CASE REPORT

Vedolizumab-induced acute pancreatitis: the first reported clinical case

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SUMMARY

Drug-induced acute pancreatitis (DIAP) is a rare, but clinically significant diagnosis. Vedolizumab, an $\alpha_4\beta_7$ integrin inhibitor, which was approved in 2015 for treatment of moderate to severe inflammatory bowel disease, is a well-tolerated medication with a favourable safety profile and minimal serious adverse events in premarketing clinical trials. We present the first reported case of acute pancreatitis directly attributable to vedolizumab.

BACKGROUND

Acute pancreatitis, an inflammatory condition of the pancreas, is associated with significant morbidity and mortality. Many commonly prescribed medications have been reported to induce pancreatic injury, with the rate of drug-induced acute pancreatitis (DIAP) ranging from 0.1% to 2%.¹ Most cases are mild and resolve with supportive management. Severe and even fatal cases, however, have been reported making identification of the offending medication essential.² Vedolizumab, a humanised monoclonal antibody that targets the $\alpha_4\beta_7$ integrin receptor and blocks gut lymphocyte trafficking, is a relatively new and increasingly used treatment for moderate to severe inflammatory bowel disease.^{3,4} It is generally well tolerated, with minimal severe adverse events reported in the premarketing phase III clinical trials.^{3,4} We present the first case of acute pancreatitis associated with vedolizumab administration.

CASE PRESENTATION

A 30-year-old man with left-sided ulcerative colitis (A2E2) was reviewed after presenting with symptoms suggestive of a flare of his colitis. His prior inflammatory bowel disease medical therapy included mesalazine with the addition of weight-based 6-mercaptopurine, 6 months prior to this presentation. He underwent a colonoscopy, which revealed an active, moderate to severe (Mayo endoscopic subscore 2) left-sided colitis.

As he had ongoing active disease, the decision was made to commence him on treatment with vedolizumab (induction and maintenance) and to continue his mesalazine and mercaptopurine. His pretreatment blood workup, including full blood picture, liver function panel and lipase, was unremarkable. He was commenced on 300 mg of vedolizumab by intravenous infusion. He received 100 mg of hydrocortisone intravenously as a premedication

as per our hospitals protocol to prevent an infusion reaction.

Immediately following his second infusion of vedolizumab, he developed severe central abdominal pain radiating to his back. He was haemodynamically stable, and physical examination revealed epigastric tenderness without rebound or abdominal rigidity.

INVESTIGATIONS

Laboratory evaluation was remarkable for an elevated serum lipase of 2327 IU/L (<350 IU/L) and C reactive protein level of 14.1 mg/L (<8 mg/L).

The patient did not have any risk factors for pancreatitis and had no major comorbidities or consume significant quantities of alcohol. A comprehensive blood panel looking for other potential causes of pancreatitis demonstrated normal lipid profile, thyroid function tests, serum calcium levels and serum immunoglobulin levels.

Magnetic resonance cholangiopancreatography scanning was performed, which demonstrated oedema in the tail of pancreas with no necrosis, consistent with acute pancreatitis (figure 1). It did not show any cholelithiasis, choledocolithiasis, pancreatic duct obstruction, pancreas divisum or pancreatic mass lesion.

OUTCOME AND FOLLOW-UP

He was managed conservatively with hydration and analgesia with improvement in his abdominal pain over the period of 1 week and subsequent normalisation of his lipase. Given his other investigations were normal and the temporal association with the infusion, the vedolizumab was considered responsible for his pancreatitis and was discontinued. He has remained well since and now has had 12 months of follow-up without any recurrence of his pancreatitis.

DISCUSSION

DIAP is a relatively rare and usually self-limiting process.^{1,2} There have been many medications that have been implicated, with the list of offending agents expected to expand with newly developed medications. DIAP accounts for 0.1–2% of all cases of pancreatitis; however, the true incidence is likely much higher, due to the lack of mandatory adverse drug reporting and the challenges in associating acute pancreatitis with medications.¹

DIAP poses a significant diagnostic challenge for clinicians as there are no specific clinical

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Figure 1 Magnetic resonance cholangiopancreatogram: T2 images demonstrating oedema within the tail parenchyma with altered perfusion in keeping with acute pancreatitis.

characteristics distinguishing it from other causes of acute pancreatitis. Alcohol and biliary disease are the most common aetiologies of acute pancreatitis accounting for 36% and 38% of all cases, respectively.⁵ In our case, the patient did not have a history of alcohol abuse and imaging studies excluded biliary disease. Further laboratory investigations excluded some of the more obscure causes of acute pancreatitis.

Vedolizumab is an effective medication for the treatment of moderate to severe inflammatory bowel disease with a favourable safety profile and low rates of serious adverse events demonstrated in clinical trials.^{3,4} This safety profile has been replicated in a large real-world cohort.⁶ There have been no previously reported cases of pancreatitis attributable to vedolizumab that we could identify in the literature.

In our case, the patient was prescribed concomitant mesalazine and mercaptopurine, both of which have been implicated in inducing acute pancreatitis. 5-Aminosalicylic acid (5-ASA) therapy and thiopurines have been linked to the development of acute pancreatitis through a dose-independent hypersensitivity reaction.⁷ The time course between first administration of either 5-ASA or thiopurine and development of pancreatitis was usually between 4 to 6 weeks.^{8,9} Our patient had been on mercaptopurine and 5-ASA therapy for a duration of 6 and 24 months, respectively. He continued on both medications following resolution of his pancreatitis with no further episodes of pancreatitis, making drug-induced pancreatitis secondary to these medications extremely unlikely. We are unsure whether being on these two medications predisposed or sensitised the vedolizumab to induce the patient's acute pancreatitis. There have been no reports of either of these agents increasing the risk of pancreatitis from other causes. These drug reactions are thought to be idiosyncratic and not directly related to the pharmacodynamic mechanisms of the drugs, making this predisposition unlikely.

The onset of symptoms immediately following the dose of vedolizumab and the absence of other potential aetiologies

strongly implicate vedolizumab as the cause of our patient's acute pancreatitis. As with most cases of DIAP, we are unsure of the mechanism by which vedolizumab induced acute pancreatitis. There are no animal studies in the literature that describe this reaction. Several potential mechanisms for DIAP have been hypothesised, including an immune-mediated reaction, direct pancreatic toxicity, pancreatic duct constriction, the influence of the medication on bile flow and hypersensitivity reactions.¹ Our patient's acute episode resolved with no long-term sequelae with the initiation of supportive management and discontinuation of the drug. A rechallenge of vedolizumab was not considered given the significant morbidity associated with acute pancreatitis.

In conclusion, we report this rare complication of vedolizumab manifested in the form of DIAP. Drug-induced pancreatitis should be considered in patients commencing vedolizumab who present with suggestive clinical symptoms.

Learning points

- ▶ Drug-induced acute pancreatitis is a relatively rare and usually self-limiting process.
- ▶ Drug-induced pancreatitis should be considered in patients commencing vedolizumab who present with suggestive clinical symptoms.
- ▶ Patients should be managed supportively and the vedolizumab should be discontinued.

Contributors All authors were involved in the synthesis of the case report. SP was the primary author who reviewed the case notes, investigations, contacted the patient and wrote up the abstract and case presentation. KV and KS were involved in writing up the discussion and conclusions as well as editing the case report. MC performed the procedures referenced in the article and was involved in writing up the case presentation and discussion. All authors were involved in editing and reviewing the final document.

Competing interests None declared.

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