abscesses? If there are case reports of drug-resistant Enterobacteriaceae, the authors should recommend broad-spectrum antibiotics (ex. carbapenems) as empirical treatment.

Response 2: We would like to thank the Reviewer's for the insightful comment and the important clinical concern. In compliance with the Reviewer's comment, relevant literature was reviewed. According to the literature, no drug-resistant Enterobacteriaceae has ever been reported in patients, who were otherwise healthy except for hepatic abscesses caused by foreign body penetration of the alimentary tract. In addition, as this disease entity occurs outside hospital, it is justifiable to assume that most of the cases would be afflicted with community-acquired infections. Therefore, for the time being, we do not recommend empirical use of carbapenems for otherwise healthy patients with this disease entity. In view of the Reviewer's professional comment and important concern, this piece of essential information has been added to the Discussion section of our revised manuscript under the subheading "Treatment strategy and hospital course": "Although the literature review in the present study showed no bacterial resistance in this clinical setting, broad-spectrum antibiotics (e.g. carbapenems) may be included in the empirical treatment regimen against drug-resistant organisms." (Page 12, second paragraph, highlighted in green)

Comment 3: The blood culture of this case was negative and the pathogen was not identified. Fortunately, this case was treated with successful outcome, but authors should show at least the positive rate of blood culture in the review of literature for the future cases with similar situations (undrainable abscesses).

Response 3: Review of literature showed six patients with undrainable abscesses for which antibiotics were the only treatment. Among these six patients, only one of them showed positive blood culture (1/6, 16.67%) with *Staphylococcus aureus* identified. Relevant information has been added into the discussion section under the subheading of "Pathogen" in the revised manuscript (Page 10, last paragraph, highlighted in green).

Comment 4: Authors should discuss why the length of hospitalization of drainage group was longer than antibiotic only group.

Response 4: Clinical symptoms, size and the presence of liquefaction of abscess are principle factors that determine the necessity of abscess drainage. If the patient is in septic condition or has large abscess with liquefaction, drainage of the abscess is considered mandatory. These patients tend to experience more complicated clinical courses, and therefore require longer hospitalizations. On the contrary, for patients with smaller abscesses and/or milder clinical symptoms, antibiotics treatment alone may be adequate, possibly accounting for their shorter hospitalization. In compliance with the insightful comment of the Reviewer, relevant discussion has been added to the manuscript (Page 12, first paragraph, highlighted in green).

Comment 5: I agree the option of conservative therapy, but authors should emphasize the general rule of treating "drainage and detection of causing organisms".

Response 5: We agree completely with the Reviewer's point of view that drainage and detection of causative organism are major points that should be kept in mind when treating liver abscesses. We have included this important fact in the "Conclusion" of the revised manuscript (Page 14, highlighted in green).

Comment 6: ceftriazone > ceftriaxone. Table 2: Streptococcus > *Streptococcus* sp.;

Bacteroides > *Bacteroides* sp.; Anaerobic Gram (+) coccus > *Anaerobic Gram (+) cocci*; *Candida* > *Candida* sp.; *Enterococcus* > *Enterococcus* sp.; Gram (-) rods > *Gram (-) bacilli*; *Proteus* > *Proteus* Sp.

Response 6: Sincere appreciation for the Reviewer's meticulous observation, all incorrect terms have been corrected in the revised manuscript (Page 6 & 28, highlighted in green).

Responses to comments of Reviewer 3 (Corresponding changes have been marked in "red" in the revised manuscript):

Comment 1: Abstract OK Introduction Until the statement "We report a case of liver abscess induced by an ingested foreign body which penetrated the gastric antrum" is OK. The statement about the treatment belong to the case report, whereas the lines starting from "Using the key words "liver abscess", "hepatic abscess", and "foreign body..." until the end should be moved into the review of the literature section.

Response 1: In compliance with the Reviewer's suggestion, the lines starting from "Using the key words "liver abscess", "hepatic abscess", and "foreign body..." until the end in the "Introduction" section of the original manuscript have been moved into the "Discussion" section of the revised manuscript under the subheading of "Review of the literature" (Page 6, second paragraph, highlighted in red). Moreover, introductory statements regarding literature review of the present study have been added to the "Introduction" of the revised manuscript to outline the review nature of this article (Page 4, last two sentences of the "Introduction", highlighted in red).

Comment 2: Case report: Was the abdominal ultrasonography performed just one time, that is 12 months after discharge, or was the abscess followed up with US? It is not clear.

Response 2: Thanks for the Reviewer's comment. After discharge, the patient underwent serial abdominal ultrasonographic examinations every two weeks for one month and then monthly to evaluate the resolution of the liver abscess. Complete resolution of the hepatic abscess was noted six months after discharge. The information has been added to the revised manuscript at the end of the "Case report" section (Page 6, first paragraph, highlighted in red).

Comment 3: Discussion: Background The first five lines are a repetition of the introduction statements and should be deleted.

Response 3: In view of the Reviewer's comment, the first five line of the "Background review" subsection of Discussion: "About 80-90 % of ingested foreign bodies pass through the gut uneventfully ... causes a hepatic abscess is rare" have been deleted in the revised manuscript to avoid repetition. The information has been shifted to the first sentence of the Introduction section (Page 4, highlighted in red).

Comment 4: Foreign bodies I suggest to give references for the unusual foreign bodies, such as clothespin, toothbrush, rosemary twig, pigtail catheter, rabbit bone, ball pen, lobster shell, metal wire, and dental plate. Also add references for the two cases in whom initial diagnosis was not established until the second visit and for the 7 cases in whom the diagnosis was not established until autopsy. Prognosis References should be given throughout.

Response 4: In accordance to the Reviewer's professional comment, references have been given for unusual foreign bodies, the two patients in whom initial diagnosis was not established until the second visit, the 7 cases in whom the diagnosis was not established until autopsy, and also in the "Prognosis" subsection in the revised manuscript (highlighted in red).

Responses to comments of Reviewer 4:

Comment: This paper provides a useful insight into the treatment of a relatively rare event. It is well written.

Response: We would like to express our sincere appreciation for the Reviewer's encouraging comments.

Thank you again for accepting and publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Sun Cheuk Kay", followed by a period.

Cheuk-Kay Sun M.D.

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