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Single Case

Listeria Monocytogenes Brain Abscess in Crohn's Disease Treated with Adalimumab

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Abstract
Listeria monocytogenes is a gram-positive bacterium that causes listeriosis. Brain abscess is a very uncommon manifestation of listeriosis and has not been reported to be associated with adalimumab (humira), one of the approved medications for treating Crohn's disease. A 45-year-old female with Crohn's disease presented with sudden onset of fever, headache, nausea, vomiting, and altered mental status for 1 day. She was on prednisone and 6-mercaptopurine. She had started taking adalimumab 17 days prior to admission. She had signs of toxicity, confusion, and nuchal rigidity, but showed neither central nervous system deficits nor focal deficits. The laboratory results revealed Gram-positive coccobacillus, positive blood and cerebrospinal fluid culture for Listeria monocytogenes, and a 5 × 5 mm ring-enhancing lesion of brain abscess on MRI. After holding off 6-mercaptopurine and adalimumab, her mental status improved on the next day. Finally, she was discharged on day 7 of hospitalization with ampicillin 2 g intravenously every 4 h for a total of 2 weeks. Two weeks later, the follow-up MRI showed a 2-mm area of residual enhancement in the left temporal lobe at the site of the previous brain abscess. Adalimumab, as a tumor necrosis factor (TNF)-alpha inhibitor, carries a risk of triggering opportunistic infection, such as listeriosis. With an altered mental status or neurological signs in patients receiving TNF-alpha antagonizing agent, physicians should suspect bacterial infection in the central nervous system and promptly initiate treatment for brain abscess if needed.

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Introduction

Listeria monocytogenes (LM), a gram-positive bacterium, is commonly found in food or water. Patients infected with LM usually have fever, muscle aches, and sometimes nausea or diarrhea. The common manifestations of listeriosis are meningitis, meningoencephalitis, and bacteremia in immunosuppressed patients. However, brain abscess is rarely found in patient with LM infection. On the other hand, adalimumab (humira), a recombinant human IgG1 monoclonal antibody directed against tumor necrosis factor (TNF), is one of the approved treatments for Crohn's disease [1]. There were a few reports about patients who developed brain abscess from LM infection [2, 3]. To the best of our knowledge, there is no reported evidence of LM brain abscesses in patient treated with adalimumab. Herein, we present a patient with Crohn's disease who developed a left temporal lobe abscess within 17 days after adding adalimumab to her standing regimen of prednisone and 6-mercaptopurine.

Case Report

A 45-year-old female presented with sudden onset of fever, headache, nausea, vomiting, and altered mental status for 1 day. She had a past medical history of Crohn's disease. Additionally, she was on oral prednisone 30 mg daily and oral 6-mercaptopurine 25 mg daily. Seventeen days before admission, she had started taking adalimumab. On physical examination, the patient had a temperature of 39.8°C, blood pressure of 133/94 mm Hg, heart rate of 122 beats/min, respiratory rate of 20 breaths/min, and oxygen saturation of 20% in room air. Apart from that, she had signs of toxicity, confusion, and nuchal rigidity. Due to the patient's discomfort, the tests for Kernig's sign and Brudzinski's sign were not performed.

A neurological examination revealed neither central nervous system (CNS) deficits nor focal deficits. For laboratory data, complete blood count was notable for leukocytosis of 12.7 k/mL with bandemia (band neutrophils 15%), hemoglobin 14.5%, hematocrit 42.5 g/dL, and platelet count 151,000/μL. Her comprehensive metabolic panel was remarkable for hyponatremia (serum sodium 132 mmol/L), hypochloremia (chloride 87 mmol/L), anion gap metabolic acidosis (anion gap 25 mmol/L and carbon dioxide 20 mmol/L), lactic acidosis (lactic acid 2.53 mmol/L), and hyperglycemia (glucose 142 mg/dL). By lumbar puncture we could extract 1.5 mL of turbid cerebrospinal fluid (CSF); CSF analysis showed white blood cell count 2,300 cells/mL (48% segmented neutrophils, 6% lymphocytes, and 43% monocytes), red blood cell count 130 cells/mL, glucose 44 mg/dL, and protein 216 mg/dL. CSF stain revealed Gram-positive coccobacilli, the patient was given vancomycin, ceftriaxone, and ampicillin. At the same time, 6-mercaptopurine and adalimumab were discontinued immediately together with tapering off prednisone. Consequently, the patient's mental status improved on the next day despite persistent headache and fever with a body temperature of 37.8°C. Since both blood and CSF culture were positive for LM, vancomycin and ceftriaxone were hence discontinued; the patient eventually defervesced.

