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Case Report

Role of Duodenal Biopsy in the Diagnosis of Giardiasis with Negative Stool Tests: A Case Report and Literature Review

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ABSTRACT

Giardia lamblia (also known as Giardia intestinalis and Giardia duodenalis) is the most frequent intestinal parasite responsible for chronic diarrhea and malnutrition. Giardia infections commonly cause nausea, abdominal cramping, bloating, and foul-smelling diarrhea in patients. Usually, Giardiasis causes a self-limiting illness, but it can progress to a severe disease in immunocompromised individuals and cause dehydration, malnutrition, and failure to thrive. As a result, early diagnosis and treatment are required to control the infection and prevent complications. Infectious Disease Society of America diagnostic guidelines recommend obtaining stool studies to diagnose Giardiasis. When stool tests are negative, but suspicion persists, a duodenal biopsy is a gold standard for diagnosis. We present the case of a patient diagnosed with Giardia by an incidental duodenal biopsy specimen obtained during a workup for malnutrition and chronic diarrhea, despite a normal stool examination. A few cases of Giardiasis have been diagnosed and reported in the literature using a duodenal biopsy. Some studies addressed the same issue, and we believe that duodenal biopsy can be a good strategy for diagnosing Giardiasis with high sensitivity and specificity.

Keywords: Duodenal Biopsy, Endoscopy, Giardia lamblia, Giardiasis, Malabsorption

INTRODUCTION

Often underestimated, Giardia lamblia is a significant contributor to global diarrheal illnesses impacting both adults and children. Approximately 200 million people fall victim to its effects annually, with 500,000 deaths reported annually.[1] In India, Giardia infection rates in diarrhea patients span from 0.4% to 70%, revealing a wide-ranging prevalence. Rural southern India reports notably high rates of asymptomatic cyst transmission, up to 50%.[2] Vulnerable populations encompass infants, young children, immunocompromised individuals, international travelers, and those with cystic fibrosis. Usually, Giardiasis causes a self-limiting illness; however, in immunocompromised cases, it can escalate into severe forms, resulting in dehydration, malnutrition, and growth issues, especially among children.[3,4] Additionally, the infection can also remain asymptomatic.

Diagnostic methodologies encompass stool antigen detection through ELISA, nucleic acid detection assays, stool examination, and duodenal biopsy. While stool examination is simple to conduct, it exhibits limited sensitivity. Duodenal aspirate with biopsy emerges as a highly sensitive and specific option.[5,6] This approach gains significance, particularly in scenarios where alternative diagnostic methods have proven ineffective, like in this case.

For individual protection, a feasible step involves boiling water vigorously for one minute, effectively eradicating Giardia cysts. In cases where boiling the water is not a viable

option, an alternative approach involves adding 2 to 4 drops of household bleach or 0.5 ml of 2% tincture of iodine to each liter of water, allowing it to stand for 60 minutes before consumption. The cold water necessitates a more extended treatment period for proper decontamination. Moreover, consuming properly cooked fresh foods plays a significant role in minimizing the intake of pathogens. Prophylaxis for giardiasis is not routinely recommended except for travel in highly endemic areas.[7]

Case History

A 21-year-old man presented with 3 months of dysphagia, abdominal pain, abdominal distention, and watery diarrhea. He did not endorse recent recreational activity like travel or camping, or exposure to animals. On arrival, he was in mild distress. Early laboratory findings were notable for eosinophils on the peripheral smear of 15% with Absolute Eosinophil Count (AEC) of 918 cells/microliter, hemoglobin of 9.6 gm/dl, from a baseline of 14.2 g/dL, and serum albumin was 3.0 (normal range: 3.5 - 5.5 g/dl) which confirmed hypoalbuminemia. Liver function tests (LFT) were baseline. Stool microscopy with Lugol's solution (Figure-1), stool culture, and Clostridium difficile toxin were unremarkable. To rule out the cause of malabsorption and eosinophilic disorder, he was taken for esophagogastroduodenoscopy and colonoscopy.

