

Do Not Miss the Diagnosis: Not All Pink Findings Mean the Same in the Gastrointestinal Tract!

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Os diagnósticos que não devem ser esquecidos – nem todos os achados cor de rosa significam o mesmo no tubo digestivo

Palavras Chave

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The diagnosis of some gastrointestinal (GI) diseases, such as GI infections or immune-mediated disorders, can be challenging not only due to the diverse array of GI (and extra-GI) symptoms they may manifest with, but also due to the nonspecific endoscopic and sometimes even histological findings. In this supplementary issue of *GE – Portuguese Journal of Gastroenterology*, we present a compilation of articles concerning GI infections and eosinophilic GI diseases (EGIDs). Indeed, GI infections pose a significant burden in patients, health systems, and gastroenterologists and the diagnosis of EGIDs is also increasing. Of note, the national thematic meeting of the Portuguese Society of Gastroenterology (Sociedade

Portuguesa de Gastrenterologia [SPG]) in 2023 was also dedicated to GI infections and this supplementary issue reinforces the importance of this problem in our beloved specialty.

GI infections can be caused by either virus, bacteria, fungi, and parasites, showcasing a wide range of clinical manifestations, and potentially leading to long-term morbidity or even mortality. In low-income countries, GI infections particularly gastroenteritis are a main cause of mortality, especially among children [1]. In high-income countries, even if mortality is lower, GI infections are also prevalent, namely, infections such as *Helicobacter pylori* (*H. pylori*) or hepatotropic virus, which still entail a considerable burden of disease. Indeed, in 2019 it was estimated that approximately 296 million people worldwide were living with chronic hepatitis B infection, and 58 million with chronic hepatitis C infection, with viral hepatitis being estimated to be the cause of roughly 1.1 million deaths per year, the majority due to both chronic liver disease and liver cancer [2]. On the other hand, *H. pylori* infects 40–50% of the world population and is one of the most common bacterial infections globally. Typically, infection occurs during childhood and becomes persistent if left untreated, with possible long-term consequences, including peptic ulcer disease and gastric cancer [3].

Although there are disparities in GI infections across different countries, the current trend of migration is altering this landscape, posing challenges for physicians in identifying, diagnosing, and treating these diseases [4]. Similarly, immune-mediated disorders like EGIDs can also pose significant clinical dilemmas [5, 6]. The best known EGID is eosinophilic esophagitis (EoE), but the non-EoE EGIDs are now the subject of new research due to increased clinical awareness of these conditions [5, 6]. Non-EoE EGIDs can involve the stomach, small bowel, and colon, either individually or in any combination of segments, and can also vary in the depth of involvement of the GI wall layers, making the clinical presentation of EGIDs widely variable – to nonspecific symptoms such as abdominal pain to ascites if the serosa is involved [6, 7].

Laboratory tests should be performed, and peripheral eosinophilia, iron deficiency, or hypoalbuminemia can contribute to the suspicion of EGIDs. Even so, it is essential to consider and rule out alternative causes of peripheral eosinophilia, such as drug reactions, infections, malignancy, connective tissue diseases, vasculitis, Crohn's disease, hypereosinophilic syndrome, among others, to ensure an accurate diagnosis of non-EoE EGIDs [6].

Endoscopic evaluation is often performed, but the majority of endoscopic findings are nonspecific and sometimes are patchy. Biopsies play a crucial role in the diagnosis of EGIDs, and due to their patchy nature, multiple biopsies should be taken from both normal and abnormal mucosae. In some cases, full-thickness biopsies may be necessary to evaluate deeper wall involvement. However, even histology may be nondiagnostic due to suboptimal sensitivity and suboptimal specificity – indeed, the definition of GI tract eosinophilia has specific thresholds for documentation of abnormal eosinophil count that differ depending on the area of the GI tract involved but a fully consensus is not yet established [5–7]. Management can also be problematic because almost all the current therapies are from retrospective studies – either case reports and small case series. Dietary therapy for highly motivated patients can be an option, but the most used class of medications is corticosteroids [5, 6].

