

A little known cause of ischemic colitis

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Abstract

Acute ischemic colitis associated with the use of neuroleptic agents is a rare but potentially life-threatening condition, and its true incidence is likely underestimated. The exact pathophysiological mechanisms underlying this complication remain poorly understood. Sigmoidoscopy or colonoscopy is considered the gold standard for diagnosis, although various imaging modalities can also aid in the diagnostic process. Preventive measures primarily involve the management of constipation and the reduction of risk factors. In cases of suspected neuroleptic-induced ischemic colitis, prompt adjustments in medication—either through dose reduction or substitution with alternative antipsychotics—should be considered. This article presents two cases of ischemic colitis caused by neuroleptic treatment, emphasizing the critical importance of early diagnosis and timely intervention. (*Acta gastroenterol belg.*, 2026, 89, 79-82).

Keywords: Ischemic colitis, neuroleptica .

Introduction

Acute ischemic colitis is the most common subtype of intestinal ischemia (1, 2). It occurs when blood flow to the colon is reduced to levels insufficient to meet the oxygen and nutrient demands of cellular metabolism. This condition can result from both occlusive and non-occlusive etiologies. Studies suggest that ischemic colitis may be more common in females (3). The diagnosis and treatment of this condition can be challenging (4).

Although neuroleptic medications are an uncommon cause, they can contribute to the development of this disorder (5, 6). We report two cases of neuroleptic-induced ischemic colitis with distinct clinical presentations, and review the existing literature on this topic (7, 8). Healthcare providers should be aware of the need to identify and manage this potentially life threatening side effect of neuroleptics (2).

Case Report (1)

A 26-year-old male was admitted to the emergency department with acute abdominal pain and diarrhea, accompanied by significant blood loss during bowel movements. His medical history included allergic asthma, allergic rhinoconjunctivitis and psychiatric problems (severe psychosis). The patient has been treated with clozapine (Leponex) for the past five years. A few months prior to admission, fluoxetine, a selective serotonin reuptake inhibitor, was added to his treatment regimen. Additionally, he was taking valproic acid (Depakine) and lamotrigine.

Abdominal ultrasound revealed thickening of the bowel wall in the region of the left colonic frame. Sigmoidoscopy demonstrated colitis involving the splenic flexure, sigmoid colon, and descending colon, findings that were primarily suggestive of ischemic colitis (Figure 1). Histopathological examination confirmed ulcerative changes of the colonic mucosa, most consistent with ischemic colitis. There was no evidence of inflammatory bowel disease or dysplasia.

Based on these findings, a diagnosis of ischemic colitis was made, and a conservative treatment was initiated, including bowel rest and intravenous fluids. In consultation with the psychiatrist, fluoxetine was gradually tapered and eventually discontinued, and the clozapine dosage was reduced. The patient responded well to treatment, with resolution of symptoms and no recurrence observed during a one-year follow-up period.

Case Report (2)

A 70-year-old woman was hospitalized because of psychiatric symptoms. She had a history of cholecystolithiasis, hyponatremia, polyneuropathy, bipolar disorder and ethyl abuse, but no specific cardiovascular risk factors and no cardiac arrhythmia. She was transferred to the gastroenterology department due to a sudden onset of colicky abdominal pain with significant red blood loss in the stool.

A comprehensive blood test was reassuring, showing no signs of inflammation, and a stool sample was negative for enteropathogens. Sigmoidoscopy revealed a pronounced presentation of ischemic colitis (Figure 2). There was a sinus rhythm, and no underlying risk for cardiogenic embolism.

She had recently been started on olanzapine (Zyprexa) and risperidone (Risperdal), after her admission to the psychiatric ward a few weeks earlier. A vascular abnormality was ruled out through computed tomography angiography (CT angiography). The suggestion was made of an olanzapine-induced ischemic colitis.

