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Strongyloides stercoralis Gastric Ulcer: A Rare Cause of Upper Gastrointestinal Bleeding

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Keywords

Strongyloides stercoralis · Gastric ulcer · Hematemesis

Abstract

Strongyloidiasis is an infection caused by *Strongyloides stercoralis*. Gastrointestinal manifestations typically include duodenitis, chronic enterocolitis, and malabsorption, while gastric involvement is very rare. In this case report, the authors present a case of upper gastrointestinal bleeding caused by a gastric ulcer with a challenging etiological diagnosis. In Portugal, there have been reports in the past century of autochthonous cases of *S. stercoralis* infection suggesting endemic zones, but with the current sanitation infrastructure strongyloidiasis is thought to be rare. A 56-year-old Caucasian male smoker with a history of significant weight loss presented to the emergency department with hematemesis and abdominal pain. Upper endoscopy revealed a giant gastric ulcer with a macroscopic appearance suggestive of malignancy. Further investigation with CT scan highlighted gastric wall thickness and a spiculated lung lesion in the upper right lobe without lymph node involvement or metastatic disease. Bronchoscopy with bronchial brushing was performed. Histological examination identified squamous cell carcinoma of the lung and the patient was referred to Oncological Pneumology. Gastric ulcer biopsies ruled out malignancy and identified fragments of nematodes with inflammatory infiltrates and fibrinogranulocytic exudate, suggestive of *S. stercoralis*. Accordingly, the diagnosis of strongyloidiasis was made and further confirmed with molecular methods and serology. The giant gastric ulcer was affirmed to be caused by *S. stercoralis* infection and the patient was treated with ivermectin with improvement of epigastric pain. On reevaluation 6 weeks later the patient was asymptomatic, had gained weight, parasitological stool examinations were negative, and upper endoscopy showed complete ulcer healing. Further tests were done targeting risk factors for strongyloidiasis, and in addition to the presence of malignancy, other underlying causes for immunosuppression were ruled out. In this case report strongyloidiasis was manifested by gastric involvement with upper gastrointestinal bleeding in a patient who was subsequently diagnosed with squamous cell carcinoma of the lung.

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Úlcera Gástrica por *Strongyloides stercoralis*: Uma Causa Rara de Hemorragia Digestiva Alta

Palavras Chave
Strongyloides stercoralis · Úlcera gástrica · Hematemeses

Resumo
A estrongiloidíase é uma infecção causada por *Strongyloides stercoralis*. As manifestações gastrointestinais tipicamente incluem duodenite, enterocolite crónica e má absorção, sendo o envolvimento gástrico muito raro. Neste caso clínico, os autores apresentam um caso de hemorragia digestiva alta causada por uma úlcera gástrica com um diagnóstico etiológico desafiante. Em Portugal no século passado existiram casos autóctones de infecção a *S. stercoralis* sugerindo zonas endémicas, mas com a actual infraestrutura de saneamento a estrongiloidíase é rara. Homem de 56 anos de idade, caucasiano, fumador, com história de perda ponderal significativa, admitido no Serviço de Urgência por hematemeses e dor abdominal. A endoscopia digestiva alta realizada revelou uma úlcera gástrica gigante com aparência macroscópica sugestiva de malignidade. A investigação subsequente com tomografia computadorizada (TC) destacou a presença de espessamento gástrico e uma lesão pulmonar espiculada no lobo superior direito, sem envolvimento ganglionar ou doença metastática. Foi realizada broncofibroscopia com escovado brônquico tendo o exame histológico identificado carcinoma pavimento celular do pulmão, pelo que o doente foi referenciado para a Pneumologia Oncológica. As biópsias da úlcera gástrica descartaram malignidade e identificaram fragmentos de nemátodes com infiltrados inflamatórios e exsudado fibrino-granulocítico, sugestivo de *Strongyloides stercoralis*. Consequentemente, foi feito o diagnóstico de estrongiloidíase, confirmado com métodos moleculares e sorologia. Admitiu-se que a úlcera gástrica gigante terá sido causada pela infecção por *Strongyloides stercoralis* e o doente foi tratado com ivermectina com melhoria da dor epigástrica. Em reavaliação, seis semanas depois, o doente estava assintomático, com ganho ponderal, os exames parasitológicos das fezes estavam negativos e a endoscopia digestiva alta mostrou cicatrização completa da úlcera. Foram realizados exames adicionais para investigação de factores de risco para estrongiloidíase, tendo sido excluídas outras causas de imunossupressão subjacente para além da presença de malignidade. Neste caso clínico, a estrongiloidíase manifestou-se por envolvimento gástrico com hemorragia digestiva alta num doente que foi posteriormente diagnosticado com carcinoma pavimento celular do pulmão.

