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CASE REPORT | INFLAMMATORY BOWEL DISEASE

Vedolizumab-Induced Acute Interstitial Nephritis in Ulcerative Colitis

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ABSTRACT

Vedolizumab is used in the treatment of inflammatory bowel disease and is generally well tolerated. We report a 20-year-old man who presented with right flank pain on a background of ulcerative colitis. He was on vedolizumab with his last dose 1 week before the onset of symptoms. Kidney function tests revealed a serum creatinine of 171 μmoL/L and a C-reactive protein of 74 mg/L. Kidney biopsy demonstrated focal acute interstitial nephritis. He was prescribed oral prednisolone and achieved complete recovery of renal function within 3 weeks. At the follow-up after 4 months, his renal function remains normal.

INTRODUCTION

Vedolizumab is a gut-selective humanized monoclonal antibody that binds to α4β7 integrin used in the treatment of ulcerative colitis and Crohn's disease.[1] The efficacy and safety of vedolizumab in inflammatory bowel disease (IBD) were demonstrated in the GEMINI trials.[2–4] It is generally well tolerated, and the common adverse effects include nausea, fatigue, and arthralgia with no reports of kidney injury.[5] There has only been 1 previous case report of acute interstitial nephritis (AIN) secondary to vedolizumab. In this article, we report a case of late-onset AIN while on vedolizumab.[6]

CASE REPORT

A 20-year-old White man presented to the emergency department in August 2020 with 3 weeks of right flank pain. He was diagnosed with ulcerative colitis 15 months earlier and was intolerant to several therapies including mesalazine, azathioprine, and infliximab because of the development of side effects. Ten months before his current presentation, he was commenced on vedolizumab and was receiving maintenance therapy with vedolizumab every 8 weeks. His last colonoscopy 3 months before admission was graded as Mayo Score 0 and fecal calprotectin 83 μg/g. His last dose of vedolizumab was 1 week before the onset of symptoms. He was not on any other medications including nonsteroidal anti-inflammatory drugs or over-the-counter or herbal supplements. He had no associated nausea, vomiting, urinary symptoms, hyperesthesia, trauma, rash, or fevers.

His vital signs revealed a blood pressure of 128/77 mm Hg, heart rate of 97 bpm, respiratory rate of 21 breaths per minute, oxygen saturation of 97% on room air, and a temperature of 37.0°C. Physical examination revealed tenderness over the right flank with no associated peritonism. There was no evidence of any rash, erythema, or signs of infection, and there was no periorbital or pedal edema.

His baseline kidney function before the commencement of vedolizumab was 73 μmoL/L, and the estimated glomerular filtration rate (eGFR) was > 90 mL/min/1.73 m2. On admission, his kidney function revealed an elevated serum creatinine of 171 μmoL/L with an eGFR of 49 mL/min/1.73 m^2, which did not improve with intravenous fluids. Laboratory findings also revealed albumin 45 g/L, hemoglobin 166 g/L, white blood cell count 10.3 × 10^9/L (neutrophils 7.22 × 10^9/L, eosinophils 0.05 × 10^9/L, and lymphocytes 2.01 × 10^9/L), C-reactive protein 74 mg/L (normal 0–5 mg/L), and negative blood cultures. Urinalysis revealed no leukocyturia (<10 × 10^6/L), eosinophiluria (<1%), hematuria (<10 × 10^6/L), or proteinuria (<20 mg/L), and urine culture was negative. Hepatitis B virus,

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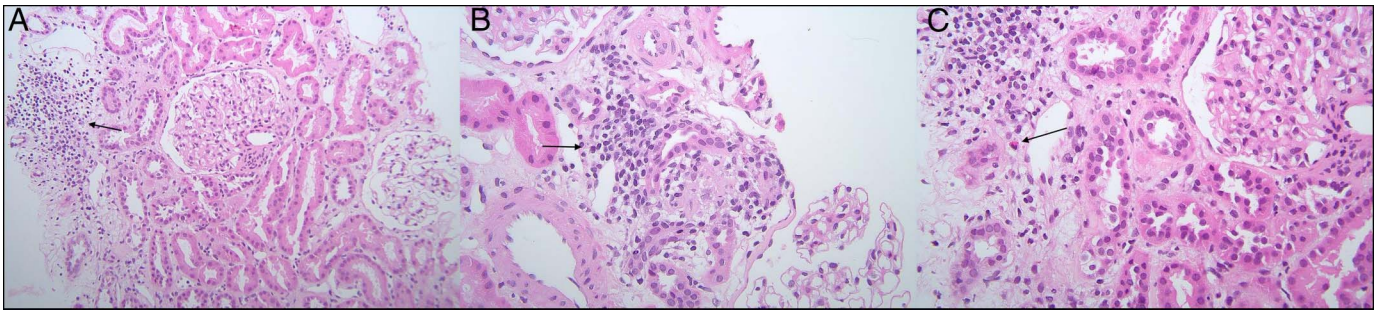