In this issue of *GE – Portuguese Journal of Gastroenterology*, several case reports are published reporting interesting non-EoE EGIDs and two case reports of GI parasite infections in immigrants, increasing awareness of heterogeneous prevalence of these diseases and the clinical challenge we may encounter in diagnosing them. Freitas et al. [8] describe a case of a young patient with white cords in stools and mild lower GI symptoms in whom initial investigation revealed 3 negative stool samples and normal upper and lower GI endoscopy. A small bowel

capsule endoscopy (SBCE) was decisive for the diagnosis since it showed a tapeworm infection in the small bowel without mucosal lesions. Despite this observation in SBCE, proglottids can be present in different cestode species, and without direct observation, the specific type is difficult to determine. However, treatment is independent of the cestode species, and in this case, a single dose of praziquantel 10 mg/kg allowed full clinical response [9]. This case highlights the remarkable diagnostic value of SBCE in patients' high clinical suspicion of parasite infection with negative stool results.

In another case, reported by Franco et al. [10], a young immigrant patient with upper GI symptoms and peripheral eosinophilia was found to have a duodenal stricture on upper GI endoscopy. Histopathology later confirmed *Strongyloides stercoralis* duodenitis inducing duodenal obstruction. Following appropriate treatment, the patient showed complete resolution of symptoms and laboratory abnormalities. This case underlines not only the importance of recognizing the global spread of infectious diseases that can be silent for several years, but also the need to always keep an open mind toward the different clinical presentations possible for the same infectious agent.

Tarrio et al. [11] describe the case of a 40-year-old male with nonspecific GI symptoms and unintended weight loss. Laboratory findings such as anemia, peripheral eosinophilia, and elevated calprotectin were observed, and CT scan revealed bilateral pleural effusion, low-volume ascites, and thickening of the terminal ileum. Endoscopic evaluation including ileocolonoscopy did not show significant abnormalities, but random ileal biopsies collected using antegrade motorized spiral enteroscopy demonstrated mucosal inflammation characterized by eosinophilic infiltration, approximately 35 eosinophils per high-power field, and altered eosinophil distribution within the ileal wall. After thorough exclusion of other possible causes, a diagnosis of eosinophilic ileitis was established and the patient was started on oral prednisolone with resolution of the case. This study illustrates not only the clinical diverse spectrum that patients can appear with, but also the difficulty that physicians may encounter in their diagnosis sometimes needing persistent efforts and invasive methods to establish a correct diagnosis allowing proper treatment. After ruling out more prevalent etiologies (including infectious ones), the histological samples obtained through enteroscopy were vital for the diagnosis and treatment of this patient.

In this era of globalization, a more recent infection, SARS-CoV-2, has also been a central player in daily clinical practice in the last years. Gonçalves et al. [12] share in this issue their experience about safety in endoscopy units

during the SARS-CoV-2 pandemic. In a retrospective analysis of 2,166 patients proposed to GI endoscopy who underwent either PCR screening for SARS-CoV-2 ($n = 1,521$) or a specific questionnaire ($n = 645$) up to 72 h before the procedure, only 1.4% ($n = 21$) tested positive pre-endoscopy. Follow-up until 14 days after endoscopy identified only 9 positive patients (0.42%) for SARS-CoV-2, concluding that by implementing symptom and risk contact screening measures along with the use of individual protective equipment, the possibility of infection in endoscopy units can be reduced to a negligible level. This study draws attention to the crucial role of preventive measures in the propagation of infectious diseases, as adherence to these measures can significantly reduce the transmission of pathogens.

Although very distant apart in terms of pathogenesis and treatment options, several GI infections and EGIDs share some common ground including the variability in clinical manifestations – from asymptomatic to serious complications (protein-losing enteropathy, for example) – and the (very real) struggle in reaching a definitive diagnosis that often requires a combination of laboratory, endoscopic, imagological, and histological findings.

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Statement of Ethics

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Conflict of Interest Statement

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