CASE REPORT

 β -lactam-associated eosinophilic colitisTamara Mogilevski,¹ David Nickless,² Sam Hume³¹Department of Medicine, The Northern Hospital, Epping, Victoria, Australia²Department of Healthscope Pathology, The Northern Hospital, Melbourne, Victoria, Australia³Department of Infectious Diseases, The Royal Melbourne Hospital, Melbourne, Victoria, AustraliaCorrespondence to
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SUMMARY

A 42-year-old man with a history of childhood asthma presented with a 2-week history of watery diarrhoea and marked peripheral eosinophilia in the setting of recent use of cephalexin. His colonoscopy revealed patchy colitis. Biopsies were consistent with eosinophilic colitis. Two months later he received a course of amoxicillin resulting in recurrence of peripheral eosinophilia. Given the time-frame of β -lactam administration to symptom onset and elimination of all other precipitating causes, he was diagnosed with β -lactam-associated eosinophilic colitis. The patient's symptoms resolved and peripheral eosinophil count decreased with no specific treatment. Eosinophilic colitis is a rare heterogeneous condition, the pathogenesis of which is likely to be an interplay between environmental and genetic factors. It can be secondary to a helminthic infection or a drug reaction and has been associated with ulcerative colitis. If secondary causes of eosinophilic colitis have been excluded, the mainstay of treatment is with corticosteroids.

BACKGROUND

Drug-induced eosinophilic colitis is a rare condition with very few case reports described in the literature to date.^{1–9} Cephalexin and amoxicillin are β -lactam antibiotics commonly used in clinical practice for the treatment of skin, urinary tract and upper respiratory tract infections, respectively. To the best of our knowledge, this is the first described case of eosinophilic colitis secondary to β -lactam antibiotic use.

CASE PRESENTATION

A 42-year-old Australian-born man with a medical history of childhood asthma presented to the emergency department with a 2-week history of non-bloody diarrhoea. He had not taken any medication for asthma for three decades and did not have a history of atopic diseases. His last overseas travel had been 5 years prior to presentation.

Three weeks prior to presentation he suffered from an upper respiratory tract infection for which his general practitioner prescribed a 1-week course of cephalexin—a medication to which he had not been exposed previously. Two weeks before presentation, his stools became soft in consistency and he experienced one episode of chills. One week before presentation his stool frequency increased to 15 bowel motions per day.

Stools were of small volume, green and contained mucus. The patient had no further episodes of fevers, chills or rigours, nor did he have abdominal pain associated with the diarrhoea. He had not had any overseas visitors or unwell contacts. His

exposure to animals was limited to his family dog. His 2-year-old daughter did not attend childcare.

On examination, the patient was dehydrated but had no abdominal tenderness or bloating. His peripheral absolute eosinophil count was $9.7 \times 10^9/L$ on presentation and peaked on day 7 of admission at $29.9 \times 10^9/L$. Examination of the peripheral blood film revealed eosinophils of normal morphology. Stool examination and culture were negative for bacteria, *Clostridium difficile* toxin and ova, cysts and parasites on three separate occasions. *Strongyloides* and *Toxocara* serology and autoimmune investigations including antinuclear antibodies, antineutrophil cytoplasmic antibodies and extractable nuclear antibodies were negative.

Colonoscopy demonstrated patchy colitis in the descending and sigmoid colon (figure 1). Multiple biopsies were taken and histopathology revealed similar changes from the rectum to the caecum. The lamina propria contained increased numbers of eosinophils with a maximum of 60 per high power ($\times 40$) field (figures 2 and 3). Eosinophils were noted to be crossing into the muscularis mucosa and submucosal layers. There was no evidence of parasite infection, nor characteristic features of inflammatory bowel or connective tissue disease noted on histopathological evaluation.

