Acute Interstitial Nephritis: A Rare and Unusual Side Effect of Omalizumab

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Abstract

Acute interstitial nephritis (AIN) is a relatively common cause of acute kidney injury with etiologies that include drug therapy, infections, and systemic diseases. Of these etiologies, drug therapy accounts for ~70% of AIN cases. Although any drug can cause AIN, there are no reported cases of AIN caused by omalizumab, a humanized monoclonal antibody that binds to and inhibits circulating immunoglobulin E. In this article, we share the first reported case of AIN following administration of omalizumab for the treatment of moderate to severe persistent asthma.

Keywords

nephrology, acute interstitial nephritis, drug-induced interstitial nephritis, omalizumab, acute renal failure

Introduction

Omalizumab is a humanized monoclonal antibody that binds to and inhibits circulating immunoglobulin E (Ig) E and is Food and Drug Administration approved for use in treating moderate to severe persistent asthma that is poorly controlled with inhaled corticosteroids.¹-³ Major adverse effects reported include anaphylaxis, cardiovascular affects, and vasculitis symptoms consistent with eosinophilic granulomatosis with polyangiitis (EGPA).⁴ In 2018, omalizumab was to be evaluated as a potential treatment of drug-induced acute interstitial nephritis (DI-AIN), a common cause of acute kidney injury (AKI), but was withdrawn due to a lack of participants.⁵ Instead of omalizumab therapy for treating DI-AIN, however, we present a rare case of AIN as a side effect of omalizumab therapy.

Case Presentation

A 71-year-old obese Filipino female with moderate to severe asthma, uncontrolled type 2 diabetes, hypertension, heart failure with preserved ejection fraction, and chronic kidney disease (CKD) stage 4 presented to the emergency department for progressively worsening shortness of breath and productive cough for 1 week with increased severity in the past 2 days. The patient was in her normal state of health up until 3 weeks prior to presentation when she received her first omalizumab injection for refractory asthma. Omalizumab was the only new medication added to her home medication regimen (Table 1). After the injection, she developed mild generalized weakness and fatigue but otherwise felt well. After receiving the second injection of omalizumab 2 weeks later, she experienced worsening of the generalized weakness, fatigue, and developed shortness of breath with a productive cough. This prompted her to go to the emergency department.

On presentation in the emergency department, the patient was in no acute distress, afebrile, and nonhypoxic with an oxygen saturation of 96% on room air. Pulmonary examination revealed decreased breath sounds, diffuse bilateral wheezing, and rales at the bilateral lung bases. The patient also had 2+ bilateral pitting edema with the rest of the physical examination unremarkable. While in the emergency department, she was treated for heart failure exacerbation with intravenous (IV) furosemide, kidney failure, and acute asthma exacerbation. She then became increasingly lethargic with obtained laboratory values significant for an elevated potassium of 8.1 mEq/L (8.1 mmol/L; Table 2), blood urea nitrogen of 139 mg/dL (49.62 mmol/L), creatinine of 8.08 mg/dL (714.27 µmol/L) from a baseline creatinine of 2.09 mg/dL (184.76 µmol/L), and urine microalbumin/creatinine ratio (MCR) of 2,092 µg/g creatinine.

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Received February 21, 2020. Revised July 1, 2020. Accepted July 6, 2020.

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by decreased to 4.8 mEq/L (4.8 mmol/L), 90 mg/dL (32.13 µmol/L), respectively. By this time, the patient was hemodynamically stable and downgraded to the medical floor. In the setting of asthma with pulmonary infiltrates on CXR, eosinophilia (1.2 × 10³ µL), and sudden-onset acute kidney failure requiring hemodialysis, there were concerns for possible AIN secondary to omalizumab therapy versus EGPA (formerly known as Churg-Strauss syndrome). The patient was started on high-dose methylprednisolone for 3 days while workup for autoimmune disorders was obtained. Her antineutrophil antibodies screening was positive with a titer of 1:640. Antineutrophil cytoplasmic antibodies (ANCA) for myeloperoxidase (MPO-ANCA) and proteinase 3 (PR3-ANCA) were both negative. A kidney biopsy was then obtained, which demonstrated moderate diffuse glomerulonephritis, focal segmental glomerulosclerosis, and moderate arterio- and arteriolosclerosis. There was no evidence of lupus nephritis or ANCA-associated necrotizing/crescentic glomerulonephritis. Focal eosinophils were noted near the corticomedullary junction, consistent with a drug-induced interstitial nephritis (Figure 1). The patient’s hospital course remained uncomplicated and she was discharged on day 7 with oral steroids and outpatient hemodialysis 3 times per week with instructions to avoid omalizumab.

