

Gastric actinomycosis facilitated by diffuse large B-cell lymphoma

Ranjit Dhillon Singh, Fransien de Boer,
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ABSTRACT

Introduction: Gastric actinomycosis is a rare endogenous infection caused by *Actinomyces* species and is usually provoked by gastric mucosal damage, for example due to previous abdominal surgery or trauma. As the clinical presentation and invasive nature of actinomycosis often mimics malignancy, the diagnosis is sometimes only established after exploratory laparotomy. **Case Report:** Here, we present a male in his seventies, with low-grade B-cell chronic lymphatic leukemia, in whom gastric actinomycosis was diagnosed by histopathological examination of endoscopic biopsies. Repeated endoscopic examination following antibiotic treatment revealed an underlying diffuse large B-cell lymphoma, interpreted as a Richter's transformation. The patient received six Rituximab, Cyclophosphamide, Adriamycin, Vincristine, and Prednisone (R-CHOP) chemotherapy courses, after which complete remission was achieved. **Conclusion:** We emphasize that a high level of vigilance is necessary to diagnose gastric actinomycosis and the possibility of a concomitant malignancy should be considered.

Keywords: *A. israelii*, B-cell lymphoma, Gastric actinomycosis, Richter's transformation

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INTRODUCTION

Actinomycosis is a rare inflammatory disease caused by anaerobic, gram positive, filamentous bacteria of the *Actinomyces* species (mostly *A. israelii*) that belong to the indigenous commensal flora of the oropharynx, gastro-intestinal tract, and urogenital tract. The main localizations of actinomycosis are cervicofacial (30–65%), abdominopelvic (20–36%), and thoracic (15–30%) [1–3]. Although the clinical presentation strongly depends on the primary site of involvement and the duration of the disease, general features of actinomycosis include abscess formation, dense fibrosis, and draining sinuses with characteristic yellow exudate containing sulfur granules [4, 5]. Within the digestive tract, actinomycosis most commonly affects the appendix, cecum, and colon [6]. Gastric involvement is uncommon in actinomycosis, presumably due to the low gastric pH that is usually sufficient to either kill or inhibit micro-organisms [7]. In most cases of gastric actinomycosis, structural disturbances of the gastric mucosa play an important role in facilitating the disease. Common predisposing factors leading to gastric mucosal disruption include previous abdominal surgery and trauma [6, 8]. The widespread use of proton

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pump inhibitors nowadays, however, might increase the incidence of this infection. Clinical manifestations of gastric actinomycosis include epigastric pain, low-grade fever, or upper gastro-intestinal bleeding [1, 9]. Prior reports are limited and the diagnosis of gastric actinomycosis was mostly established postoperatively following exploratory laparotomy for a suspected malignancy, reflecting that the disease typically behaves as a progressive and invasive spreading mass [2, 7, 10–12].

CASE REPORT

A 72-year-old Caucasian male presented to the hospital with postprandial back pain lasting for several weeks. He lost three kilograms in two months. He had a history of hypertension, type 2 diabetes, an occipital infarction, and an asymptomatic B-cell chronic lymphatic leukemia classified as RAI0, BINETA with no indication for treatment. There was no history of abdominal surgery or trauma. Over the past years, the patient received the following medications: clopidogrel, nifedipine, atenolol, metformin, atorvastatin, and pantoprazole. Physical examination revealed unremarkable vital signs together with a soft and non-tender abdomen without signs of acute pathology. Laboratory investigations showed expected values with low-grade B-cell chronic lymphatic leukemia (leukocytes $11.0 \times 10^9/l$ [$n = 4.3 - 10.0$], lymphocyte percentage 56.0) without signs of progression or Richter's transformation (LDH 182 U/l $n < 450$). A chest X-ray showed no abnormalities, and especially no signs of pulmonary infiltrates. Subsequent gastroscopic examination revealed a tumorous process within the corpus and antrum of the stomach, which was considered suspicious for malignant disease (Figure 1). Biopsies obtained from the edge and center of the mass demonstrated an ulcerative inflammation with multiple actinomyces. Furthermore, the specimens showed a monoclonal B-cell population. The typical morphology of the organisms was considered sufficient; therefore, there was no confirmation through culturing (Figure 2). The patient was then treated with high doses of intravenous (IV) benzylpenicillin (10×10^6 IE/day) for two weeks. During this period, the patient's major complaint (back pain after eating) had disappeared completely. A follow-up gastroscopy was performed to evaluate the effectiveness of antibiotic treatment. Again, multiple biopsies were taken and sent for histopathological examination. The biopsies revealed, apart from an active inflammation, diffusely present large B-lymphocytes with prominent nucleoli, without discernable lymphoepithelial lesions. The immunohistochemical staining profile was consistent with a diffuse large B-cell lymphoma (DLBCL, GCB type), i.e. CD3⁻, CD5⁻, CD10, CD20⁺, CD21⁻, PAX5⁺, Cyclin D1⁻, BCL2⁺, BCL6⁺, with 80% nuclear ki67 expression. A subsequent CT-scan of the neck, chest and abdomen as well as a

