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## Single Case

# Vedolizumab as a Potential Culprit in the Development of Ovarian Teratoma?

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## Keywords

Vedolizumab · Ovarian teratoma

## Abstract

Vedolizumab is a new humanized monoclonal antibody that has been reserved for those with moderate-to-severe Crohn's disease and ulcerative colitis who have failed immunomodulator and TNF- $\alpha$  antagonist therapy, and for those who have an increased risk for developing progressive multifocal leukoencephalopathy. Because it targets gastrointestinal tract-specific lymphocytes, meta-analyses and integrated studies have shown that vedolizumab causes fewer extraintestinal adverse effects, such as opportunistic infections and malignancies, compared with anti-TNF therapies. We present the case of a patient who developed an ovarian teratoma after initiation of vedolizumab therapy.

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## Introduction

Vedolizumab is a new humanized monoclonal antibody that has been reserved for those with moderate-to-severe Crohn's disease (CD) and ulcerative colitis who have failed immunomodulator and TNF- $\alpha$  antagonist therapy, and for those who have an increased risk for developing progressive multifocal leukoencephalopathy [1, 2]. It selectively antagonizes  $\alpha_4\beta_7$ -integrin receptors in the gastrointestinal tract, decreasing mucosal degradation and

inflammation [3, 4]. Since the FDA approved vedolizumab for the treatment of CD and ulcerative colitis in May 2014, it has been studied for its association with cancer during treatment. Because it targets gastrointestinal tract-specific lymphocytes, meta-analyses and integrated studies have shown that vedolizumab causes fewer extraintestinal adverse effects, such as opportunistic infections and malignancies, compared with anti-TNF therapies [2, 5, 6]. We present the case of a patient who developed an ovarian teratoma after initiation of vedolizumab therapy.

### Case Presentation

A 36-year-old female with a past medical history of severe CD and multiple sclerosis presented to the emergency department after 1 week of left lower abdominal pain. The patient had initially been diagnosed with severe CD 5 years prior to current presentation. The initial therapy had included sulfasalazine and azathioprine, with mild improvement in symptoms. Azathioprine was stopped due to development of painful blisters. She was also treated with 6-mercaptopurine, infliximab, and adalimumab, which were stopped due to side effects. 6-Mercaptopurine caused loss of appetite, infliximab caused infusion reactions, and adalimumab caused severe migraines. After starting certolizumab, her symptoms were controlled, but it subsequently unmasked and exacerbated the underlying multiple sclerosis. Further evaluation revealed that she was also positive for the JC (John Cunningham) virus. Thus, certolizumab was stopped as well.

About 18 months prior to current presentation, she was admitted for cramping right lower quadrant abdominal pain that worsened after eating. It was associated with occasional nausea but no vomiting. Computed tomography (CT) of the abdomen and pelvis at that time showed wall thickening of the distal ileum, terminal ileum, and segments of the small intestine, as well as intermittent inflammatory worsening of the ileocecal valve, suspicious of the enteroenteric and enterovesical fistulous tract. Colorectal surgery was advised and an exploratory laparotomy performed with lysis of adhesions, resulting in an ileocectomy. After this event, she remained without any therapy for her CD until starting vedolizumab 2 months prior to current presentation due to intolerance to immunomodulators, and inability to receive anti-TNF therapy due to multiple sclerosis and JC virus positivity. She received 3 doses of vedolizumab, causing significant improvement in symptoms.

