Adalimumab Induced Aseptic Meningitis and Focal Partial Seizures in Patient with Crohn’s Disease

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Received July 14, 2019; Revised August 18, 2019; Accepted September 01, 2019

Abstract
Tumor necrosis factor α inhibitors (TNFα-i) are a commonly prescribed class of medications for the treatment of inflammatory bowel disease. With the increasing use of this medication class, some uncommon adverse effects have been reported. We present a case of a young male recently prescribed adalimumab for Crohn’s disease who developed aseptic meningitis with associated focal partial seizures.

Keywords: anti-inflammatory agents/adverse effects, crohn disease/drug therapy, adalimumab, meningitis, aseptic/chemically induced, meningitis, aseptic/drug therapy


1. Introduction

Tumor necrosis factor α inhibitors (TNFα-i) are an increasingly prescribed class of medications for the treatment of inflammatory bowel disease. Their use in the treatment of Crohn’s disease was first approved by the US Food and Drug Administration (FDA) in 1998. The latest American Gastroenterology Association guidelines on the treatment of Crohn’s disease listed TNFα-i as a primary medication class to induce and maintain symptom remission. [1] With increasing use of this medication class, some uncommon adverse effects, including aseptic meningitis, have been reported. The first case of TNFα-i induced aseptic meningitis (TAAM) was published in 2001. [2] To date, there have been 13 published cases describing the correlation between TNFα-i and aseptic meningitis. [3,4,5] Presented is a case report on a young male recently prescribed adalimumab for Crohn’s disease who developed aseptic meningitis with associated focal partial seizures.

2. Case

A 24-year-old male presented to the Emergency Department (ED) with acute onset right-sided headache with left-sided paresthesia. The patient reported left facial droop and two episodes of left-sided weakness and numbness, each lasting 15 minutes before spontaneous resolution. These weaknesses started distally in his toes and fingers and migrated proximally. He did not have complete paralysis. The patient’s past medical history was significant for a recent diagnosis of Crohn’s disease. He had received his third dose of adalimumab (i.e., dosed every two weeks) 12 days prior to his presentation. Surgical history and family history were non-contributory. The patient denied tobacco, ethanol, or drug use, and was currently employed as a service technician.

The patient was admitted for further evaluation. Head computed tomography scan and computed tomography angiography of head/neck were both unremarkable. Electroencephalogram was normal. Cluster headaches were suspected, and the patient was discharged home on day two with a prescription for sumatriptan.

The day after discharge the patient had a third episode of acute onset right-sided headache with left-sided weakness that was unresponsive to sumatriptan, prompting his return to the ED. Patient’s vitals included temperature 100 F°, blood pressure 179/93 mmHg, pulse 74 beats/minute, respiratory rate 16 breaths per minute, and oxygen saturation 94%. His neurologic exam was normal. Laboratory studies were also normal including: serum white blood cell count of 8.6 x 10³/µL (i.e., 49% neutrophils, 36% lymphocytes), hemoglobin 16.3 g/dl, sodium 135 mEq/L, potassium 3.6 mEq/L, chloride 99 mEq/L, bicarbonate 26 mEq/L, BUN 14 mg/dL, creatinine 1.10 mg, glucose 105 mg/dL, and calcium 9.8 mg/dL.

The patient was re-admitted. Neurology was consulted, and another electroencephalogram was conducted revealing rhythmic and semi-rhythmic delta waves in the right frontotemporal region. A second head/neck computed tomography angiography was conducted and failed to show vasospasm. Magnetic resonance imaging of brain with contrast was normal. A lumbar puncture was performed with findings presented in Table 1.
With the increased use of TNFα-i, general knowledge of both common and uncommon adverse drug effects is important. Commonly described side effects are headache, fever, infection, arthralgia, and rash. [6] TNFα-i aseptic meningitis (TAAM) is a rare but potentially serious side effect with an increasing number of reports. Most of these patients presented with fever and meningeval signs. Although most cases describe mild symptoms with resolution within 24 hours, [7] one prior case demonstrated TAAM as being fatal. [8]

The pathophysiology of TAAM remains unclear. It has been hypothesized that the mechanism is a type III hypersensitivity reaction akin to serum sickness. [7] Another proposed mechanism is an altered cytokine milieu resulting from peripheral inhibition of TNFα-i, which then upregulates pro-inflammatory pathways in the brain of susceptible individuals. [2] Direct drug toxicity to the brain is not considered a viable mechanism due to its inability to cross the blood brain barrier. [3]

Since the first report of TAAM was published in 2001, [2] several other cases have now been published. [3,4,5] In addition, other, even less common, neurologic manifestations have been reported including: Guillain-Barre, [9] multiple sclerosis, [10] optic neuritis, [11,12] demyelinating encephalomyelitis, [13] and mononeuritis multiplex. [14] While most patients with TAAM had normal neurologic exams, some did have objective lower extremity weakness [9] or positive Kernig/Brudzinski signs. [6] To date, there has been only one other case report of seizure activity related to TNFα-i. [8] The publication reported a patient with generalized seizure. To the authors’ knowledge, this is the first case of a patient presenting with aseptic meningitis with focal partial seizures while on adalimumab.

A pertinent clinical question is whether a patient that developed TAAM should be re-trialed on the medication. In one case report, severe adverse effects associated with Crohn’s disease led to resumption of TNFα-i therapy. [15] Authors of the report noted no reoccurrence of the adverse reaction despite resuming the same medication. However, the time frame for re-introduction of the medication was unclear in the article. In the presented case report, due to safety, the reintroduction of TNFα-i therapy was not assessed since the patient’s Crohn’s disease has remained controlled when off TNFα-i therapy. Further research in this area is needed to better understand and study this topic.

In summary, the presented case describes the first reported patient to date who developed aseptic meningitis complicated by focal partial seizures in association with administration of adalimumab for treatment of Crohn’s disease. More research is needed to determine if a patient can safely resume the class of medication after experiencing a severe adverse event. This will become an important question to answer as TNFα-i is increasingly prescribed. It is also important that gastroenterologists provide patient education on rare but significant side effects.

**Acknowledgements**

There are no acknowledgements.

**Disclosures**

The authors have no competing interests.
Abbreviations

TNFα-i: tumor necrosis factor α inhibitors
TAAM: TNFα-i induced aseptic meningitis.

References


