## t is illegal to post this copyrighted PDF on any website. Repeat Ischemic Colitis

## in a Patient Taking Quetiapine

**To the Editor:** Some atypical antipsychotic medications such as clozapine and quetiapine antagonize the muscarinic receptors, which lead to anticholinergic side effects such as constipation and gastric outlet obstruction. We present a case of repeat ischemic colitis in a patient taking quetiapine. According to our review of the literature, this is the only case depicting 2 episodes of ischemic colitis in the same patient taking quetiapine.

**Case report.** Ms A is a 65-year-old woman with *DSM-5* bipolar I disorder with history of psychotic features, unspecified anxiety disorder, borderline personality disorder, and alcohol use disorder in full sustained remission. Her medical history was significant for gastroesophageal reflux disease, hypertension, hyperlipidemia, overweight, chronic constipation, and asthma. She presented with abdominal pain, nausea, vomiting, light-headedness, and constipation and was admitted to the medical floor. Computed tomography scan of the abdomen and pelvis showed wall thickening involving the transverse, descending, and sigmoid colon consistent with colitis. Testing showed her white blood cell count was elevated at  $12.7 \times 10^9$ /L; her erythrocyte sedimentation rate, which was initially 48 mm/h at admission, rose to 69 mm/h; and her creatinine level was elevated at 1.36 µmol/L.

The gastroenterology department performed flexible sigmoidoscopy, which showed ischemic colitis with evidence of moderate, nongangrenous ischemia proximal to rectosigmoid until at least the distal transverse colon. This patient had 1 prior episode of ischemic colitis 10 years earlier. Leading up to the first episode, quetiapine had been slowly titrated up from 50 mg to 600 mg. Her other psychiatric medications during the first episode of ischemic colitis included long-acting risperidone injection 50 mg every 2 weeks, hydroxyzine 25 mg twice/day, amitriptyline 25 mg at bedtime, and lamotrigine 250 mg at bedtime. Her ischemic colitis resolved with symptomatic treatment, and her psychiatric medications, including quetiapine, were continued. These 2 episodes of ischemic colitis were unexpected given that Ms A had few risk factors for this vascular disease. Psychiatry evaluation was requested due to concern that psychiatric medications could be involved.

Her mental illness was well-controlled on quetiapine 200 mg 3 times/day and 50 mg at bedtime, long-acting risperidone injection 50 mg every 2 weeks, hydroxyzine 25 mg 3 times/day as needed for anxiety, lamotrigine 250 mg at bedtime, and amitriptyline 25 mg at bedtime with no recent changes. She had been taking quetiapine for over 10 years.

Quetiapine and amitriptyline have been associated with ischemic colitis. We recommended that she taper off quetiapine, discontinue amitriptyline, and add melatonin with close outpatient follow-up with her psychiatrist. Ms A's medical condition stabilized, and she was discharged 2 days later. At outpatient psychiatry follow-up, her depression was noted to have worsened. Thus, she was started on aripiprazole 10 mg and quetiapine was discontinued. At her follow-up gastrointestinal appointment, the physician documented resolution of symptoms including "no melena, no hematochezia, and no nausea, vomiting, or abdominal pain."

Major risk factors for ischemic colitis include cardiovascular disease, diabetes mellitus, chronic obstructive pulmonary disease,

independent risk factor, but older patients are more likely to have identified risk factors. However, American College of Gastroenterology clinical guidelines<sup>1</sup> indicate that there are no specific identifiable risk factors for ischemic colitis in most patients. The heterogeneity of risk factors in most patients points toward a multifactorial pathogenesis.<sup>1</sup>

Medication-induced colonic ischemia is uncommon and has largely been reported in the form of case reports, with the most recent available review<sup>5</sup> published in 2009. Wellestablished associations include cocaine, ergotamine, estrogens and progesterones, and sodium polystyrene in sorbitol. Probable associations include alosetron,  $\alpha$ -interferon, amphetamines, digitalis, dopamine, epinephrine and norepinephrine, methysergide, nonsteroidal anti-inflammatory drugs, pseudoephedrine, vasopressin, tricyclic antidepressants, and atypical antipsychotics.<sup>2</sup> We present the first case report, to our knowledge, of repeat ischemic colitis in a patient taking an atypical antipsychotic, as this patient had 2 incidents of ischemic colitis while taking quetiapine separated by a 10-year interval.

Several atypical antipsychotic medications are commonly associated with gastrointestinal side effects, including constipation and gastric outlet obstruction. Rarely, gastrointestinal hypomotility and constipation can promote ischemia by increasing intraluminal pressure and compression of mucosal vessels. Subsequently, bacterial translocation, inflammation, and ischemia of the bowel wall can occur, resulting in ischemic colitis. The mechanism of action underlying this process is attributed to antagonism of the  $M_1$ ,  $M_2$ ,  $M_3$ , and  $M_4$  muscarinic receptors, resulting in anticholinergic side effects.<sup>3</sup> Clozapine has the highest affinity for muscarinic receptors, followed by olanzapine and quetiapine.<sup>4</sup>

Case reports<sup>5,6</sup> have identified that clozapine, quetiapine, olanzapine, and haloperidol can induce ischemic colitis. Additive effects from other anticholinergic medications, including tricyclic antidepressants or dual antipsychotic use, may also increase risk.<sup>5</sup>

Most reports<sup>6</sup> describe ischemic colitis that occurs soon after initiation of therapy with an atypical antipsychotic. Interestingly, our patient had been maintained on the same dose of quetiapine for years prior to onset of ischemic colitis; however, her first episode occurred after titration of quetiapine. We recommended discontinuation of quetiapine because this was the second episode of ischemic colitis during quetiapine treatment. Amitriptyline was also discontinued due to concern for additive anticholinergic effects. We continued long-acting risperidone depot injections, as this type of antipsychotic is not associated with anticholinergic side effects.

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### Letter to the Editor

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Potential conflicts of interest: None. Funding/support: None.

**Patient consent:** Consent was obtained from the patient to publish this case, and information was de-identified to protect anonymity.

Published online: November 8, 2018.

Prim Care Companion CNS Disord 2018;20(6):17l02250

*To cite:* Arkfeld DV, Svingen LA, Sutton S, et al. Repeat ischemic colitis in a patient taking quetiapine. *Prim Care Companion CNS Disord.* 2018;20(6):17102250.

To share: https://doi.org/10.4088/PCC.17I02250 © Copyright 2018 Physicians Postgraduate Press, Inc.