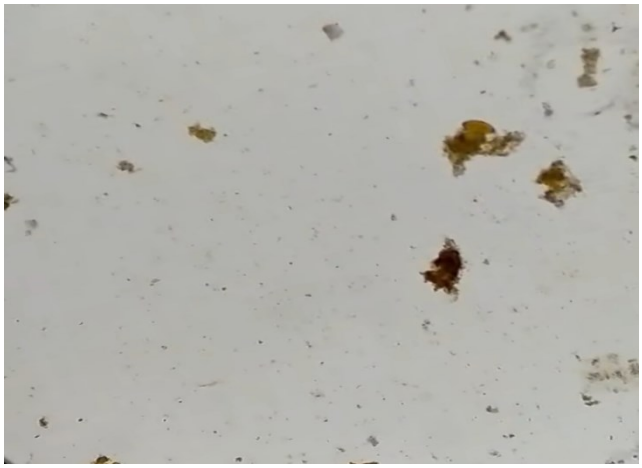

Figure-1: Stool examination with Lugol's solution (unremarkable)

An endoscopy was done which showed a normal gastric surface and duodenum. Biopsy was taken from the first and second part of the duodenum, and its microscopy revealed teardrop (pear) shaped trophozoites of Giardia between the villi (Figure-2). No granulomas, subepithelial collagen band, or neoplasm were found. The above findings confirm Giardiasis. He was treated outpatient with 2 gm of tinidazole and the follow-up was uneventful.

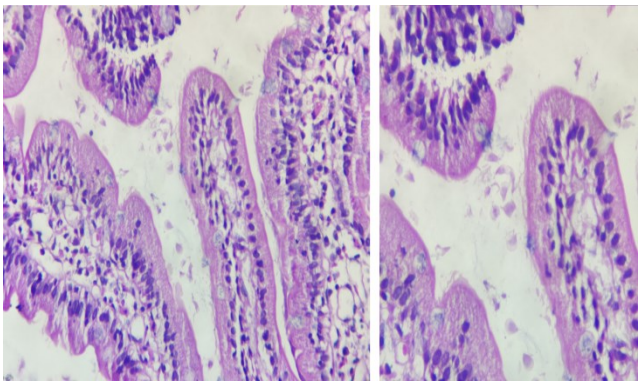

Figure-2: H & E stain showing tear-drop-like Giardia lamblia trophozoites

DISCUSSION

Giardia has two main life cycle stages: the cyst (infective) and the trophozoite (vegetative).[8] Cysts are acquired through contaminated water, occasionally from food, or via direct fecal-oral contact.[9] Following exposure to the stomach's acidic conditions, cysts transform into trophozoites in the upper small intestine. Here, they replicate and give rise to symptoms such as diarrhea and malabsorption. Subsequently, upon encountering biliary fluid, some trophozoites convert into cysts within the jejunum, eventually excreted in the faeces.[9]

Individuals affected by giardiasis can manifest in three ways: as asymptomatic carriers, acute, or chronic.[7] Asymptomatic patients can carry and shed the organism for up to six months, remaining infectious.[10] Acute infections present with a range of symptoms, including diarrhea, fatigue, nausea, and abdominal discomfort. Chronic giardiasis can be even more difficult to diagnose due to its vague abdominal symptoms. In rare instances, Giardia lamblia infection can mimic intestinal pseudo-obstruction.[11]

In Giardia lamblia infection, the epithelial barrier is compromised due to claudin-1 tight junction protein downregulation and heightened epithelial cell apoptosis. This leads to impaired sodium-dependent D-glucose absorption and the initiation of active electrogenic anion secretion. Consequently, diarrhea mechanisms in chronic giardiasis involve leak flux, malabsorption, and secretory components.[12] Following Giardia infection, post-infectious bowel dysfunctions are associated with increased duodenal mucosal cholecystokinin (CCK), with a stronger correlation to postprandial dyspeptic symptoms than serotonin (5-HT) metabolism.[13]

The diagnosis of giardiasis is made by various methods, including stool antigen assays (counter-immuno-electrophoresis, double-antibody sandwich EIA technique, nucleic acid amplification test-NAAT, indirect or direct

immunofluorescence - detect cyst or trophozoite antigens in the stool using Giardia-specific antibodies), stool microscopy, duodenal aspirate, and biopsy.[5,7,10] Every method has its advantages and limitations. While examining a single stool specimen yields only 30% to 50% sensitivity, investigating at least three stools before considering alternatives is advised.[5] However, stool assays remain valuable due to their cost-effectiveness and easy to perform. Despite stool assays' simplicity and reasonable specificity, their relevance decreases in asymptomatic cases, given the risk of false negatives.

