Ecilizumab, Neuromyelitis Optica, and Tuberculosis: We Live An Era of Challenging Combinations

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Received 13 July 2015; revision 23 August

2015; accepted 25 August 2015

doi: 10.1111/cns.12465

Dear Editor

Ecilizumab is a recently developed monoclonal antibody that blocks the cleavage of human complement protein C5 by C5-converter, thereby preventing the formation of the pro-inflammatory complement components C5a and C5b-9 [1]. C5a is a very potent mediator that induces chemotactic migration, enhances cell adhesion, stimulates the oxidative burst, and induces the release of various inflammatory mediators [2,3]. C5b-9 is known as the membrane attack complex and has multiple functions, including cytolysis [3].

Ecilizumab has been shown to be an effective treatment for paroxysmal nocturnal hemoglobinuria (PNH) [4], and it is currently used to treat this condition. More recently, ecilizumab has become a therapeutic option for patients undergoing kidney transplant and for those with atypical hemolytic uremic syndrome [5]. Consequently, ecilizumab may prove to be a therapeutic tool for other severe inflammatory disorders [5], including neuromyelitis optica (NMO). A clinical trial of ecilizumab for patients with refractory NMO is currently recruiting patients [6], following the report of successful results from Pittock et al. [7]. Here, we report the case of a patient with NMO and tuberculosis, treated with ecilizumab. The report was approved by the Ethics Committee of Universidade Metropolitana de Santos, SP. The patient signed a consent statement for the case report and also for the off-label therapeutic option of ecilizumab.

The patient was a woman aged 31 years, who developed NMO at the age of 22 years. At disease onset, she had presented optic neuritis and extensive myelitis (C4-T10). NMO was confirmed by clinical manifestations, magnetic resonance findings, and the presence

of anti-aquaporin-4 antibodies, which were assessed using the cell-binding assay (CBA). During the 9 years of the disease, she presented another nine episodes of myelitis and one severe bout of optic neuritis, despite therapy. She received corticosteroids, azathioprine, methotrexate, cyclosporine, mycophenolate mofetil, and rituximab, all to no avail. After 16 months of therapy with rituximab, she developed lung tuberculosis and was treated with rifampicin, isoniazid, pyrazinamide, and ethambutol for 2 months, followed by rifampicin and isoniazid for maintenance. Due to the severity of NMO, which gave rise to a high degree of neurological disability (EDSS 6.0) [8], bimonthly infusions of ecilizumab were proposed. She accepted this alternative and started with 900 mg/infusion for 1 month, followed by 600 mg/infusion thereafter. This treatment regimen was concomitant with isoniazid. The presence of tuberculosis and the choice of a new and very potent drug, although a worrisome association, did seem to be rational. Inhibition of C5 is not associated with the reduction of tumor necrosis factor-alpha (TNF-alpha) and, therefore, should not interfere with the evolution of tuberculosis [9]. On the other hand, concomitant presence of tuberculosis and ecilizumab is not the usual scenario in clinical practice.

The washout period between rituximab and ecilizumab was 10 months. At present, the patient has undergone eight months treatment with ecilizumab at full dose.

Figure 1 shows the extent of the central nervous system lesions on magnetic resonance imaging and imaging of the lung tuberculosis.

The patient has not presented any complications or adverse events over the eight months of ecilizumab therapy. Although

Figure 1 Magnetic resonance imaging (MRI) of the spinal cord (A–C) and brain (D, E), and tomographic (F) and radiographic (G) images of lung tuberculosis. MRI shown here is previous to the use of eculizumab, and chest radiography and tomography were obtained at the time of the diagnosis of tuberculosis.

the follow-up period is relatively short and infections may still develop, the authors feel reassured that NMO is under control and tuberculosis has not reactivated. Hematological and biochemical profile testing remain normal, as do chest radiographs.

NMO is a complex and severely disabling disease [10]. Patients do not progress with disability, as they do in multiple sclerosis, but they accumulate disability at every relapse of NMO. To be able to

avoid the relapses is crucial for controlling the neurological damage. To the best of our knowledge, this is the first medical report of eculizumab used for refractory NMO in a patient with tuberculosis.

Conflict of Interest

The authors declare no conflict of interest.

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