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Single Case

Acute Chest Pain as an Infusion Reaction to Vedolizumab

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Keywords
Vedolizumab · Adverse reaction · Chest pain

Abstract
Vedolizumab-associated adverse effects, including infusion reactions, are generally uncommon. Less than 5% of patients experience an infusion-related reaction. We report a 67-year-old male with ulcerative colitis under prolonged maintenance therapy who presented with recurring chest pain occurring immediately after consecutive vedolizumab infusions. Medical workup of possible etiologies for chest pain were investigated and excluded. Vedolizumab drug trough levels were negative, accompanied by high detectable levels of anti-vedolizumab antibodies. These findings demonstrate an uncommon case of an infusion reaction to vedolizumab infusion.

Introduction

Vedolizumab, a gut-selective monoclonal antibody targeting α4β7, is approved for the treatment of moderate to severe inflammatory bowel disease [1, 2]. As the integrin α4β7 is found solely in the intestine, vedolizumab is considered relatively target specific. The most common vedolizumab-related adverse effects reported are nasopharyngitis, upper respiratory tract infections, headaches, and arthralgia [1–3]. Few additional rare adverse events have been described in the literature including dermatologic- and pulmonary-related adverse events [4–6]. Cases of infusion reactions following vedolizumab administration are uncommon. Only ≤5% of patients receiving vedolizumab experience an infusion-related reaction, much

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rarer than with anti-TNFα [7, 8]. Here, we describe an atypical presentation of an infusion reaction toward vedolizumab occurring following prolonged maintenance therapy.

Case Report

We present a case of a 67-year-old male with a past medical history positive for left-sided ulcerative colitis (UC) diagnosed at the age of 64 years. His history is also notable of chronic ischemic heart disease after coronary artery bypass surgery at the age of 47 years and several percutaneous coronary interventions since. Since the last coronary intervention at the age of 63 years, his heart disease was stable, and no symptoms of angina were reported.

One year following UC diagnosis, biologic therapy with vedolizumab was initiated. After standard induction, the patient received infusions every 8 weeks for maintenance treatment. Due to clinical and endoscopic exacerbation of his left-sided colitis, which necessitated hospitalization and steroidal therapy, therapy intervals were shortened to every 4 weeks.

One-hundred and thirteen weeks after initiation of vedolizumab therapy, the patient presented with acute chest pain that started immediately upon commencement of a vedolizumab infusion. He reported intense pain radiating to the jaw, with relief several minutes after infusion cessation. On presentation, vital signs were normal, and no signs of an allergic reaction were evident. Medical workup including chest x-ray, electrocardiogram, and laboratory blood tests for cardiac enzymes were negative excluding any other major reason for chest pain. After discharge, trough vedolizumab levels and anti-vedolizumab antibodies were obtained. Vedolizumab levels measured were zero, and antibodies were detectable (195 mg/dL, shown in Fig. 1; Table 1).

One month later, several minutes after initiation of the next vedolizumab infusion, similar symptoms of chest pain recurred. The infusion was halted, and the patient was referred to the emergency department. The symptoms subsided within hours and once again, no abnormal findings on workup were detected. Cardiac enzymes and an electrocardiogram were intact.

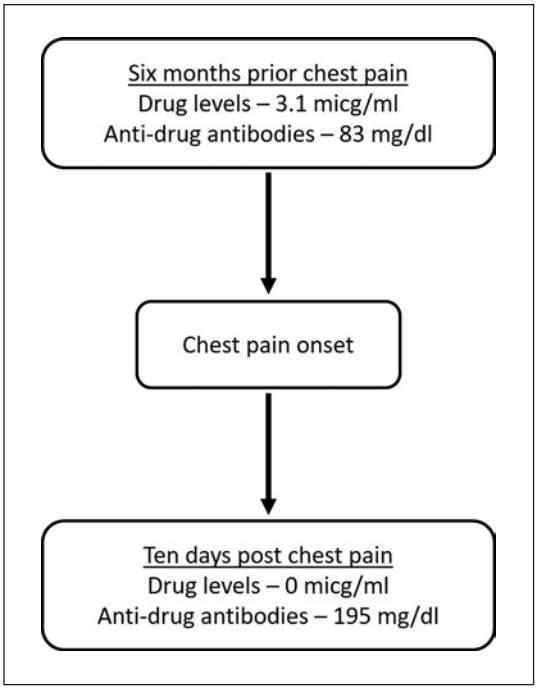

Fig. 1. Flowchart showing vedolizumab drug levels and antidrug antibodies 6 months before and 10 days after acute chest pain.