The patient had started experiencing new-onset abdominal discomfort 1 week prior to the current admission. The pain was pressure-like and squeezing, wrapping around her abdomen in a belt-like fashion. It was worse on her left flank and radiated to her left leg. She had associated nausea and over 10 episodes of nonbloody, nonbilious emesis. The physical examination was remarkable for left lower abdominal tenderness without guarding or rigidity. The laboratory data revealed an elevated white blood cell count of  $15.73 \times 10^3/\mu\text{L}$ . Serum C-reactive protein was 0.7 mg/dL and the erythrocyte sedimentation rate was 23 mm/h, which was lower than during her previous episodes of CD flare-ups, with C-reactive protein up to 2.2 mg/dL and the erythrocyte sedimentation rate up to 31 mm/h in the past. A CT scan of the abdomen and pelvis revealed an approximately 10-cm left ovarian mass that was cystic in nature with soft tissue and a bony component, suggestive of a dermoid cyst (Fig. 1a). A previous CT scan 18 months prior to current presentation had not revealed any findings regarding any ovarian lesions (Fig. 1b, c). Obstetric-gynecological care and colorectal surgery were consulted, and the patient underwent an exploratory laparotomy with left salpingo-oophorectomy and lysis of adhesions. Surgical pathology confirmed the mass to be

a mature cystic teratoma, measuring 12.6 × 7.8 × 7.5 cm with extensive hemorrhagic necrosis consistent with ovarian torsion. The patient did well postoperatively and was discharged with outpatient follow-up.

## Discussion

Vedolizumab is a humanized monoclonal antibody targeting  $\alpha_4\beta_7$ -integrins [3]. The introduction of vedolizumab and other anti-integrin therapy has been a landmark for patients with moderate-to-severe inflammatory bowel diseases on whom biologic and/or immunomodulator therapies cannot be used [1]. The theoretic risk of systemic side effects with vedolizumab is extremely low due to its gut selectivity. Previously, an integrated study of 6 clinical trials found 18 cases of malignancy that were associated with vedolizumab therapy [5]. The malignancies included colorectal, hepatocellular, dermatological, breast, lung, and B-cell lymphoma. Although another meta-analysis of gut-specific anti-integrin antibodies did not show a statistically significant elevation in the relative risk of malignancy [6], one study examining the microdissection of mature teratomas found aggregates of lymphoid tissue [7]. Since  $\alpha_4\beta_7$ -integrins are expressed by mucosal lymphoid tissue, this could suggest a potential mechanism by which vedolizumab induces the growth of teratomas.

Our report is unique because our patient developed an ovarian teratoma within 2 months of initiation of vedolizumab therapy. The sudden development of an ovarian teratoma raises the question about the potential role of vedolizumab. Our patient had undergone abdominal and pelvic imaging, as well as exploratory laparotomy (for enterovesical and enteroenteric fistulas), 18 months prior to current presentation, which showed some insignificant fullness of the left ovary but no evidence of an ovarian mass (Fig. 1). A study evaluating expectant management of ovarian dermoid cysts with ultrasound followed the growth of teratomas for an average of 12.6 months [8]. It found that the mean growth rate of these cysts was 1.67 mm per year, which was not affected by any factors. This is a drastic difference from our patient's dermoid cyst development of 12.6 cm after about 1.5 years. Thus, the natural history of dermoid cysts alone does not explain the rapid development of the tumor. The patient did not have any new exposures after her abdominal imaging and exploratory abdominal surgery 18 months prior to her current presentation, except for the introduction of vedolizumab therapy 2 months prior to her current presentation.

Our case raises the concern that vedolizumab therapy might be associated with the development of ovarian teratoma. This correlation is strengthened by the timing of exposure and by the rapid growth of the tumor that is generally not seen in the natural history of this tumor. Our case, along with other reports of malignancies with vedolizumab use, highlights the possibility that there might still be more unknown aspects of this drug. Increased reporting of side effects from anti-integrin therapy will help to better understand the safety profile of these agents.

## Statement of Ethics

Informed consent was obtained.

## Disclosure Statement

The authors of this case report have no conflicts of interest.

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**Fig. 1.** **a** Computed tomography scan of the abdomen and pelvis with contrast depicting the left ovarian mass at its largest diameter. **b, c** The corresponding anatomical planes from a CT scan 18 months prior do not show any evidence of the ovarian mass.