The patient had a baseline creatinine of 2.09 mg/dL (184.76 µmol/L) and estimated glomerular filtration rate of 23 mL/min 1 month prior to admission. After 3 days of methylprednisolone 1 g IV with an 8-week taper of oral prednisone 40 mg outpatient, her urine micro-albumin/creatinine ratio decreased from 2524 µg/mg on admission to 889 µg/mg (Table 1). Eight weeks after being discharged, the patient recovered from her AKI and no longer required hemodialysis.

### Discussion

Omalizumab was approved by the Food and Drug Administration in 2003 for the treatment of moderate to severe persistent asthma in patients 12 years and older with elevated IgE level whose symptoms were not adequately controlled with inhaled corticosteroids. Omalizumab is also approved for treating chronic idiopathic urticaria in patients 12 years and older who continue to be symptomatic despite H1 antihistamine treatment. Our patient continued to have asthma exacerbations requiring multiple emergency room visits despite being on high-dose inhaled glucocorticoids, antileukotriene agents, and long-acting muscarinic antagonists (Table 1). She was a good candidate for a trial of omalizumab versus EGPA (formerly known as Churg-Strauss syndrome). The patient was started on high-dose methylprednisolone for 3 days while workup for autoimmune disorders was obtained. Her antineutrophil antibodies screening was positive with a titer of 1:640. Antineutrophil cytoplasmic antibodies (ANCA) for myeloperoxidase (MPO-ANCA) and proteinase 3 (PR3-ANCA) were both negative. A kidney biopsy was then obtained, which demonstrated moderate diffuse glomerulonephritis, focal segmental glomerulosclerosis, and moderate arterio- and arteriolosclerosis. There was no evidence of lupus nephritis or ANCA-associated necrotizing/crescentic glomerulonephritis. Focal eosinophils were noted near the corticomedullary junction, consistent with a drug-induced interstitial nephritis (Figure 1). The patient’s hospital course remained uncomplicated and she was discharged on day 7 with oral steroids and outpatient hemodialysis 3 times per week with instructions to avoid omalizumab.

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omalizumab as a potential treatment for AIN with the goal of shortening the duration of prednisone use in treating DI-AIN; however, due to a lack of participants, the study was withdrawn.6 Currently, there are no studies or reports of omalizumab causing AIN.

Drug-induced acute interstitial nephritis is a common cause of AKI and is estimated to be the cause in approximately 20% of patients with unexplained AKI.7 Many drugs are known to cause AIN with the most common being antibiotics, NSAIDs (nonsteroidal anti-inflammatory drugs), and proton pump inhibitors.7 Other drugs that demonstrate an increase in nephrotoxicity with a predominance for AIN are immune checkpoint-inhibitors (CPIs) used in cancer therapy.7 Immune CPIs are monoclonal antibodies that activate quiescent T-cells and stops a cancer cell’s ability to turn off activated T-cells that would allow for unchecked tumor cell proliferation.8 AIN caused by CPIs is slower to develop compared with known drugs that cause AIN and may be missed in the outpatient setting.9 Although not used in cancer therapy, omalizumab is also a monoclonal antibody like CPIs and may have similar effects on the kidneys.

The definitive treatment for DI-AIN is stopping the offending agent with no current consensus on the use of steroid therapy.10 Small case series along with anecdotal reports have suggested that the use of corticosteroids in treating DI-AIN may be beneficial in some patients.10 However, there are no randomized controlled trials to determine the efficacy of steroids in treating DI-AIN, leaving the decision to be based on clinical judgement. In this patient, because of her acute asthma exacerbation and early concerns for EGPA, methylprednisolone 1 g IV was started early. She received 3 days of methylprednisolone 1 g IV with an 8-week oral prednisone 40 mg taper. Her proteinuria significantly decreased from 2524 µg/mg on admission to 889 µg/mg 15 days post discharge.

In conclusion, this patient had stage III CKD in the setting of uncontrolled diabetes; however, the acute changes in her kidney function and worsening of proteinuria were attributed to omalizumab. The kidney biopsy confirmed the acute changes of CKD with AIN. The patient has recovered from AKI with corticosteroids. DI-AIN can be caused by any drug, including novel drugs that have been considered for potential treatment of DI-AIN. Our case highlights the first report of AIN as a side-effect of omalizumab therapy and the importance of continued surveillance of possible rare side effects from current medications on the market.

Authors’ Note
An abstract of this work was presented at the 2020 Western Medical Research Conference in Carmel, California, from January 23 to 25, 2020.

Declaration of Conflicting Interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics Approval
Kern Medical Institutional Review Board granted ethical approval to report this case, Study #19034.

Informed Consent
Written informed consent was obtained from the patient for their anonymized information to be shared in this case report for presentation/publication.

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Figure 1. Renal biopsy: eosinophils (arrow) at the corticomedullary junction consistent with acute interstitial nephritis.
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