LETTERS TO THE EDITOR

A Case of Autoimmune Encephalitis Probably Due to Adalimumab in a Patient Treated for Rheumatoid Arthritis

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A Case of Autoimmune Encephalitis Probably Due to Adalimumab in a Patient Treated for Rheumatoid Arthritis

To the Editor:

Tumor necrosis factor α (TNF-α) blockers are widely known to possess a good efficacy in treating rheumatoid arthritis (RA) and other inflammatory diseases. Besides, these agents even are more effective than common disease-modifying antirheumatic drugs in preventing structural damage due to RA.[1,2] However, studies reveal that anti-TNF agents might trigger severe adverse effects, including susceptibility to infections, malignancies, and neurological complications, especially autoimmune encephalitis (AE).[3] Besides, some indicate that administrating anti-TNF agents seemed to be associated with other neurological complications, such as demyelination, optic neuritis, chronic inflammatory demyelinating polyneuropathy, mononeuritis multiplex, and Guillain-Barré syndrome.[4] However, it would be challenging for clinicians to differentiate the etiologies of the aforementioned neurological manifestations. Clinicians could reach the diagnosis by a thorough medical history taking and a precise evaluation of manifestations and findings through paraclinical tests, which can rule out other possible etiologies. Studies indicated that anti–*N*-methyl-D-aspartate receptors (NMDARs) might play a role in developing encephalitis triggered by anti-TNF agents. Thus, it would be a good measure to evaluate the level of anti-NMDAR antibodies in a patient when clinical suspicion of AE is present. Herein, we report an RA patient who experienced AE following anti-TNF therapy with adalimumab.

CASE PRESENTATION

A 67-year-old woman presented to the emergency department with sudden dyspnea, dizziness, sudden blurry vision, a mild chest pain beginning some days before, and a mild headache initiating a week earlier.

The patient was a known case of RA, under treatment with prednisolone, hydroxychloroquine, and methotrexate for 12 years. She also received etanercept over the preceding year, without any response. As the RA could not be controlled, adalimumab 40 mg was administered for her for 6 months (every other week). It is worth noting that the patient discontinued taking methotrexate on her own without consulting her physician. She also had a history of hypertension, hyperlipidemia, diabetes mellitus, and ischemic heart disease (had undergone 2 courses of angioplasty before). However, she did not mention any previous history of neurological complications, such as seizures or decreased level of consciousness.

Clinical evaluations revealed a low-grade fever of 38.2°C, rhonchi and rales on pulmonary auscultation, and a slight decrease in the sounds of the base of the lungs. Mild edema of the lower limbs (1+) was also present. Further physical examination showed no other abnormal findings, except for a positive Babinski sign, whereas other neurological evaluations were normal.

During the second day of hospitalization, the patient deteriorated suddenly, became lethargic, and experienced a generalized tonic-clonic seizure for 30 minutes. Further investigations uncovered a leukocytosis, a high C-reactive protein level, and a bilateral pleural effusion on the chest computed tomography scan, whereas computed tomography scan and magnetic resonance imaging of the brain (with and without contrast) and electroencephalogram were all clear and normal. Moreover, a lumbar puncture was performed, and the cerebrospinal fluid (CSF) analysis was also in the reference range, reported in detail in Table; other laboratory tests are presented in Supplementary Table 1, http://links.lww.com/RHU/A208.

Empirical therapy with acyclovir, intravenous antibiotics (vancomycin, ceftriaxone, and ampicillin), and prednisolone (1 mg/kg of body weight) was initiated immediately to cover any probable infectious encephalitis. After 3 days, no significant response was observed, and the patient was still confused and agitated, and her speech was indistinguishable. At that point, further results on the anti-NMDAR antibodies test were obtained, and they were positive, which led us to think of AE. Therefore, treatment with intravenous immunoglobulin (IVIg) was initiated (20 g daily), and a dramatic response was observed; adalimumab was discontinued, and treatment with IVIg successfully continued for 5 days, whereas there was a significant improvement from the first dose of the treatment. The patient, eventually, was discharged after 9 days, in good condition, and we put her on treatment with leflunomide (20 mg, daily), prednisolone (20 mg, daily), methotrexate (15 mg, weekly) because etanercept was ineffective. After 1 year, there was no recurrence at her follow-up, and the patient's general condition was stable.

DISCUSSION

Autoimmune encephalitis is known as one of the most common causes of acute noninfectious encephalitis, and the possible triggers for AE include tumors, infections, cryptogenic causes, and autoimmune diseases. It could have different clinical manifestations, such as behavioral and psychological symptoms, autonomic dysfunction, motor disorders, and seizure.[5]

Moreover, anti-NMDAR encephalitis is one of the most common causes of AE, which was initially reported in 2007 in 12 patients, 11 of whom had ovarian teratomas[6]; it should be noted that this condition mostly affects young children and women. Concerning anti-NMDAR encephalitis, some recent studies incriminated adalimumab, as it occurred in patients under treatment with

TABLE. Cerebrospinal Fluid Analysis of the Patient

	Patient's Result	Laboratory Reference Range
Opening pressure, cm H_2O	10	5–20
WBC	2	<5
RBC	1	0
Protein, g/L	0.35	0.15–0.6
Glucose, mg/L	40	45–80
Microscopy	No organisms seen	
Culture	No growth	
Cytology	No malignant cells detected	
PCR	Negative for herpes simplex virus 1 and 2 (HSV1 and 2)	

WBC, white blood cells; RBC, red blood cells; PCR, polymerase chain reaction.