Introduction

Strongyloidiasis is an infection caused by the helminth *Strongyloides stercoralis*, an intestinal nematode which is endemic in rural areas of tropical and subtropical regions of the world, particularly in hot and humid climates as well as countries with inadequate sanitary conditions, but it can also be transmitted in temperate regions such as North America and Southern Europe [1, 2] (Fig. 1).

The global prevalence of strongyloidiasis is unknown, but experts estimate that there are between 30 and 100 million infected persons worldwide [3]. In Portugal there are no recent epidemiological data, but between 1914 and 1985 autochthonous cases of *S. stercoralis* infection were reported, suggesting endemic zones within the country in the past [4–6].

Distribution of *S. stercoralis* closely coincides with the geographic distributions of soil regimes, moisture, and temperature. The filariform larvae can survive with significant motility in water, greatly increasing their transmission potential. The most frequent mode of transmission is via skin contact with contaminated soil and poor water quality, which explains how the lack of adequate sanitation has a major influence, making strongyloidiasis a public health issue in these regions. Less common modes of transmission include fecal-oral transmission and person-to-person transmission via contact with fecally contaminated fomites.

The authors present a case of upper gastrointestinal bleeding with a challenging etiological diagnosis and propose to highlight an often-neglected parasitic disease.

Case Presentation

A 56-year-old Caucasian male, chronic smoker (63 pack-years), with a previously unremarkable medical history, complained of loss of appetite, postprandial fullness, epigastric discomfort, and a significant weight loss of 10 kg in the past year. The patient presented to the emergency room with hematemesis, dysphagia, and worsening of postprandial abdominal pain. Symptoms such as fever, diarrhea, or skin lesions were ruled out as well as journeys to tropical countries, rural areas, or contact with animals. The patient had not taken any medication, including nonsteroidal anti-inflammatory or immunosuppressive drugs.

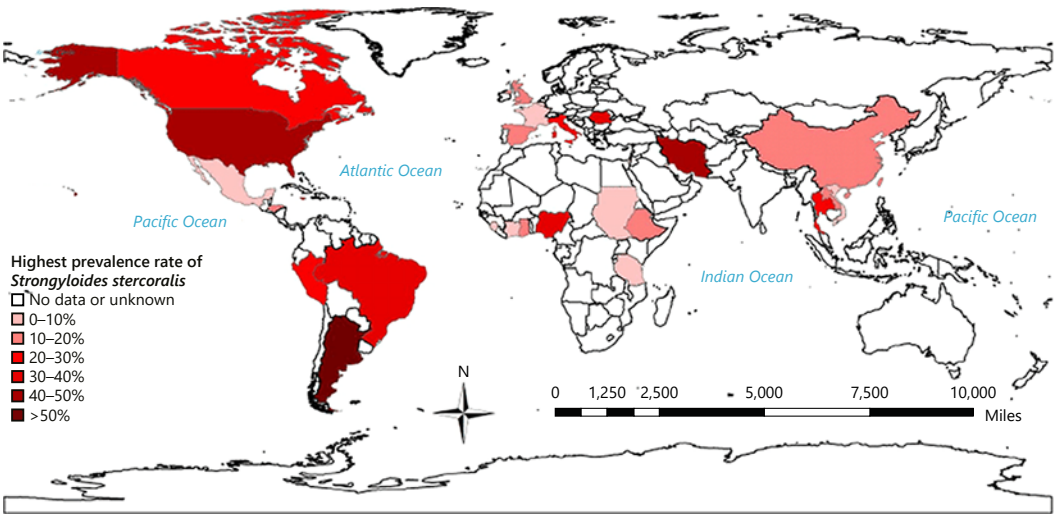

Fig. 1. Map showing reports of the global prevalence of *Strongyloides stercoralis* infection in 2014 [1].

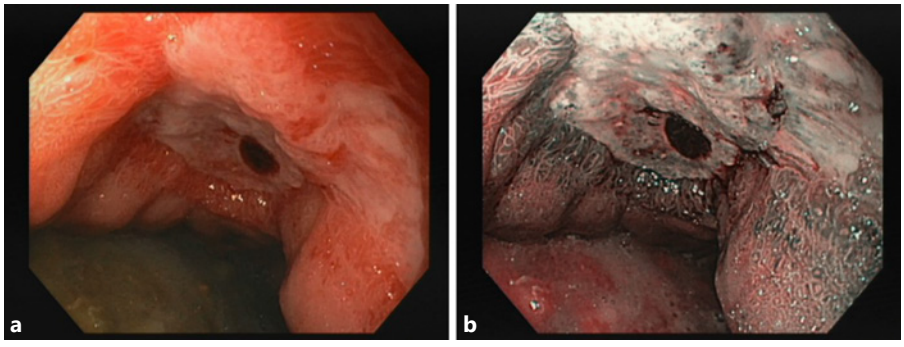

Fig. 2. Upper endoscopy showing a giant ulcer (30 mm) of the gastric antrum – Forrest class IIb. **a** Standard endoscopic view. **b** Narrow band imaging.