Then, the initial MRI of the brain came back showing a 5 × 5 mm ring-enhancing lesion in the left temporal lobe with surrounding increased T2 and FLAIR signal consistent with brain abscess (Fig. 1). The patient was discharged on day 7 of hospitalization with ampicillin 2 g intravenously every 4 h for a total of 2 weeks. The follow-up MRI at 2 weeks after the initial treatment of ampicillin revealed decreasing signs of a ring-enhancing lesion in the left temporal lobe (Fig. 2). After completing 3 weeks of ampicillin, the patient received an additional week of trimethoprim/sulfamethoxazole 10 mg/kg/day. A repeat MRI of the brain

was performed 4 weeks after the initial treatment, showing no evidence of a ring-enhancing lesion in the left temporal lobe (Fig. 3).

Discussion

LM is one of the most harmful food-borne pathogens, as the Center for Disease Control estimates that listeriosis causes approximately 1,600 illnesses and 260 deaths per year in the United States [4]. As an intracellular organism, LM can invade tissues normally resistant to infection, such as the CNS, the gravid uterus, or a fetus [5]. Thus, cellular immune response plays an important role for protective immunity against LM; any conditions or medications associated with impaired cellular immunity may prone to LM infection [3].

Brain abscess accounts for approximately 10% of CNS infections by LM [6]. The diagnosis of LM brain abscess may be suspected from the clinical findings. However, there is no clinical method to separate LM brain abscess from other infectious diseases that can lead to fever, constitutional symptoms, headache, and focal neurological deficits. For this reason, a positive blood or CSF culture is required for a definite diagnosis. However, there was a report that patients with LM brain abscess were tested positive for LM based on blood culture in 79% and CSF culture in 23% of all cases [3].

In this case, the patient had started taking adalimumab, a TNF-alpha inhibitor, as a treatment for Crohn's disease. Consequently, adalimumab suppressed the inflammatory response, which led to listeriosis. In 2011, the risk of developing listeriosis from TNF-alpha inhibitors was added to the drug label according the US Food and Drug Administration [7]. It is also worth noting that most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids [7, 8]. A recent review article identified 26 cases of LM infection associated with adalimumab: 36% were CNS infections (i.e., meningitis or encephalitis) and 90% were taking concomitant immunosuppressants (i.e., steroid, methotrexate, or azathioprine) [8]. To the best of our knowledge, there is no reported evidence of LM brain abscess in patients following adalimumab therapy. Yet, right thalamus cerebral toxoplasmosis was reported in a 67-year-old man with rheumatoid arthritis who underwent treatment with adalimumab [9].

Unlike other reported incidences, this patient developed LM brain abscess at the left temporal lobe 17 days after adding adalimumab to a standing regimen of prednisone and 6-mercaptopurine. Although the patient carried a risk for brain abscess from prednisone and 6-mercaptopurine, she had never been reported to have brain abscess before. The addition of adalimumab could have accelerated a serious opportunistic infection such as LM brain abscess. We strongly encourage physicians to maintain a high level of suspicion of listeriosis in patients, who are on a TNF-alpha antagonizing agent, with an altered mental status or neurological signs and promptly initiate treatment for brain abscess if needed.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

There are no financial disclosures for any of the authors.