whole-body PET/CT-scan did not show evidence of other lymphoma localizations besides the gastric mass (Figure 3). After two weeks of IV benzylpenicillin, medication was converted to oral doxycycline and continued for another six months. The patient also underwent six chemotherapy sessions over the course of six months consisting of Rituximab, Cyclophosphamide, Adriamycin, Vincristine, Prednisone (R-CHOP q21 days) and Pegfilgrastim. The chemo-immunotherapy was well-tolerated by the patient and complete remission of the diffuse large B-cell lymphoma was achieved after six cycles. A control gastroscopy seemed to show a slightly thickened, probably reactive, remaining area around the gastric antrum, but biopsies showed no evidence of malignancy. Moreover, a CT-scan of the neck, chest, and abdomen as well as a whole body PET/CT-scan showed normalization of the gastric mass.

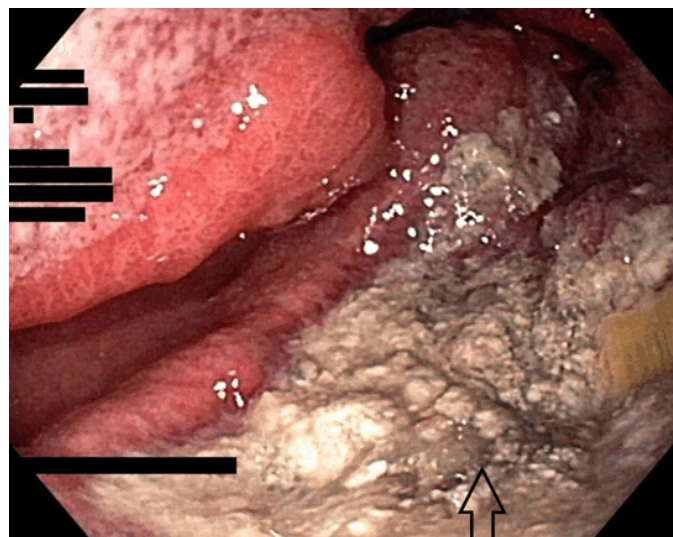


Figure 1: Gastroscopic examination revealing a large, centrally ulcerated mass (arrow), with yellowish-green precipitation, located in the antrum of the stomach.

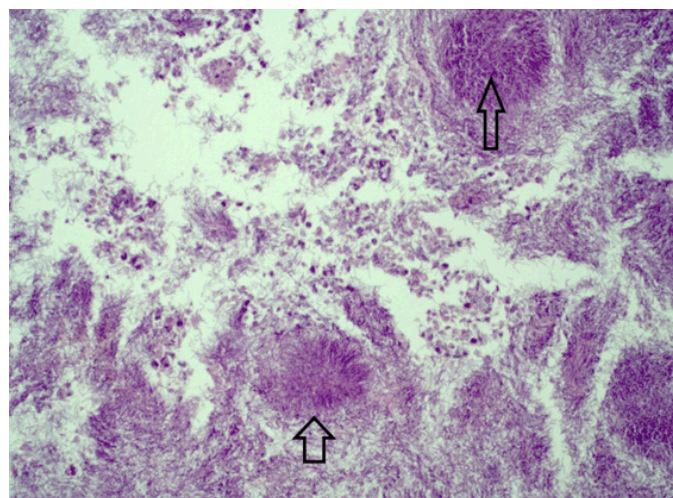


Figure 2: Multiple lesions (arrows) characteristic of Actinomyces. Staining with haematoxylin-eosin, original magnification x20.

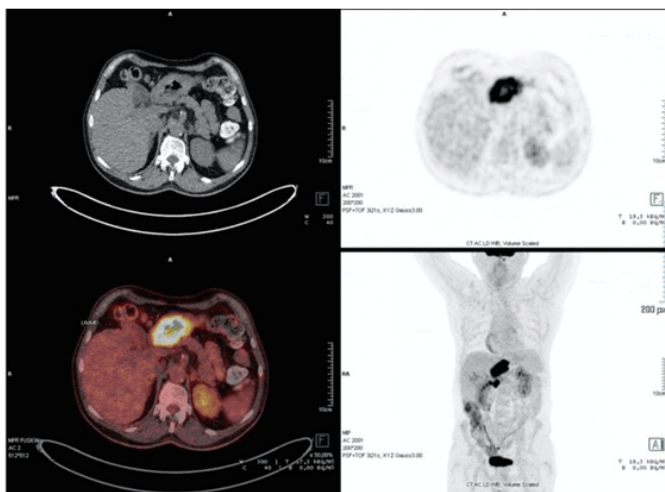


Figure 3: Whole-body position-emission tomography (PET) – CT scan with 18F-fluorodesoxyglucose (FDG), showing intense stomach uptake.