On admission, the patient was hemodynamically stable and besides a mild epigastric pain without tenderness, physical examination was unremarkable. Intravenous treatment with high-dose bolus of proton pump inhibitor followed by continuous infusion was initiated. Laboratory tests showed normocytic normochromic anemia with Hb 9.8 g/dL (previous value 14 g/dL) and a significant elevation of inflammatory parameters with leukocytosis 21,230/μL (normal range: 4,000–11,000/μL), neutrophilia 84% without eosinophilia, increased C-reactive protein 29.3 mg/dL (normal range: <0.5 mg/dL), and erythrocyte sedimentation rate 120 mm/h, with a normal platelet count and INR. Subsequent laboratory examinations revealed iron deficiency (reduced serum iron 15 μg/dL and transferrin saturation 6%, with normal ferritin 194 ng/mL) and folic acid deficiency (plasma folate 1.8 ng/mL).

Upper endoscopy performed in the first 12 h revealed a giant gastric ulcer (30 mm) with regular borders and an adherent clot at the base – Forrest class IIb – comprising the distal third of the lesser curvature, extending through the anterior wall of the gastric body (Fig. 2); multiple biopsies were performed. The patient was discharged to outpatient consultation waiting for biopsy results and treated with pantoprazole 40 mg/day.

Given the macroscopic appearance of the gastric ulcer and the clinical presentation, neoplastic etiology was suspected, and a CT scan was performed highlighting gastric wall thickness, bronchiectasis, and a spiculated lung nodule with 16 mm in the upper right lobe, which was not previously known (Fig. 3). Imaging with both CT and PET scans excluded lymph node involvement or metastatic disease.

Bronchoscopy with bronchial brushing was performed and was positive for cancer cells, with histological examination revealing squamous cell carcinoma of the lung; the patient was referred to Oncological Pneumology. There was no evidence of filariform larvae in the bronchoalveolar lavage fluid.

Four weeks later, despite treatment with pantoprazole, the patient complained of persisting abdominal pain. Evaluation of the gastric ulcer biopsies identified fragments of partially destroyed parasites with inflammatory infiltrates and fibrinogranulocytic exudate, indicative of *S. stercoralis* (Fig. 4). In the multiple biopsies evaluated there was no evidence of malignancy or *Helicobacter pylori*.

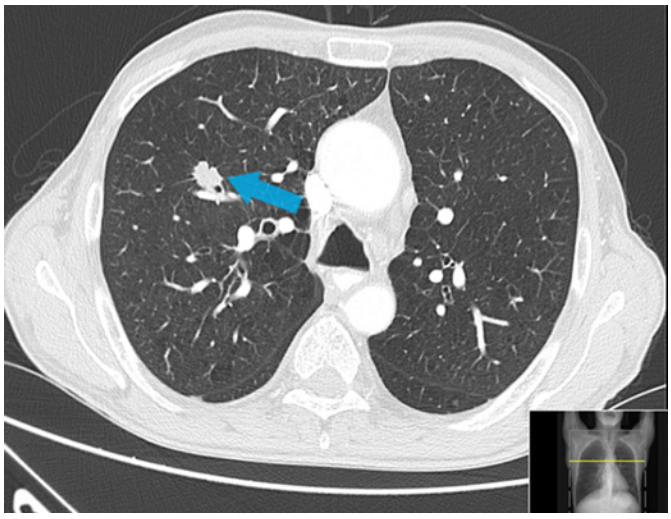

Fig. 3. CT scan showing a spiculated lung lesion.

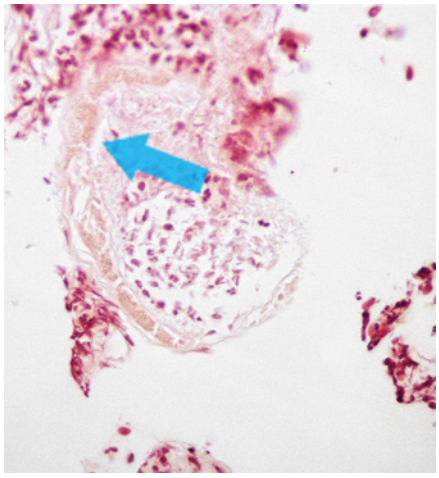

Fig. 4. Hematoxylin-eosin stain of the biopsy sample from the gastric ulcer showing a partially destroyed *Strongyloides stercoralis* nematode.