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Table 1. Anti-vedolizumab antibody levels before and after acute chest pain reaction

Timeframe	Antidrug antibodies
Six months prior chest pain	83 mg/dL
Ten days post chest pain	195 mg/dL

In addition, a subsequent echocardiography ruled out structural heart disease or cardiac wall abnormalities that may imply of ischemia.

Discussion

In this case report, we present an infusion reaction to long-term vedolizumab therapy manifesting as acute chest pain. Acute chest pain is a symptom generally divided to cardiac or noncardiac causes. The causes range from life-threatening to relatively benign conditions. In primary care, the most common causes of chest pain are chest wall pain, gastroesophageal reflux disease, and costochondritis. However, cardiac-related conditions such as acute myocardial infarction and unstable angina are the leading causes of death. Chest pain can be a drug-related adverse effect. A variety of common therapeutic agents have been documented as potential causes including analgesics, antidepressants, antihistamines, hormones, antibiotics, and beta-agonist inhalers [9]. Chest pain related to anti-TNFα therapy has been reported, manifesting as pleural effusion and pericarditis in a patient with Crohn's disease that developed drug-induced lupus [10]. In our case, possible etiologies for chest pain were investigated and reasonably excluded twice based on clinical data and laboratory findings in the emergency department and the internal medicine ward. In addition, the rechallenge of vedolizumab provided a certain diagnosis of the culprit agent.

The recurrent chest pain following a consecutive infusion as well as the antidrug antibody pattern narrow down the manifestation to an uncommon case of an infusion reaction. Infusion reactions to vedolizumab are rare and are generally well tolerated by patients. The landmark studies in UC and CD have reported infusion-related reaction rates of 5% and 4% of patients, respectively [7, 8]. The majority of infusion-related reactions occurred within the first 2 h after completion of infusion [11]. One of the patients had a serious reaction (dyspnea and bronchospasm) that started 13 min after infusion initiation. Premedication including corticosteroids and antihistamines was seldom used. Nausea and headache were the most common infusion-related reactions.

Infusion reactions to anti-TNFα and mostly to infliximab have been extensively reported. It is considered that up to 20% of patients would develop infusion reactions associated with neutralizing antibodies [12–14]. These events generally include headache, dizziness, flushing, tachycardia, and edema. Hanauer and colleagues reported chest pain as one of the possible infusion reactions among patients who received maintenance infliximab therapy [12]. These hypersensitivity reactions are mainly explained by antidrug antibody formation which occurs in anti-TNFα therapy, more frequently with infliximab than adalimumab [13].

Thus far, the impact of anti-vedolizumab antibodies formation on clinical outcomes has not been proven. Detectable anti-vedolizumab antibodies did not correlate with clinical outcomes during induction and maintenance [15]. In addition, the relationship between detectable anti-vedolizumab antibodies and clinically important infusion reactions is unclear. Wyant and colleagues [16] demonstrated similar rates of infusion reactions to vedolizumab among patients with detectable and undetectable anti-vedolizumab antibodies.

In this case, an immediate reaction to vedolizumab was observed upon two consecutive infusions. Trough vedolizumab levels were negatively accompanied by a high level

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of anti-vedolizumab antibodies. To our knowledge, this is the first documented case of acute chest pain reaction associated with vedolizumab infusion.

Statement of Ethics

This retrospective review of patient data did not require ethical approval in accordance with local guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case.

Conflict of Interest Statement

Shomron Ben-Horin has received consulting and advisory board fees and/or research support from AbbVie, MSD, Janssen, Takeda, and CellTrion. Uri Kopylov has received speaker fees from Abbvie, Janssen, and Takeda; research support from Takeda and Janssen; and consulting fees from Takeda and CTS. Bella Ungar has received consultation fees from Janssen and Abbvie. The remaining authors disclose no conflicts.

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Author Contributions

Asaf Levartovsky and Bella Ungar drafted the original manuscript and collected clinical data; Ella Fudim and Miri Yavzori extracted drug serum levels and acquired laboratorial data; Shomron Ben-Horin and Uri Kopylov revised the manuscript and approved the final version.

Data Availability Statement

The clinical data regarding the patient are available in the electronic medical records in our medical center. Further inquiries can be directed to the corresponding author.

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