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CASE REPORTS

Olanzapine-induced ischemic colitis

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ABSTRACT

Background: Ischemic colitis (IC) is an uncommon adverse event associated with antipsychotic agents, more commonly found with phenothiazine drugs and atypical neuroleptics such as clozapine. The risk of developing ischemic colitis increases when anticholinergic drugs are associated.

Case report: We report the case of a 38-year-old woman with a history of schizoaffective disorder who had been on chronic quetiapine for 3 years, and presented to the ER because of diarrhea for 5 days. Four months previously, olanzapine had been added to her psychiatric drug regimen. Physical examination revealed abdominal distension with abdominal tympanic sounds and tenderness. Emergency laboratory tests were notable for increased acute phase reagents. Tomography revealed a concentric thickening of the colonic wall in the transverse, descending and sigmoid segments, with no signs of intestinal perforation. Colonoscopy demonstrated severe mucosal involvement from the sigmoid to the hepatic flexure, with ulcerations and fibrinoid exudate. Biopsies confirmed the diagnosis of ischemic colitis. The only relevant finding in her history was the newly added drug to her baseline regimen. An adverse effect was suspected because of its anticholinergic action at the intestinal level, and the drug was withdrawn. After 6 months of follow-up clinical, laboratory and endoscopic recovery was achieved.

Discussion: Antipsychotic medication should be considered as a potential cause of ischemic colitis, particularly atypical antipsychotics such as clozapine and olanzapine; despite being uncommon, this adverse event may result in high morbidity and mortality.

Key words: Ischemic colitis. Olanzapine. Antipsychotic drugs.

INTRODUCTION

Ischemic colitis (IC) is the most common cause of intestinal ischemia, and represents around 50% of cases. It results from transient vascular flow deprivation in the colon (1,2). Most cases resolve spontaneously, but others progress to more severe presentations that require surgical management (2). Incidence rates vary with age, and oscillate from 1.1 per 100,000 inhabitant-years among patients younger than 40 years to 107 per 100,000 inhabitant-years among those at or above 80 years of age. It typically involves elderly patients with multiple comorbidities, and is associated with high in-hospital mortality (11.5%) and surgery (17%) rates (3). In clinical practice many cases are overlooked because of mild or transient presentations with no clear trigger.

Several drugs have been associated with the development of intestinal ischemia, including digitalis, diuretics, estrogens, antibiotics, and non-steroidal anti-inflammatory drugs (4). IC is an uncommon adverse event of antipsychotic drugs, particularly phenothiazines and atypical or second-generation compounds (5). The effect of these drugs is enhanced when anticholinergics are associated. Clozapine is the atypical antipsychotic most commonly described in the literature as a cause of IC (6). In contrast, the IC risk associated with quetiapine is lower given its milder anticholinergic potential (7).

CASE REPORT

We report the case of a 38-year-old woman with a history of schizoaffective disorder on quetiapine (Seroquel®) (300 mg/day) for 3 years who presented to the emergency room with diarrhea (4-5 liquid stools for 5 days, without abnormal components). Four months previously another atypical antipsychotic agent, olanzapine (Zyprexa®) (20 mg/day), had been added to her regimen for improved symptom control. Physical examination was notable for: fever at 38.5 °C, fast heart rate at 116 beats per minute, and blood pressure at 120/74 mmHg. Her abdomen exhibited distension with marked tympanism and highly reduced peristaltism, had tenderness in the lower third, and no masses or visceromegalies could be discerned.

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Emergency labs were notable for leukocytosis at 12,000 cells/mm^3, hemoglobin at 11.2 g/dl, C-reactive protein (CRP) at 249.1 mg/dl, erythrocyte sedimentation rate (ESR) at 89 mm/h, and fibrinogen at 876 mg/dl. Blood culture, urine culture, fecal parasites and coproculture were tested, as well as *Clostridium difficile* toxin. All results were negative.

Computerized tomography (CT) revealed a smooth, diffuse, concentric dilation and thickening of the colonic wall with extensive transverse, descending and sigmoid colon involvement (Fig. 1). Suspicion of inflammatory/infectious colitis prompted colonoscopy, which confirmed the colonic segmentary involvement from the sigma to the hepatic flexure in the form of ulcerations and fibrinoid exudates (Fig. 2). Biopsies were taken from the affected colonic mucosa. Histology revealed exuberant granulation tissue in association with thick fibrinoid necrosis bands, interstitial edema with capillary congestion, and extensive RBC extravasation alternating with focally hyalinized fibrotic areas. These findings were consistent with ischemic colitis. A thyroid function profile and hypercoagulability and autoimmunity studies were ordered at the gastroenterology ward, which yielded negative results.

