CASE REPORT

Colitis possibly induced by quetiapine

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SUMMARY

A 39-year-old man with bipolar disorder was hospitalised for depression. He was started on quetiapine (titrated up to 300 mg), lactulose (a laxative) and tropatepine (an anticholinergic). Valpromide (a mood stabiliser) and prazepam were later added and rapidly withdrawn. Seven days after quetiapine initiation, the patient reported abdominal pain and constipation; 2 days later, CT revealed an important distention of the colon including the caecum and a pre-perforation. A subtotal colectomy was performed and histology confirmed necrotising ischaemic colitis. The patient survived. This is the first case reported so far of ischaemic colitis related to quetiapine, in the absence of other antipsychotics simultaneously prescribed. Tropatepine likely acted as a cofactor to determine colitis. Clinicians need to be aware of the potential danger of the co-prescription of quetiapine with tropatepine (and possibly other anticholinergics).

BACKGROUND

Ischaemic colitis is a rare but severe complication of antipsychotic treatments. All types of antipsychotics can be involved, with phenothiazines and clozapine more frequently implicated.^{1–3} The role of anticholinergic drugs has also been stressed.^{1,4} Only one case of ischaemic colitis involving quetiapine has been reported in the literature.⁵ However, in that case, quetiapine was co-prescribed with a phenothiazine, making it difficult to attribute responsibility to quetiapine alone in the occurrence of colitis. In the present paper, we report a case of ischaemic colitis in a patient treated with quetiapine without any other antipsychotics. It is important for clinicians to know that quetiapine antipsychotic monotherapy can induce ischaemic colitis.

CASE PRESENTATION

A 39-year-old man with a history of bipolar disorder and severe depressive episodes was hospitalised for the treatment of major depressive disorder with suicidal ideation. He had been hospitalised 10 times over the past 15 years. He had a history of poor responsiveness to mood stabilisers, largely because of non-compliance. The patient had been out of treatment for 1 year, except for an irregular administration of haloperidol decanoate, the last injection of which (150 mg) had been made 2 months (precisely 62 days) before the present hospitalisation. He had been taking no medication between the injection and the hospitalisation. He had no history of established risk factors for ischaemic colitis (dyslipidaemia, diabetes, cardiovascular disease, irritable bowel syndrome, constipation).^{6,7} He was a smoker (around 25 cigarettes per day) and was of normal

weight. He had never been treated before by quetiapine.

Three drugs were introduced the first day of hospitalisation: quetiapine 100 mg (200 mg the second day and 300 mg from the third day on), lactulose (a laxative) 10 g twice a day and tropatepine (an anticholinergic) 10 mg twice a day. It should be noted that the patient was not constipated, but that, in this hospital, laxatives are systematically given to patients who are prescribed antipsychotics. Tropatepine was given to prevent potential antipsychotic-induced motor side effects. Valpromide (a valproic acid prodrug marketed in France for bipolar disorder) 300 mg was introduced on day 5 and prazepam 20 mg on day 7. On day 7, the patient started to report abdominal pain and constipation. On day 8, valpromide and prazepam were withdrawn. On day 9, tropatepine, quetiapine and lactulose were withdrawn. On day 9, the physical examination revealed a painful abdomen with generalised defence, distended and tympanic abdomen, with mottling on the flanks. An enema was administered to no effect, and the patient was transferred to a surgery unit.

INVESTIGATIONS

Laboratory tests revealed a white cell count at 20 500/mm³ and metabolic acidosis. Contrast-enhanced abdominal CT revealed an important distention of the colon including the caecum and a pre-perforation. A scarce peritoneal effusion appeared, but no faecal impaction in the rectum or sigmoid was found.

TREATMENT

A subtotal colectomy was first performed (all colon, except sigmoid). Three days later, a subtotal sigmoidectomy with partial resection of the ileon was performed because of necrosis of the proximal part of the sigmoid. Macroscopic view and histology confirmed ischaemic colitis, partly necrotising, limited to the mucosa.

OUTCOME AND FOLLOW-UP

The patient survived. Intestinal continuity was re-established 3 months later.

