

Title:

Late metastases: a rare cause of diarrhea

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Late metastases: a rare cause of diarrhea

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Dear Editor,

We present the case of a 64-year-old female, who was diagnosed in 2011 with invasive lobular breast carcinoma locally advanced, treated with surgery, chemo and hormone therapy, and discharged from the Oncology service after 10 years disease-free.

In November 2022, she underwent an endoscopic study due to 2 years of diarrhea and weight loss. A complete colonoscopy with ileoscopy demonstrated the colon's mucosa, haustra and distensibility without alterations. Following clinical guidelines, biopsies were taken from cecum, ascending colon, transverse colon, descendent-sigmoid colon and rectum to study diarrhea.

Histological study of the samples showed multifocal infiltration of the large intestine's lamina propria by cells with morphology and immunophenotype (positive for CKAE/AE3 and GATA 3 and negative for estrogen receptors and HER2) compatible with lobular breast carcinoma (Fig. 1 A-D).

The patient is referred to the Oncology department which performs disease staging, revealing pancreatic lesions and splenic vein thrombosis suggesting metastatic origin. The patient is currently ongoing treatment with chemotherapy with Folfirinox regimen.

Breast cancer is the most common malignant tumor in women, with a 5-year survival rate of 31% in disseminated stages (1). Up to 30% of patients develop metastases during the disease (2), usually through the lymphatic system (3). Given the type of dissemination, metastases in the gastrointestinal tract are extremely rare (4): estimated by clinical case series in less than 5% and



up to 35% in autopsy series (2). Stomach is the most frequently affected location (60%) (5), followed by esophagus (12%), colon (11%), and rectum (4). The timeframe for diagnosis goes from 3 months up to 25 years after the detection of the primary tumor (3).

Only 20% of cases present symptoms, the most common ones being bowel obstruction (40.6%), followed by bleeding and perforation (3). Up to 30.1% of patients present non-specific symptoms such as change in bowel habits (3). Gastrointestinal metastases darken the prognosis(4), with a survival rate median of 12 months after diagnosis (3).

Diagnosis is challenging due to nonspecific findings (table 1). Imaging modalities frequently show mural thickening. Endoscopic findings may vary from showing normal macroscopic mucosa to showing erosions, ulcers or nodularity. Definitive diagnosis is histological.

In conclusion, secondary gastrointestinal affectation due to cancer is rare with nonspecific symptoms and long latency periods, thus needing a high level of suspicion. Biopsy sampling by segments in patients with diarrhea allows the diagnosis of entities such as microscopic colitis, but also for less frequent entities such as the case presented.

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TABLES

Table 1. Differential diagnosis of chronic diarrhea	
With macroscopic findings by endoscopic examination	Without macroscopic findings by endoscopic examination
Chronic infectious diseases	
Bacterial infection: intestinal tuberculosis, Whipple's disease, Yersinia infection Viral infection: Cytomegalovirus infection, VIH enteritis Parasitic infection: amebic colitis, Giardia lamblia, <i>Strongyloides stercoralis</i> infection, Cyclospora infection Fungal infection: Histoplasma infection	Bacterial overgrowth
Inflammatory bowel diseases	
Crohn's disease Ulcerative colitis Diverticulitis Behçet's disease Celiac disease Post-radiation colitis	Eosinophilic gastroenteritis Microscopic colitis
Neoplasms	



Table 1. Differential diagnosis of chronic diarrhea

Gastrointestinal metastases Colon cancer Gastrointestinal malignant lymphoma Villous adenoma of rectum	Gastrointestinal metastases VIPoma, somatostatinoma, gastrinoma Pheochromocytoma, carcinoid syndrome Medullary thyroid cancer Pancreas cancer
Malabsorption syndrome	
	Lactose intolerance Dumping syndrome Bile acid diarrhea Exocrine pancreatic insufficiency
Motility disorders	
	Irritable bowel syndrome Functional diarrhea
Drug-related	
	Drug-induced collagenous colitis: non-steroidal anti-inflammatory drugs, proton pump inhibitors, angiotensin receptor antagonists. Ursodeoxycholic acid, antibiotics, DPP4 inhibitors, immune checkpoint inhibitors, lactulose and other laxative medication abuse Alcohol
Vascular diseases	
Ischemic colitis	
Systemic disorders	