A satisfactory outcome was obtained with fluid therapy and antibiotics. Diarrhea and abdominal distension improved gradually. The patient's ischemic colitis was deemed related to the prior introduction of olanzapine because of this drug's anticholinergic action and impact on intestinal motility. A psychiatric consultation was called for evaluation, and olanzapine was replaced with a different antipsychotic drug, paliperidone (Invega®). The patient evolved satisfactorily following discharge, and was in clinical, laboratory and endoscopic remission at 6 months. Endoscopic follow-up at 1 year showed complete lesion healing. After 2 years the patient remained on psychiatric therapy with quetiapine and paliperidone, and free from intestinal ischemia.

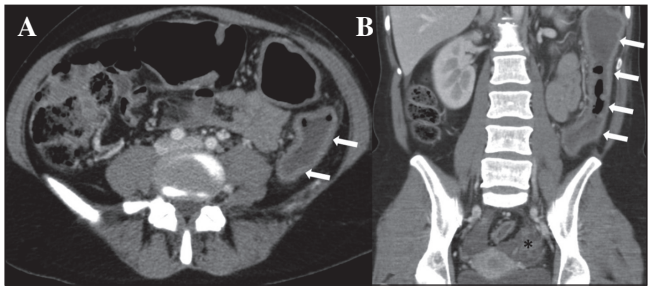

Fig. 1. Transversal (A) and coronal reconstructed (B) CT scans, where a smooth, concentric thickening of the descending colonic wall may be seen (white arrows), with a minimal amount of free fluid within the pelvis (asterisk).

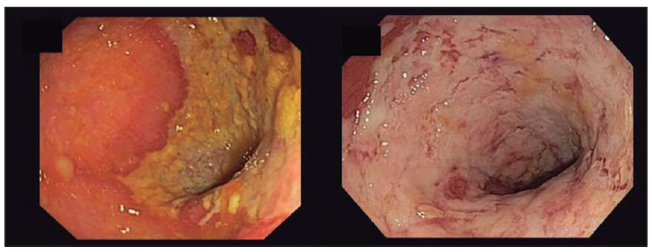

Fig. 2. Endoscopic findings consistent with ischemic colitis.

DISCUSSION

IC is the most common form of intestinal ischemia (1). It develops typically in elderly patients with multiple comorbidities. It has been associated with various medical conditions: cardiovascular disease (blood hypertension, diabetes mellitus, dyslipemia, heart failure, ischemic heart disease, atrial fibrillation), cerebrovascular disease, history of abdominal or cardiovascular surgery, and systemic ailments such as vasculitis (2,3). Furthermore, various drug types have been related to IC development, including chemotherapy agents, antibiotics, digitalics, psychiatric drugs, nonsteroidal anti-inflammatory drugs, diuretics, and laxatives (4).

IC is a rare adverse effect of antipsychotic medication. It is more common with phenothiazines and atypical or second-generation antipsychotics (particularly those with anticholinergic activity) (5,6). The effect of these drugs is enhanced when other anticholinergic drugs are associated. Hypomotility and constipation resulting from the anticholinergic and antiserotonergic effects of antipsychotic drugs have been suggested as the primary precipitants of intestinal ischemia (4-6). Constipation has been recognized as a common issue among the psychiatric population as a result of psychoactive drugs such as antipsychotics (8). Several cases have been reported suggesting the role of olanzapine and clozapine in IC development (8,9). However, clozapine is the antipsychotic agent most commonly described as a cause of IC in the literature. Despite this, the incidence of clozapine-induced IC is low (6).

In this paper we report the case of a young woman (38 years of age) who developed IC following the addition of a second antipsychotic drug (olanzapine) to her baseline chronic regimen (quetiapine) for three years. Following the discontinuation of olanzapine and introduction of paliperidone, another antipsychotic with much lower anticholinergic activity, the patient rapidly experienced clinical, laboratory and endoscopic improvement (10).

In the literature, quetiapine has demonstrated a lower association with IC development as compared to other antipsychotics because of a milder anticholinergic effect (7). The association of both antipsychotics likely resulted in a synergistic enhancement of anticholinergic effects on intestinal motility, hence triggering IC. Therefore, the joint administration of drugs with anticholinergic actions, including benztropine, tricyclic antidepressants and anti-

psychotics, may enhance intestinal hypomotility and result in functional intestinal obstruction with increased intraluminal pressure. Thus, colonic mucosal perfusion is compromised with the result of intestinal ischemia and colonic necrosis or perforation (5).

Currently there is no clear evidence that lower antipsychotic doses may reduce gastrointestinal adverse effects. Therefore, close monitoring and patient education on the potential side effects of this medication is crucial. To prevent the constipation associated with these drugs a high-fiber diet may be recommended, as well as abundant fluid intake and physical activity to minimize the anticholinergic effects of antipsychotic medications (11). Furthermore, the association of other psychoactive drugs with anticholinergic properties should be avoided.

To conclude, it is important that antipsychotic drugs, particularly atypical neuroleptics such as clozapine and olanzapine, are considered as a potential cause of IC, as this adverse effect, although uncommon, may result in high morbidity and mortality.

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