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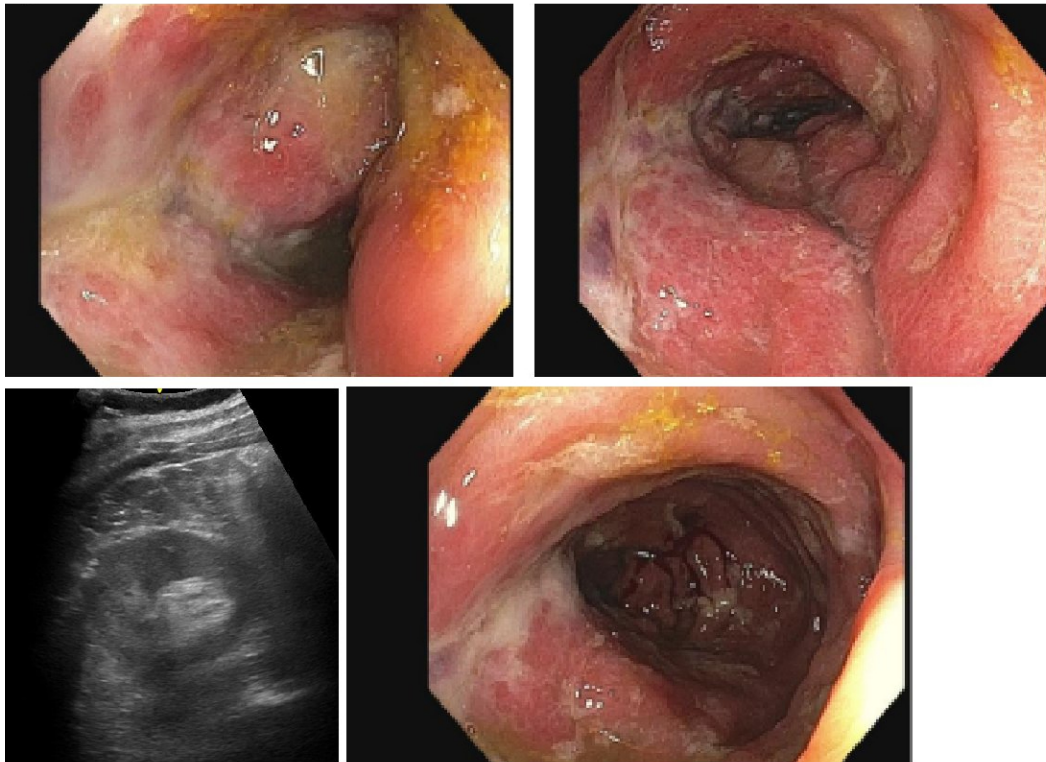


Figure 1. — Endoscopic and ultrasound findings of patient 1. Sigmoidoscopy revealed colitis affecting the splenic flexure, sigmoid colon, and descending colon. Abdominal ultrasound showed thickening of the bowel wall in the left colonic region.

A conservative treatment was started with bowel rest, intravenous fluids and antibiotics (levofloxacin and ornidazol) for seven days. In consultation with psychiatric colleagues, olanzapine was replaced by aripiprazol (Abilify). There was a favourable clinical outcome, and the patient was discharged from the hospital in good general condition, without any recurrence.

Discussion

Acute ischemic colitis is caused by transient vascular flow deprivation (1, 2). The incidence is likely underestimated, with an approximate annual rate of 4 to 5 cases per 100,000 people (3). One of the most important risk factors is age - up to 90% of cases occur in patients older than 60 (3). There is an association with various medical conditions, including cardiovascular diseases (such as hypertension, diabetes mellitus, dyslipidemia, heart failure and atrial fibrillation), viral/bacterial infections, inflammatory diseases (such as Crohn's disease and coeliac disease), cerebrovascular diseases and vasculitis (3, 4).

Several medications or drugs have been linked to ischemic colitis, including digitalis, diuretics, non-steroidal anti-inflammatory drugs (NSAID), sumatriptan, oral decongestant containing pseudoephedrine or phenylephrine, and cocaine (2, 4). Although rarely, neuroleptics have also been associated with this disease (5-8).

Ischemic colitis is a rare side effect of antipsychotics, especially phenothiazines and atypical antipsychotics (6, 8). Published in 1984, the article 'Ischaemic Colitis Associated with Psychotropic Drugs' by Gollock and Thomson was the first to document neuroleptic induced ischemic colitis in the medical literature (8). The study by Blayac et al. retrospectively reviewed all cases of ischemic colitis and intestinal necrosis related to antipsychotics registered in the French Pharmacovigilance Database (FPD) up to December 2006 (6). A total of 38 patients were included, of whom 24 underwent surgical intervention, ranging from partial to total bowel resection. Meanwhile, several case reports have been published on ischemic colitis in patients treated with clozapine, olanzapine or SSRI (5-7).

The exact underlying mechanism remains unclear. Several causes are considered, including blockage of peripheral anticholinergic receptors, blockage of antiserotonergic receptors and anti-dopamine effects (6, 7). This could explain the significantly higher incidence of ischemic colitis with clozapine, compared to olanzapine, as the first one has a higher affinity for cholinergic and serotonergic receptors (6). Blocking these receptors limits gastrointestinal smooth muscle contraction, leading to slowed intestinal transit (6, 7). Severe fecal constipation could increase intraluminal pressure, causing a reduction in blood flow and leading to ischemia. Loss of mucosal integrity can eventually cause transmural necrotizing colitis with bacterial translocation and sepsis (6, 7, 9).