Considering the differential diagnosis of the gastric ulcer, in the absence of risk factors for stress ulcer and persisting pain despite proton pump inhibitors, with biopsies ruling out malignancy or *H. pylori* and having recognized *S. stercoralis* in the histopathological examination, the most likely etiological diagnosis was strongyloidiasis. Moreover, the patient had significant weight loss with folate and iron deficiencies representing a malabsorption state, which is a manifestation of strongyloidiasis. A PCR-based assay was performed in repeated stool samples and was positive for *S. stercoralis*. Serological tests using ELISA were positive and consistent with the diagnosis of strongyloidiasis. Treatment with ivermectin 200 μg/kg was administered on 2 consecutive days and pantoprazole was interrupted. On reevaluation 6 weeks after the ivermectin treatment, the patient was asymptomatic, had gained weight, folic acid and iron levels were within the normal range, parasitological stool examinations were negative, and the upper endoscopy showed complete ulcer healing. This significant improvement after ivermectin treatment is consistent with the etiology of the gastric ulcer being caused by the parasite.

Further tests were performed targeting risk factors for strongyloidiasis [7] considering the likelihood of immunosuppression in addition to the presence of malignancy. Laboratory tests including human T-lymphotropic virus type 1 (HTLV-1) and HIV 1/2 were negative and primary immunodeficiency was also ruled out.

Discussion

Gastrointestinal manifestations of strongyloidiasis typically include duodenitis induced by the adult worms, chronic enterocolitis, and malabsorption resulting from the high intestinal worm burden, while gastric involvement is very rare [8]. An underlying malignancy constitutes an impairment of the cell-mediated immunity which translates into an immunosuppressed state, having increased risk of developing a hyperinfection syndrome [9].

The diagnosis of strongyloidiasis is hampered by the lack of a gold standard as traditional parasitological tests including direct microscopic examination, although specific, have insufficient sensitivity. Hence, novel molecular methods have been implemented, using PCR to detect the DNA of the parasite, with the aim of achieving higher sensitivity and preserving the specificity for *S. stercoralis* infection, which ranges from 93 to 95% according to the reference test [10]. Other diagnostic tools include serological tests which have high diagnostic sensitivity and specificity and can be used as a screening tool for early detection. Several immunodiagnostic tests are available to identify anti-*Strongyloides* antibodies in serum, from which enzyme assays are recommended because of their greater sensitivity (>90%), but there are concerns about their specificity due to cross-reactions with other parasites and long-term persistence of antibodies after an effective treatment [11]. Eosinophilia typically associated with parasitic infections is often present but is not a reliable marker, and its absence does not exclude strongyloidiasis [12].

This case highlights the gastric involvement by strongyloidiasis, demonstrated by hematemesis due to a giant gastric ulcer in a patient who was subsequently diagnosed with early-stage lung cancer. Diagnosis of strongyloidiasis was made by microscopic examination and further confirmed with molecular methods and serology. The

significant improvement after ivermectin treatment and without proton pump inhibitors suggests that the ulcer was induced by the parasite infection.

Regarding environmental factors, the adequate sanitation infrastructure in Portugal justifies that cases of strongyloidiasis are currently extremely rare. Nonetheless, reports suggesting endemic areas within the country in the last century makes one consider how many asymptomatic individuals might have *S. stercoralis*, which can remain quiescent in the host's intestine for as long as 30 years. The advent of modern medicine with recognition of immunocompromised states, immunosuppressive treatment, cytostatic regimens, increased incidence of diabetes, cancer, and autoimmune diseases may result in strongyloidiasis reactivation and hyperinfection syndrome in those patients.

In conclusion, strongyloidiasis is an often-underdiagnosed parasitic disease due to its low parasitic load, irregular excretion of larvae, and nonspecific symptoms. Increasing diagnosis in developed countries and nonendemic regions may occur with globalization and transmission potential to immigrants, travelers, and immunosuppressed patients. Accordingly, as a key message, it is important that physicians consider this hypothesis in the differential diagnosis of cases in which diagnosis is unclear and have an integrated approach towards control of this parasitic disease.

Statement of Ethics

The authors state that the patient provided written informed consent to publish his case, including publication of images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

International Committee of Medical Journal Editors (ICMJE) criteria were used to define authorship. Each author was considered to fulfil these criteria.

Ryan Costa Silva, Joana Rita Carvalho, Joana Rosa Martins, and Rui Tato Marinho: substantial contributions to the conception of the manuscript and interpretation of the case report; drafting the work and revising it critically for important intellectual content.

Ricardo Crespo and Nídia Zózimo: substantial contributions to the conception of the manuscript and acquisition of data for the work; critically revising the work for important intellectual content.

All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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