Unexpected outcome (positive or negative) including adverse drug reactions

Adverse drug reaction: rosuvastatin as a cause for ischaemic colitis in a 64-year-old woman

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Summary

Rosuvastatin (Crestor, AstraZeneca) is a commonly used drug for managing hypercholesterolaemia. It is a very safe medication with mostly acceptable side effects. Rare but serious side effects are not well known. A 64-year-old woman presented with bloody diarrhoea after starting rosuvastatin for hypercholesterolaemia. Stool microscopy and culture ruled out infective causes. Abdominal CT scan revealed normal calibre celiac axis and superior mesenteric artery. Colonoscopic biopsy revealed ischaemic colitis as the final histological diagnosis. The patient is in complete remission after ceasing the medication. Rosuvastatin causing ischaemic colitis should be considered a rare but serious adverse drug reaction.

BACKGROUND

Rosuvastatin is a competitive inhibitor of HMG-CoA (3-hydroxy-3-methyl-glutaryl-CoA) reductase enzyme, which belongs to the 'statin' group of cholesterol lowering medication.¹ Unique to other statins, it has a safer pharmacological profile such as higher hydrophilic and

Figure 1 Diffuse bowel wall thickening involving the colon from splenic flexure (red arrow).

Figure 2 Fat stranding around the same loop of bowel (red arrow).

hepatoselective properties and lower systemic bioavailability than the predecessor statins.² Since its launch in 2003,³ this medication has been a commonly prescribed cholesterol lowering medication. Despite its ability to reverse the atherosclerotic effect,⁴ rosuvastatin is known to have infrequent side effects⁵ like arthralgia (10.1%), myalgia (2.8%–12.7%), abdominal pain (2.4%), nausea (2%–3.4%), asthenia (0.9%–4.7%) and headache (3.1%–5.5%). The more serious documented side effects⁵ are altered liver enzymes, and rhabdomyolysis (<1%). There is limited report of other serious side effects such

as ischaemic colitis. On the FDA database, there are two reported cases of ischaemic colitis⁶ at the time of writing. On MIMS Australia online, a commonly accessed database for clinicians, ischaemic colitis is not listed as a potential side effect. At present, no large-scale primary or secondary prevention clinical trials on rosuvastatin have documented its long-term safety.⁷ This case study intends to highlight ischaemic colitis as a possible but rare adverse drug reaction of rosuvastatin.

CASE PRESENTATION

A 64-year-old lady presented to hospital for sudden onset bilateral lower abdominal pain. The abdominal pain is associated with 8 bouts of bloody diarrhoea. On presentation, she was hypertensive, tachypnic and diaphoretic. Just 4 weeks before she had a screening colonoscopy which was normal apart from pre-existing diverticular disease. She had been recently started on rosuvastatin by her regular doctor for cholesterol control. The patient also reported similar episode of abdominal pain with bloody diarrhoea after starting rosuvastatin approximately 1 year ago but did not seek medical attention. She reportedly stopped the medication on her own accord and her pain resolved.

Her medical history includes osteoarthritis, fibromyalgia, diabetes mellitus type 2 and irritable bowel syndrome (associated with painful diarrhoea). She does not smoke and does not consume alcohol. Digital rectal examination was unremarkable with no haemorrhoids, empty rectum, no melena and good anal tone. The abdomen was

Figure 3 Mucosal ulceration and sloughing (red arrow) on colonoscopy.

Figure 4 Patent celiac axis and SMA (green arrow) of the patient.

Figure 5 Patent inferior mesenteric artery (green arrow).

soft but with mild general tenderness, more in her lower quadrants. The initial blood test in emergency department showed elevated white cell count at $16.8 \times 10^9/l$ of which neutrophil count was $14.6 \times 10^9/l$. Her Hb was 161 (g/l), and her C reactive protein was <1.0 (mg/l). Abdominal CT scan with intravenous contrast reported a long segment of colon wall thickening suspicious of colitis from splenic flexure to proximal sigmoid colon (figures 1 and 2). The stool culture returned negative for infective causes of colitis. The only change identifiable to her medication regime was the addition of crestor (rosuvastatin calcium). This was ceased temporarily on the ward.

She was managed conservatively with intravenous fluids and bowel rest. Her symptoms gradually resolved over 3 days. A colonoscopy was performed which showed mucosal ulceration (figure 3) and diverticulosis but otherwise normal colon. Biopsies were taken and histology later revealed an ischaemic colitis picture. A retrospective radiological review of her abdominal CT-scan revealed no pre-existing atherosclerotic vasculopathy in the celiac axis, superior mesenteric artery and inferior mesenteric artery (figures 4 and 5).

The final histological diagnosis was ischaemic colitis secondary to a rare adverse drug reaction. Upon discharge, the patient was reviewed in outpatient clinic 2 weeks later after ceasing rosuvastatin, and reported to be in complete remission.

DISCUSSION

Rosuvastatin as a cause for non-occlusive, non-infective ischaemic colitis is a very rare occurrence. This side effect is not listed in the potential side effects in the prescriber index of the 2011 edition of MIMS Australia (July 2011). Six hundred and twenty three patients reported side effects when taking rosuvastatin calcium⁶ (Crestor, AstraZeneca), two of whom were reported to have ischaemic colitis.⁶ These cases were reported in 2008 and 2009 from the FDA database. No mechanism was suggested in those two cases. However, the mechanism is likely to be idiopathic until more clinical data arises. Both previously reported cases were females in the 60–69 age group.⁶ These epidemiological data correspond to our case study. We query if this group is particularly at risk. The fact that this patient had a history of similar episode with rosuvastatin 1 year previously means this presentation represents a re-challenge of rosuvastatin to the patient. This patient's recent normal colonoscopy 4 weeks before presentation, and her recent commencement of rosuvastatin is a strong temporal indicator that rosuvastatin is responsible for her case of non-occlusive, non-infective ischaemic colitis. Ischaemic colitis is a serious diagnosis with considerable morbidity and mortality. Mortality is quoted to be approximately 6% by Longo⁸ in 1992. More clinical data, such as this case, maybe required to definitely confirm the causal relationship between rosuvastatin and ischaemic colitis.

Learning points

- ▶ Rosuvastatin is a relatively new medication now commonly prescribed for hyperlipidaemia.
- ▶ Rosuvastatin can rarely cause non-occlusive, non-infective ischaemic colitis.
- ▶ Ischaemic colitis should be considered in patients presenting with abdominal pain after initiation of rosuvastatin.

Competing interests None.

Patient consent Obtained.

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