Table 1. Differential diagnosis of chronic diarrhea

Cap polyposis	Endocrine disorders: diabetes mellitus, hyperthyroidism, hypoparathyroidism, adrenal insufficiency Deposition diseases: amyloidosis Immune related diseases: mastocytosis, hypogammaglobulinemia
Postsurgery disorders	
Short bowel syndrome	Blind-loop syndrome Post-cholecystectomy Postvagotomy, postsympathectomy

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FIGURES

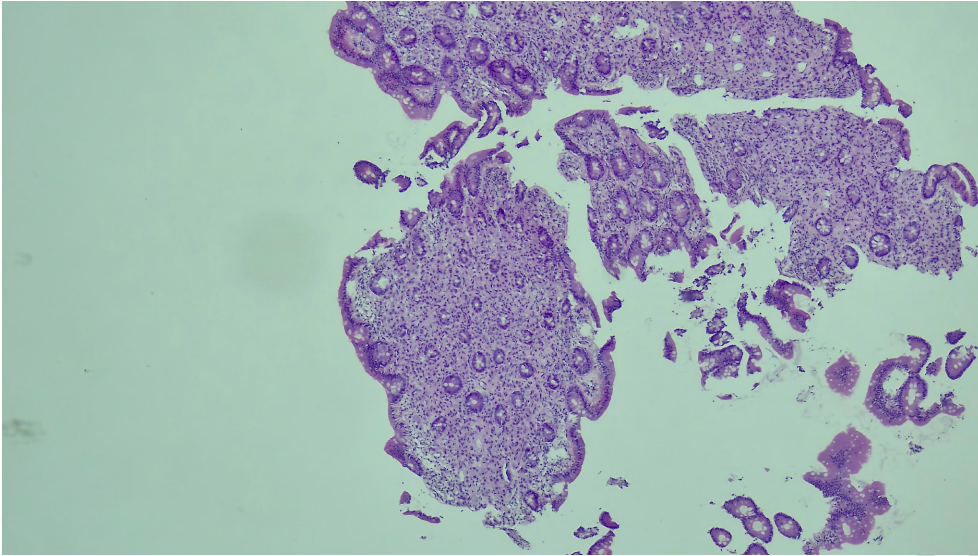


Fig 1. Densely cellular neoplastic population infiltrating colonic lamina propria (H&E, x40).

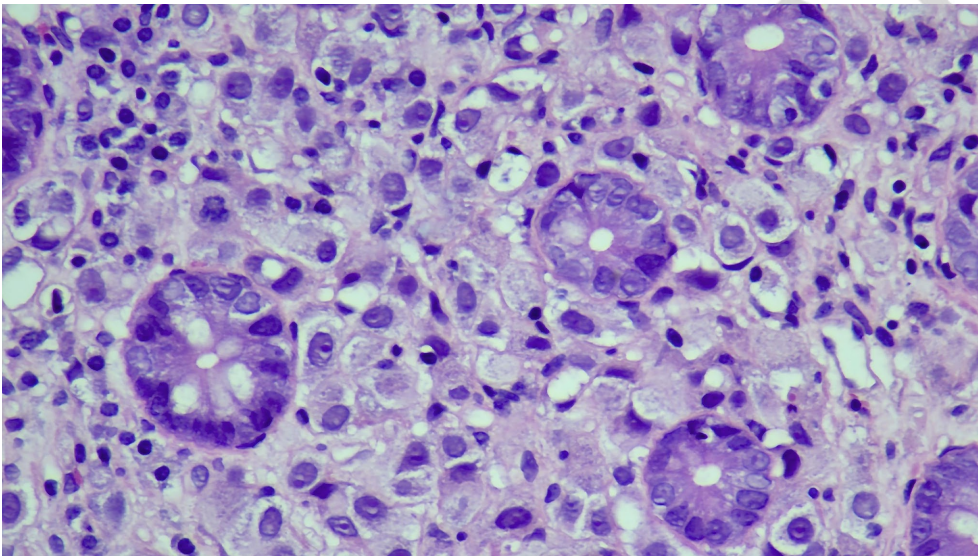


Fig 2. Intermedium-sized discohesive cells with abundant clear eosinophilic cytoplasm, round nuclei and prominent nucleoli (H&E, x400).

