

**Dear Editor-in-Chief,**

Thanks for the Editor's and the Reviewers' comments on our manuscript entitled "Gastric syphilis mimicking gastric cancer: a case report. (No: 63785)". These comments are of utmost value to help us revise and improve our paper. We have studied the comments carefully and made amendments which we hope could meet with your approval.

I enclose here with a revised manuscript which includes the full details of our responses to the Editor's and the Reviewers' comments. The revised portions are underlined in red. Please find enclosed our point-by-point responses to these comments and questions.

**Response to Reviewers:**

**Reviewer #1:** *To keep the report chronology, the anatomopathological results of biopsies taken in the first endoscopy should be presented following the first endoscopy results.*

**Response:**

We appreciate Reviewer #1's comments. We added the anatomopathological results of biopsies (Figure 2) in accordance with Reviewer #1's request,

*2. Contradictory comment in the Discussion Section vs Information provided in Case Presentation.*

*The authors inform in the Case Presentation section that the patient started complaining of "pain in the middle and upper abdomen without apparent cause for one week, which was aggravated for two days". However,*

**Response:**

Thanks for the comments. In the Discussion Section, they considered the long course of disease but no obvious symptoms is one of the reasons for the misdiagnosis of patient disease. The right sentence has been added into the revised manuscript.

*3. Conclusion. In this section, the authors stated that "two-thirds of patients have no clinical findings of syphilis" without references. A citation should be provided to give support to this statement.*

**Response:**

Thanks for the comments. A citation has been added into the revised manuscript.

**Reviewer #2:**

*1. In the abstract section; the case presentation and conclusion can be more interesting to cover main finding of study.*

**Response:**

Thanks for the comment. The abstract has been modified in the revised manuscript.

*2. Core tip is not appropriate. the author should suggested main findings of the study, and discuss about key diagnosis and therapeutic point using their own experiences and literature review*

**Response:**

Thanks for the comments.

Syphilitic gastritis is one of the rare manifestations of syphilis, which has not been recognized by doctors. The majority of patients affected by syphilitic gastritis lack other signs and symptoms of syphilis and have no previous history of primary infection. The diagnosis of syphilitic gastritis depends on the combination of medical history, physiological, radiological, serological and pathological findings. According to the clinical stage of syphilis, penicillin treatment is effective.

*3. Introduction was too small. - The author should be specified the purpose of the study in last paragraph in the introduction section.*

**Response:**

Thanks for the comments.

Syphilis is a sexually transmitted disease, and the earliest cases of syphilis were reported in the 15th century<sup>[1]</sup>. Most cases of syphilis are sexually acquired, and the clinical manifestations depend on the stage of the disease and the organs involved. Two-thirds of patients have no clinical findings of syphilis, which easily leads to misdiagnosis of other diseases, including infiltrating tumor, lymphoma and Crohn's disease. Due to the rarity of the disease and the non-specific symptoms and signs, it is not well recognised by many physicians. Low incidence and nonspecific clinical presentation of gastric syphilis emphasize the importance of diagnostic suspicion<sup>[2]</sup>. Eighty-three percent of confirmed patients received penicillin and their symptoms resolved, while 17% of patients underwent surgical treatment due to complications or

misdiagnosis of tumor or lymphoma<sup>[3]</sup>. In this article, we report a rare case of so serious misdiagnosis that the patient would have proceeded to surgical ward for surgery.

*4. The figure resolution was not sufficient; in addition, figure legends should support your figure entirely, meaning that the reader of your paper should be able to understand your figure. i suggest use arrow and etc. to give more details.*

**Response:**

Thanks for the comment. More detail figure legends has been added into the revised manuscript.

*5. please give more details about Treatment and Outcomes and follow-up such as treatment duration, adverse event, etc.*

**Response:**

Thanks for the comment. Treatment and Outcomes have been modified in the revised manuscript.

*6. In discussion section, the author should make a table regarding your case and all previous published cases you mention in the discussion, with al characteristics and treatment approach, duration of treatment and outcomes, etc.*

**Response:**

A citation has been added into the revised manuscript. Mylona conducted a systematic review of the English literature for cases of Gastric Syphilis (GS) in the last 50 years Mylona EE, Baraboutis IG, Papastamopoulos V, et al. Gastric syphilis: a systematic review of published cases of the last 50 years. Sex Transm Dis. 2010 Mar;37(3):177-83. doi: 10.1097/OLQ.0b013e3181c0d51f. PMID: 20023597.

*7. Conclusion and Core tip was repetitive, it is not acceptable. the authors should substantially revised the conclusion.*

**Response:**

The conclusion has been modified in the revised manuscript.

Our case of patient has a large and irregular gastric ulcer, which is difficult to distinguish from gastric cancer under endoscopy. Pathological biopsy is necessary to confirm Gastric

syphilis is unusual with vague symptoms. After immunohistochemistry and inquiring about a history of syphilis, it was confirmed as gastric syphilis. gastric syphilis can be easily misdiagnosed as ordinary gastritis, gastric ulcer or even gastric cancer, if its microscopic pathological characteristics (a vast number of plasma cells and vasculitis) or HE filming results aren't representative enough. When necessary, gastric spirochete syphilis immunohistochemical staining or real-time fluorescent PCR detection can be used in the diagnosis making of spirochete syphilis.

With best regards,

Yours sincerely,

Prof. Feiyun He, MD