Author's response to reviews

Title: Primary gastric actinomycosis: Report of a case diagnosed in a gastroscopic biopsy

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RESPONSE TO REVIEWERS’ CONCERNS

Reviewer: Jeff Garner

Background

• A Google advanced search was performed on January 2, 2015. An additional report was found in 2011 of a case of primary gastric actinomycosis diagnosed by gastroscopy. The text was modified to include that case report and the relevant reference was added (reference “8”).

• The importance of the fact that the diagnosis was made by gastroscopy is already clarified in the discussion as follows: “Because of the submucosal localization of the inflammatory process, gastroscopic biopsy specimens usually reveal nonspecific inflammatory changes [3,14,18,19]. In most cases, the diagnosis was made after surgery and histopathological examination of the resected specimen [9,12,19,20,27]. Only two cases are reported in which the diagnosis of gastric actinomycosis was made on microscopic evaluation of a gastroscopic biopsy specimen [6,8].” (see Discussion, lines 190-194).

Case presentation

• The white cell count at presentation was 16.6 K/ul with 89% segmented cells, so the patient was put on empiric antibiotic coverage with levofloxacin and metronidazole for 5 days. This has been clarified in the text (see Case presentation, lines 113 & 119).

• The patient's was in a good health status by the time of discharge and a third biopsy revealed atrophic gastritis with no Actinomyces identified. A plan was set up to start him on the appropriate antibiotic therapy for actinomycosis with follow up gastroscopy after one month. However, the patient chose to continue treatment somewhere else. So he was discharged on his request and he never showed up again in our institution. This has been clarified in the text (see Case presentation, lines 144-149).

Discussion

• Medications received by the patient since four years included, mainly, acetylsalicylic acid 81mg, atorvastatin 40mg, ibesartan 300mg and hydrochlorothiazide 25mg, daily. This has been added to the text (see Case presentation, lines 110, 111).

• Lines 168-173 have been rephrased with repeated information omitted as per the reviewer’s instruction (see Discussion, lines 183-186).

• Anaerobic culture was not specifically ordered by the clinician. Consequently Actinomyces, known to be strictly anaerobic, were not detected. We did not repeat
culturing after the second biopsy as the typical morphology of the organisms in tissue sections confirmed by positive Grocott, PAS and Gram staining was considered sufficient for the diagnosis of Actinomyces infection with no necessity for confirmation by culture, particularly when it is realized that culturing is negative in most cases of gastric actinomycosis. This has been clarified in the text ([See Case presentation, lines 139-143 and Discussion, lines 205-208]).

- As already mentioned, a plan was set up to start the patient on the appropriate antibiotic therapy for actinomycosis with follow up gastroscopy after one month. However, the patient chose to continue treatment in somewhere else and was lost to follow up ([see Case presentation lines 146-149]).

Conclusion

- We think there is no irony. In that line we alert the pathologist to perform appropriate “special stains” (not specific cultures) to reveal the causative organism. Such stains are to be done on paraffin tissue sections as we did. We did not recommend culture as this often yields negative results as mentioned above. Demonstration of Actinomyces in tissue sections is sufficient for diagnosis.

Reviewer: Sergio Morini

1. The diagnostic path

- The second gastroscopy and biopsy was performed because a diagnosis of malignancy was still in suspicion despite the negative result of the first gastroscopic biopsy. This has been added to the text ([see Case presentation, lines 134-136]).
- Plain X-ray was performed in the ER at presentation. Contrast CT-scan preceded the gastroscopy to rule out an organic cause for the gastric outlet obstruction by which the patient presented. This has been clarified in the text ([see Case presentation lines 116 & 121, 122]).
- Empiric antibiotic coverage with levofloxacin and metronidazole for 5 days was started immediately after admission. This has been clarified in the text ([see Case presentation line 119]).
- The patient's was in a good health status by the time of discharge and a third biopsy revealed atrophic gastritis with no Actinomyces identified. A plan was set up to start him on the appropriate antibiotic therapy for actinomycosis with follow up gastroscopy after one month. However, the patient chose to continue treatment somewhere else. So he was charged on his request and he never showed up again in our institution This has been clarified in the text ([see Case presentation lines 144-149]).

2. Although, an associated paralytic ileus due to acute pancreatitis may be an alternative explanation for the functional gastric outlet obstruction as suggested by elevated serum lipase and amylase levels ([see below]), concomitant organic disease was not likely since repeated biopsies from various sites of the stomach and follow up of the patient did not reveal other
pathologies. This has been added to the text (see Case presentation, lines 127, 128 & 144, 145).

a) Drugs received by the patient since four years included, mainly, acetyl salicylic acid 81mg, atorvastatin 40mg, ibesartan 300mg and hydrochlorothiazide 25mg, daily. This has been added to the text (see Case presentation, lines 110, 111).

b) Biopsies were obtained from the edge and the centre of the fundic mass during both gastroscopies. This has been added to the text (see Case presentation, lines 127 & 128). No biopsies were taken from the pylorus as this appeared endoscopically unremarkable.

c) This cannot be ruled out. We added in the text that “Age related mucosal atrophy may have also contributed to diminished mucosal resistance” (see Discussion, lines 163, 164).

d) This is possible. We added in the text that “An associated paralytic ileus due to acute pancreatitis may be an alternative explanation for the obstruction as suggested by elevated serum lipase and amylase levels” (see Discussion, lines 186-188).

e) Follow up data have been added to the text (see Case presentation, lines 140-145, also see “diagnostic Path” above).

3. The discussion session has been amended with parts omitted and others added (highlighted in red font).

4. Anaerobic culture was not specifically ordered by the clinician. Consequently Actinomyces, known to be strictly anaerobic, were not detected. We did not repeat culturing after the second biopsy as the typical morphology of the organisms in tissue sections confirmed by positive Grocott, PAS and Gram staining was considered sufficient for the diagnosis of Actinomyces infection with no necessity for confirmation by culture, particularly when it is realized that culturing is negative in most cases of gastric actinomycosis. This has been clarified in the text (See Case presentation, lines 139-143 and Discussion, lines 205-208).

5. As already mentioned, the typical morphology of the organisms in tissue sections confirmed by positive Grocott, PAS and Gram staining is sufficient for the diagnosis of Actinomyces infection. We, therefore do not find it necessary to confirm the diagnosis by culture. This has been added to the text (see Discussion, line 207, 208).

6. This point was corrected with the sentence rephrased as follows: “In our case, culturing yielded only Streptococcus viridans, another endogenous aerobic/anaerobic facultative commensal present in the oral and GI-tract flora” (see Discussion, lines 203-205).

**Reviewer: Kiseok Jang**

No concerns raised.