Figure 1. Kidney biopsy. (A–C) Light microscopic examination of the kidney biopsy showing focal interstitial inflammation composed of lymphocytes with occasional eosinophils. H&E ×20.

hepatitis C virus, human immunodeficiency virus, Epstein-Barr virus IgM, cytomegalovirus IgM, and QuantiFERON Gold were all negative. Peripheral anti-neutrophil cytoplasmic antibody was elevated at a titre of 40; however, his anti-nuclear antibody, antiglomerular basement membrane, and complements (C3 and C4) were within normal range.

An ultrasound and computed tomography of the abdomen with contrast of the kidneys revealed no abnormalities. Kidney biopsy demonstrated focal interstitial inflammation composed of lymphocytes with occasional eosinophils without evidence of necrotizing lesions, sclerosis in glomeruli, or evidence of diffuse tubular damage (Figure 1). Immunofluorescence was not performed because of the nonavailability of a fresh sample.

The patient was diagnosed with AIN secondary to vedolizumab. He was prescribed oral prednisolone 40 mg and achieved complete renal recovery within 3 weeks with a serum creatinine of 89 μmoL/L and eGFR of $>$ 90 mL/min/1.73 m^2. He was subsequently commenced on adalimumab for the treatment of his ulcerative colitis, and at the follow-up after 4 months, his renal function remains normal.

DISCUSSION

Vedolizumab is an α4β7 integrin antagonist that has been approved for the treatment of Crohn's disease and ulcerative colitis.[1] The α4β7 integrin, a cell surface glycoprotein, is expressed on T cells and binds to mucosal addressin cell adhesion molecule-1.[7] By blocking α4β7, vedolizumab inhibits migration of memory and effector T cells as well as subsequent leukocyte extravasation to the affected gastrointestinal mucosa.[7] There are multiple integrins that play a critical role in the kidney; however, the role of α4β7 in kidney disease is unknown.[8]

Renal manifestations of IBD, such as nephrolithiasis, have been increasingly reported with the suggestion that they may be considered as an extraintestinal manifestation of the disease.[9] However, only a few case reports have described rare complications such as glomerulopathy and AIN.[10,11] The most common diagnosis found on kidney biopsy is immunoglobulin A nephropathy, followed by interstitial nephritis and arterionephrosclerosis, suggesting a shared pathophysiology between intestinal and kidney diseases.[12]

Interstitial nephritis is an immune-mediated form of tubulointerstitial kidney injury that may occur secondary to drugs, autoimmune disease, infections, or hematological disorders. The symptoms are often nonspecific, and hence, the diagnosis is made by kidney biopsy.[13] AIN is characterized by interstitial inflammation, edema, and tubulitis with a predominance of CD4+ T lymphocytes and mononuclear cells with variable numbers of eosinophils.[13] Early recognition is crucial because AIN can progress to a chronic kidney disease triggered by fibroblast activation leading to interstitial fibrosis and tubular atrophy.[14] Extrarenal symptoms are often absent with no albuminuria.

The mainstay of therapy is removal of the causative agent and frequently requires corticosteroid therapy.[14] Drug-induced AIN can occur in up to 27% of all biopsies performed for an acute kidney injury and is characteristic because of a delayed hypersensitivity reaction.[15] Antibiotics are the most implicated class of drugs associated, followed by the use of proton pump inhibitors, nonsteroidal anti-inflammatory agents, 5-aminosalicylates, antiepileptic drugs, and allopurinol.[15] After administration, the drug can act as a tubulointerstitial antigen, deposit in the interstitium, or form a hapten. The inflammatory reaction that occurs is associated with leukocyte recruitment, activation of complement, and secretion of chemokines and cytokines.[16] Tubulointerstitial nephritis in IBD can occur while on 5-aminosalicylates; hence, it is often believed to be drug-induced.[17] There are a number of reports that demonstrate the recovery of renal function once the offending drug is removed.[18] Our patient was not on any other drug which may have caused interstitial nephritis. He was also in clinical and biochemical remission at the time of presentation, and extraintestinal manifestation of disease was believed to be unlikely. Although the patient was not rechallenged to confirm the diagnosis, based on our evaluation, we think that AIN secondary to vedolizumab was the most likely diagnosis.

DISCLOSURES

Author contributions: D. Subhaharan is the article guarantor. D. Subhaharan, PK Ramaswamy, and N. Ishaq were directly

responsible for the patient's management as well as the analysis and, drafting of the submission. S. Francisco was responsible for pathology analysis and contributed to the drafting of the submission. All authors approved the final submission.

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