DIFFERENTIAL DIAGNOSIS

A patient presenting with profuse watery diarrhoea, eosinophilic infiltrates in the colonic mucosa and a raised peripheral eosinophil count should have other secondary causes of eosinophilic colitis investigated, including helminth infections, early inflammatory bowel disease, drug reaction or hypereosinophilic syndrome. Given the degree of this patient's eosinophilia, a haematological malignancy was an important diagnosis to consider.

Figure 1 Patchy colitis—sigmoid colon.

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Figure 2 Colonic biopsy— $\times 200$ H&E stain—preserved crypt architecture with eosinophilic infiltrate.

TREATMENT

The patient did not receive any corticosteroids or antihelminthic treatment. His symptoms subsided with supportive care throughout his 1 week hospital stay.

OUTCOME AND FOLLOW-UP

At initial follow-up 4 weeks postdischarge, the patient was well with 1–2 normal bowel actions per day, and had not lost weight or experienced any abdominal pain. His peripheral eosinophil count had reduced to $1.1 \times 10^9/L$. Two months later, his general practitioner prescribed him a course of amoxicillin. This resulted in similar symptoms and recurrence of peripheral eosinophilia. A diagnosis of eosinophilic colitis secondary to β -lactam exposure was made based on spontaneous clinical and haematological recovery, timing of drug exposure and symptom onset, and the exclusion of other possible precipitants.

Figure 3 Colonic biopsy— $\times 400$ H&E stain—high number of eosinophils present in crypt epithelium.

DISCUSSION

Eosinophilic colitis is an exceptionally rare condition, thought to be part of a larger spectrum of eosinophilic gastrointestinal disorders. It is a heterogeneous disorder, both in its clinical presentation and histopathological appearance, and can affect infants as well as adults.

The pathogenesis of eosinophilic colitis is incompletely understood, but thought likely to be a combination of genetic predisposition and environmental exposure. This theory is supported by a large multinational registry, which showed that among patients with eosinophilic gastrointestinal disease, 80% had coexisting atopic disease and 16% had an immediate family member with a similar disorder.¹⁰

The diagnosis of eosinophilic gastrointestinal disease is made from the presence of gastrointestinal symptoms, peripheral eosinophilia, endoscopic and histological findings, and eosinophilic ascites, with no well-defined causes of eosinophilia on thorough evaluation.¹¹

Eosinophilic colitis has been associated with a number of helminthic infections including *Strongyloides stercoralis*,¹² *Enterobius vermicularis*¹³ and *Trichuris trichiura*.¹⁴

Drug-induced eosinophilic gastroenteritis is an exceptionally rare phenomenon with few case reports in the literature linking it to various medications. Tacrolimus in the setting of liver transplantation has been implicated in the development of eosinophilic gastroenteritis in a dose-dependent manner.¹ Other medications associated with this condition include clozapine,^{2–4} carbamazepine,⁵ rifampicin,⁶ gold⁷ and non-steroidal anti-inflammatory drugs.^{8,9}

One case report describes two patients in whom eosinophilic colitis was thought to have been a precipitant of ulcerative colitis. The association is thought to be through the activation of a T-cell-mediated response.

No prospective randomised trials exist to guide clinicians on specific therapy for eosinophilic colitis; owing in part to the rarity of the condition. All efforts to rule out helminthic infections must be made and a causative drug should be sought in all cases of eosinophilic colitis. If no precipitating factor can be identified, the condition should be treated as an idiopathic eosinophilic colitis. Small case series suggest that corticosteroid therapy should be the mainstay of treatment. Up to 90% of patients seem to respond to a 2-week course of treatment, followed by a slow taper of corticosteroids. Recurrence of the idiopathic form of eosinophilic colitis is common.¹⁵

Learning points

- ▶ Eosinophilic colitis is a rare heterogeneous condition—a drug history needs careful consideration when searching for triggers.
- ▶ Spontaneous recovery is known to occur if the trigger is removed; steroid treatment is not mandatory immediately.
- ▶ The reintroduction of a known precipitant can result in disease recurrence.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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