DISCUSSION

An antipsychotic-induced ischaemic colon is a target for pathogenic bacterial organisms, leading to mucosa necrosis, and, in a context of septic shock, spontaneous outcome is towards death within 48–72 h.^{1,2,4,5,8} The literature shows that all antipsychotics do not have the same propensity to cause ischaemic colitis, and that, except for clozapine, colitis occurs more often in patients treated with several antipsychotics, with a relationship between

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the number of antipsychotics given and the severity of colitis.⁸ The occurrence of ischaemic colitis also appears to be facilitated by concomitant absorption of anticholinergic drugs in antipsychotic-treated patients.^{1 4 5}

Although several cases of constipation due to quetiapine have been reported,⁹ to the best of our knowledge, only one case of ischaemic colitis due to quetiapine has been published so far.⁵ In this case, quetiapine (150 mg) had been given for 9 months without noticeable side effects; however, because of worsening of symptoms, quetiapine was increased (to 600 mg), and cyamemazine (450 mg) and tropatepine (30 mg) were added. Two days later, symptoms of intestinal occlusion appeared, and 3 days later, the clinical picture being one of septic shock, the patient was transferred to surgery. This case therefore shows that, while a low dose of quetiapine was well tolerated by the patient for a long period of time, ischaemic colitis occurred in the presence of, or more likely, in the simultaneous presence of, the following three factors: increase in quetiapine dose, addition of cyamemazine and addition of tropatepine. Our case differs from the preceding case in two aspects: absence of any other antipsychotics and a moderate dose of quetiapine. The two cases have the prescription of the anticholinergic tropatepine in common. In our case, the ischaemic colitis cannot be ascribed to tropatepine alone because the patient had been taking tropatepine (10 or 20 mg daily) for long periods of time in the past while treated with haloperidol decanoate, as well as with other antipsychotics, including phenothiazines. Valpromide and prazepam have never been linked to ischaemic colitis. We therefore propose that in our case, ischaemic colitis may have been the consequence of the association of quetiapine and tropatepine.

An anticholinergic effect probably plays an essential role in determining the occurrence of medication-induced intestinal colitis. Antipsychotics that have no intrinsic anticholinergic activity, such as aripiprazole and ziprasidone, although they can produce constipation, have never been linked to ischaemic colitis, while those with high anticholinergic activity (phenothiazines, clozapine, olanzapine, quetiapine) have been reported to cause ischaemic colitis.^{1-5 8} However, the rule may not be absolute, since antipsychotics with low or no anticholinergic activity, such as haloperidol and risperidone (given alone), and amisulpride (in association with other antipsychotics), have been associated with ischaemic colitis.¹ Second generation antipsychotics are also serotonin 5HT₂ antagonists, and some of them (including quetiapine) are dopamine D₁ antagonists:¹⁰ these mechanisms may contribute to intestinal motility alterations,¹¹ and have possibly played a role in our patient. It is mentioned in the Peyrière *et al*¹ article that 68.4% of patients who developed antipsychotic-induced colitis were taking anticholinergic drugs. There are no reports in the literature showing that anticholinergic drug monotherapy can cause ischaemic colitis.

Anticholinergic drugs likely act as cofactors, when given in association with antipsychotics, facilitating the occurrence of antipsychotic-induced ischaemic colitis. Valpromide and prazepam have no known anticholinergic activity. Quetiapine may therefore be considered as the primary factor responsible for ischaemic colitis in our case, tropatepine acting as a cofactor by lowering the putative threshold for ischaemic colitis.

Learning points

- ▶ Quetiapine antipsychotic monotherapy can cause ischaemic colitis.
- ▶ Tropatepine, and possibly other anticholinergics, likely act as cofactors to facilitate ischaemic colitis.
- ▶ Ischaemic colitis is a severe side effect of medications with anticholinergic properties, and clinicians should know that polytherapy with medications having anticholinergic properties may progressively lower the threshold for ischaemic colitis.

Contributors IT, SG and MT analysed the data. RdB wrote the article.

Competing interests None.

Patient consent Obtained.

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