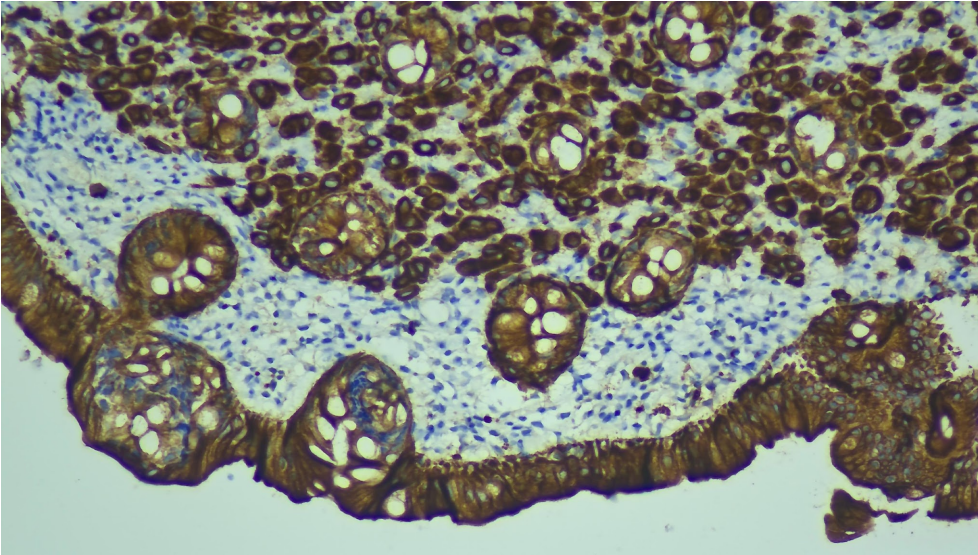


Fig. 3. Pan-keratin (AE1/AE3) cytoplasmic positivity in tumoral cells (x200).

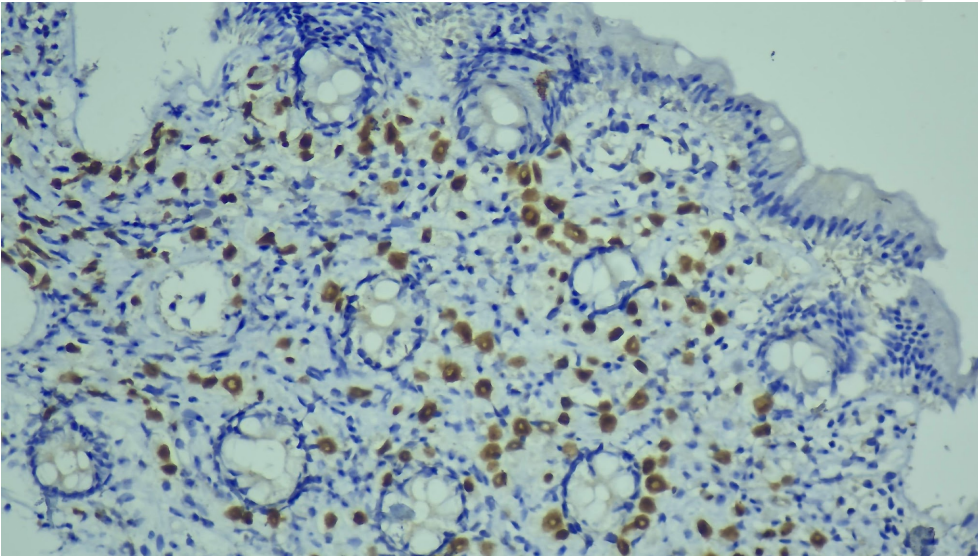


Fig 4. GATA3 nuclear positivity in tumoral cells (x200).