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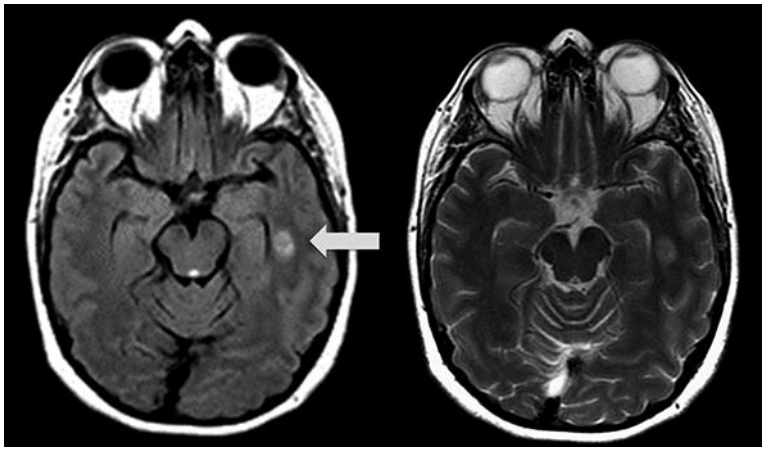

Fig. 1. MRI brain on admission day showing a 5 × 5 mm ring-enhancing lesion in the left temporal lobe.

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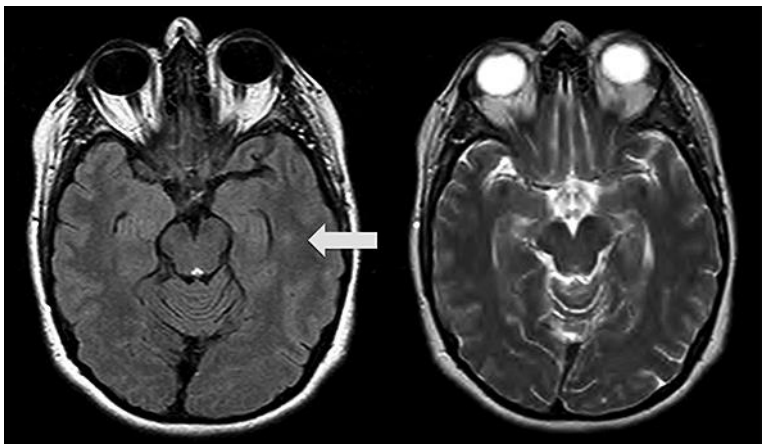

Fig. 2. MRI brain at 2 weeks after treatment showing decreasing signs of a ring-enhancing lesion in the left temporal lobe.

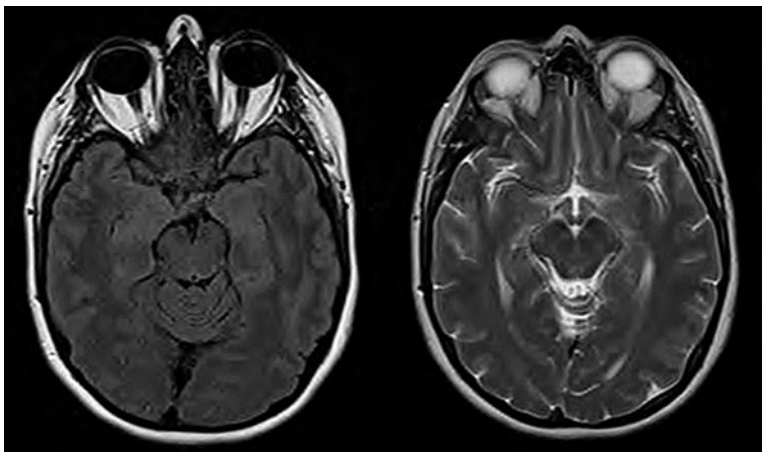

Fig. 3. MRI brain at 4 weeks after treatment showing no evidence of a ring-enhancing lesion in the left temporal lobe.