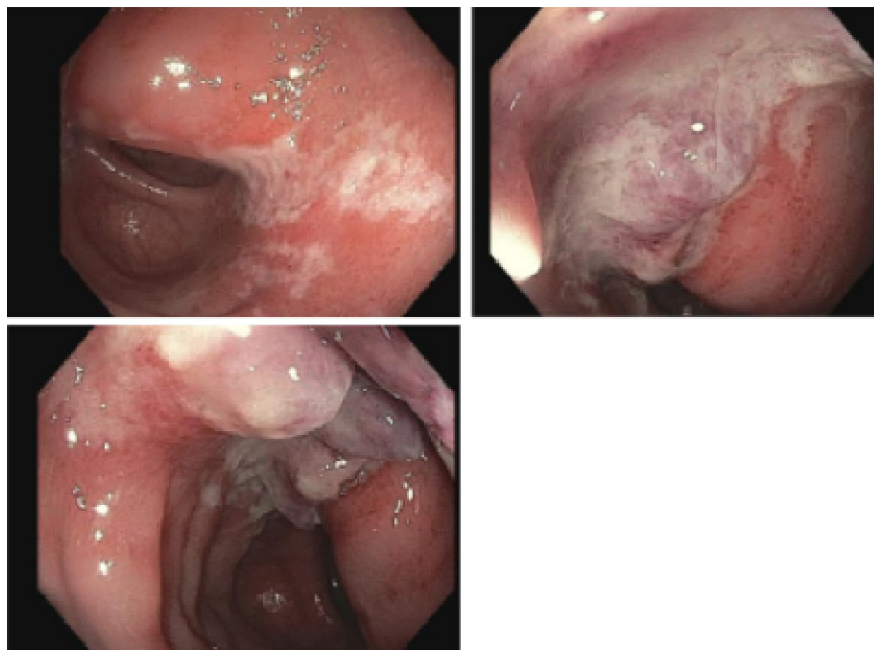


Figure 2. — Endoscopic findings of patient 2. Sigmoidoscopy revealed a pronounced presentation of ischemic colitis, similar to the findings in patient 1.

A risk factor for developing ischemic colitis when using neuroleptics is the combination with other therapies that have anticholinergic effects, such as tricyclic antidepressants and antiparkinsonians (6). The effect of neuroleptic dose and duration of use on the development of this disease is unknown. Inhibition of mesenteric vasodilation through interaction with dopamine receptors, particularly D1 and D2 receptors, could also play a role (2, 6).

The clinical presentation is atypical. The hyperactive phase occurs shortly after the effective occlusion or relative hypoperfusion and is characterized by severe pain and bloody stools, while clinical examination often remains normal (3, 4). This is followed by a paralytic phase, during which the pain diminishes but becomes more diffuse and continuous, accompanied by abdominal distension (4). Finally, in rare but severe cases of transmural ischemia, a shock phase can occur, involving leakage of fluids, electrolytes, and proteins through the gangrenous mucosa, leading to hypovolemic shock and metabolic acidosis (3, 4). A differential diagnosis should be considered, including diverticulitis, radiation enteritis, solitary rectal ulcer, lymphoma, and carcinoma (3, 4).

The gold standard for diagnosing ischemic colitis is sigmoidoscopy or colonoscopy. These procedures allow assessment of both the severity and extent of the disease and provide the option to take biopsies (3, 4). However, they are contraindicated in severe cases or when signs of peritonitis are present. Blood tests are also an important step in the diagnostic process, although no specific markers exist. A normal lactate level does not rule out ischemic colitis.

There are also various imaging techniques. Findings on an abdominal x-ray are usually nonspecific.

However, the thumbprinting sign, which indicates edema of the mucosal folds, is observed in 20% of the cases. This radiological sign is not exclusive to ischemic colitis; it can also be seen in diverticulitis, infectious or inflammatory colitis, lymphoma, and amyloidosis (3, 4).

In abdominal CT scans, initial findings are often normal. However, in some cases, thickened bowel wall, pneumatosis, an irregular bowel wall, or free fluid may be detected. The presence of a double halo sign suggests reduced blood flow, a finding commonly associated with colitis. In contrast, abdominal ultrasound can rapidly reveal abnormalities such as bowel wall thickening, pericolic fat changes, and stratification of the wall layers. This allows for a rapid and clear assessment of the severity and extent of colitis. Of course, a skilled operator is crucial for ensuring accurate evaluation. Angiography is rarely helpful in diagnosing ischemic colitis (4).

The first step in preventing ischemic colitis is primarily to avoid or treat constipation, especially in psychiatric patients who are often sedentary and polymedicated (6, 7). This can be achieved through regular physical activity, adequate hydration, and sufficient fiber intake. Patient education plays a crucial role in this process. Carefully reviewing the medication list, with the aim of avoiding combinations of different anticholinergic drugs, is an important responsibility of the physician (6). Treatment may involve a conservative approach for the majority of mild and self-limiting cases, including bowel rest (parenteral nutrition) and intravenous fluids.

Reduction of doses or switching to other antipsychotic drugs should always and immediately be considered.

For example, aripiprazole is not as strongly linked to ischemic colitis as other antipsychotic drugs (9).

Only in rare and more severe cases might intestinal decompression through nasogastric tube placement or enemas be necessary, along with the initiation of broad-spectrum antibiotics to reduce the risk of bacterial translocation when signs of localized peritoneal inflammation are present (1, 4). In the most severe cases involving transmural ischemia, surgical intervention will be required, involving the placement of a temporary stoma. Restoration of intestinal transit in a second phase may or may not be performed, depending on the extent of the disease (3, 9).

In conclusion, ischemic colitis associated with neuroleptics is an uncommon but potentially serious condition. Efforts should focus on preventing constipation in these patients, in order to eliminate this risk factor and thereby reduce the incidence of ischemic colitis (6, 7). The impact of neuroleptic dose and duration of use on the development of this disease remains unknown, and the exact mechanism causing the ischemia is still unclear (2, 6, 7).

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