DISCUSSION

Actinomycosis is a rare infectious disease caused by gram-positive filamentous anaerobic *Actinomyces* bacteria living endogenously in the oral cavity, intestinal flora and urogenital tract [1–3]. General features of actinomycosis include formation of abscesses, draining sinuses and dense fibrosis, although presenting symptoms largely depend on the affected site [4, 5]. The cervicofacial region is most commonly affected, while intra-abdominal involvement occurs less frequently and has a penchant for the terminal ileum, cecum and appendix [6]. The rarity of gastric involvement by actinomycosis has been attributed to the high luminal acidity of the stomach that inhibits bacterial growth [7]. Factors that precipitate gastric actinomycosis include previous abdominal surgery and perforating abdominal trauma, since *A. Israelii* can typically only invade through an injured mucosal barrier as an opportunistic endogenous infection [6, 8]. In most cases, however, no obvious portal of entry can be identified and the mechanism by which *Actinomyces* has reached the gastric wall cannot be traced. In the present case, we believe gastric actinomycosis was facilitated by gastric mucosal damage due to a Richter's transformation of an existing B-cell chronic lymphatic leukemia to a diffuse large B-cell lymphoma in the stomach. The immunocompromised state of our patient, associated with his leukemia, could have also made him more vulnerable to opportunistic infections such as actinomycosis [4, 6]. In the present case, initial gastroscopic findings also suggested malignancy, particularly gastric carcinoma or lymphoma. However, pathological examination of the initial biopsies revealed actinomycosis and a monoclonal B-cell population that could not be further specified. In many cases, the diagnosis of gastric actinomycosis is only made after surgical resection for suspected malignancy and histopathological examination of the resected specimen. To our knowledge, this is the fourth reported

case in which gastric actinomycosis was diagnosed based on endoscopic biopsies [12–14]. Furthermore, the large amount of oral medications, including a proton pump inhibitor, that our patient used over the past years could have contributed to gastric mucosal damage and might have facilitated the entry of actinomyces into the gastric wall [15]. Age related mucosal atrophy might have also played a role in the diminished mucosal resistance.

Typical clinical manifestations of gastric actinomycosis are low-grade fever, epigastric pain and upper gastrointestinal hemorrhage [1, 9, 14]. In the present case, no such manifestations were demonstrated. Instead, our patient presented with rather atypical complaints of back pain after eating meals and weight loss.

The diagnosis of gastric actinomycosis is often difficult to establish because of the non-specific clinical, radiological or endoscopic presentation of the disease and the similarities to malignant processes. CT-findings mostly demonstrate an infiltrative lesion with diffuse gastric wall thickening, while endoscopic findings often simulate gastric neoplasm and include tumor-like or infiltrative lesions [14].

Uncomplicated actinomycosis can be treated medically by antibiotics (usually penicillin) and requires a prolonged treatment course (6–12 months) because of the poor penetration of antibiotics into the fibrotic tissue [1, 9]. Our patient was initially treated with IV benzylpenicillin for two weeks. Biopsies taken during a second gastroscopy to evaluate the effect of antibiotic treatment revealed a diffuse large B-cell lymphoma, which is an aggressive lymphoma usually appearing as an infiltrative lesion at endoscopy, as seen in the present case. In addition to continued antibiotic treatment with oral doxycycline for six months, our patient underwent six chemo-immunotherapy sessions to treat the underlying lymphoma, after which complete remission was achieved.

CONCLUSION

It is likely that the presence of gastric actinomycosis obscured and delayed the diagnosis and treatment of the underlying lymphoma in our patient. We emphasize that a high level of vigilance is necessary to diagnose gastric actinomycosis and the possibility of a concomitant malignancy should be considered.

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Author Contributions

Ranjit Dhillon Singh – Substantial contributions to conception and design, Acquisition of data, Analysis

and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be Published

Fransien de Boer – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Thea Marieke Teune – Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Adriaan Dees – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor of Submission

The corresponding author is the guarantor of submission.

Source of Support

None.

Consent Statement

Written informed consent was obtained from the patient for publication of this case report.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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