As per IDSA (Infectious Disease Society of America) guidelines, duodenal aspirate microscopy is recommended for suspected infections like Giardia, Strongyloidiasis, Cystospores, or Microsporidia when stool studies are negative. This approach is sensitive due to the abundance of trophozoites in the proximal small bowel, aided by their motility and the clear appearance of aspirate fluid. Drawbacks encompass invasiveness, potential sample contamination, and challenges in cultivation under standard culture conditions. Here, a recommended option is duodenal biopsy. While more accurate than stool tests and microscopy, duodenal biopsy is often overlooked due to its invasiveness and complexity. Surprisingly, it is not consistently mentioned in key guidelines like the IDSA.[6,14] A duodenal biopsy is a preferred choice, especially when stool tests are negative, though it requires higher expertise than stool tests.

In Giardiasis, the duodenum often appears normal during endoscopy.[15,16] However, duodenal biopsy reveals villous atrophy, elevated intraepithelial lymphocyte count, increased lymphoid follicles, and the presence of Giardia lamblia trophozoites.[15] Importantly, obtaining duodenal mucosal biopsies for histological evaluation might eliminate the need for separate duodenal aspirates targeting Giardia.[16]

When assessing unexplained malnutrition or persistent diarrhea with normal lab results, duodenal biopsy often detects Giardia lamblia. Seven studies back our suggestion of using duodenal biopsy when stool tests and microscopy fail to identify the pathogen (Table-1).

Treatment includes supportive care and antimicrobial therapy.[3] Tinidazole is the main medication, while metronidazole is preferred for children and paromomycin for pregnant women.[3] In pomegranate extract-treated animals, histological and scanning electron microscopy showed restored villi structure, reduced atrophy, fewer lymphocytes, and protected intestinal cells from apoptosis.[20]

Table-1: Reported cases that required duodenal biopsy for diagnosis of Giardiasis

Patients	History	Authers
A 27-year-old man	Abdominal pain and weight loss without change in appetite	M Ammar Kalas [10]
A 42-year-old woman	Chronic abdominal discomfort, change in bowel movement, and normal initial laboratory work-up	Vito Domenico Corleto[17]
A woman in her 40s	Clinical features of pseudo-obstruction for the last 2 weeks and abdominal discomfort, loose stool and weight loss for the last 6 months	Tommaso Pessarelli[11]
A 64-year-old male	Fatigue and abdominal pain for the last 6 months and his laboratory work-up showed only microcytic hypochromic anemia	Isma Javed [3]
A 9.5-year-old child	Diarrhea or pasty stools and abdominal pain. The feces from patient were processed seeking for pathogenic bacteria and the microscopic examination looking for cysts and ova after the centrifugation-concentration method was negative for cysts and eggs.	Mario Noe' Martinez-Gordillo[18]
A 59-year-old man	Alcoholic cirrhosis, chronic hepatitis C, and hepatocellular carcinoma presented with 2 weeks of abdominal distention, watery diarrhea, and prior to arrival, a half cup of bright red blood per rectum. Stool studies were negative	Kevin Groudan[6]
21 children with suspected giardiasis	Out of them, duodenal biopsy confirmed 12, while duodenal aspirate confirmed only 10 and stool microscopy confirmed only 6	Kamath and Murugasu[19]
A 21-year-old man	3 months of dysphagia, abdominal pain, abdominal distention, and watery diarrhea	This study

CONCLUSIONS

Diagnosis of giardiasis can be challenging, especially when the patient presents with malnutrition with negative stool tests or in asymptomatic patient. Despite good sensitivity, there is a high chance of false negative results with non-invasive tests. At the same time, duodenal biopsy has reasonable sensitivity and specificity and is essential in identifying causative pathogens and ruling out other causes of malnutrition in such cases.

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