Safety and efficacy of secukinumab treatment in a patient with ankylosing spondylitis and concomitant multiple sclerosis

Sirs,

Here we describe the clinical impact of IL-17 blockade with secukinumab, a human IgG1κ monoclonal antibody that binds to the protein interleukin (IL)-17A, on the signs and symptoms of rheumatologic and demyelinating disease in a patient with ankylosing spondylitis (AS), who developed multiple sclerosis after treatment with tumour necrosis factor (TNF)-blocking agents.

A 41-year-old man with AS was admitted in December 2017. The diagnosis of AS was made in 2009, due to the presence of inflammatory back pain, radiographic bilateral grade 3 sacroiliitis, syndesmophytes and HLA-B27 positivity (1). In 2010 treatment with infliximab was started, continued for five years and suspended for secondary loss of response. Etanercept treatment was then introduced and administered for the next two years achieving a good clinical response. In January 2017, the patient developed blurry vision with intermittent diplopia and paresthesia affecting his right arm. Brain MRI was performed, revealing multiple encephalic demyelinating lesions. A diagnosis of multiple sclerosis (MS) was made, etanercept discontinued and treatment with intravenous steroids started. However, the patient continued to experience acute neurological relapses and reactivation of the rheumatological symptoms. In February 2018, based on the data coming from the clinical trial demonstrating the efficacy of IL-17 blockade in the treatment of MS, secukinumab treatment was initiated. At that time, inflammatory low back pain was also present, and the patient had a C-reactive protein (CRP) level of 8 mg/L, with a disease activity evaluated by ASDAS CRP of 3.2. Although the cumulative number of combined unique active (CUA) lesions was not modified by secukinumab treatment, no new CUA lesions were observed in the next 12 months follow-up (Fig. 1). Interestingly, remission of rheumatologic symptoms (ASDAS CRP 1.4) was achieved and it was accompanied by the complete remission of neurological symptoms with no evidence of active neurological disease.

Multiple sclerosis is an immune-mediated demyelinating disease of the central nervous system (CNS). The role of anti-TNF-α blocking agents in inducing new demyelinating disease or triggering pre-existing demyelinating predisposition still remains controversial (2). *In vitro* studies and preclinical animal models indicate that IL-17A is a crucial cytokine involved in the pathogenesis of multiple sclerosis (3-4). IL-17A, produced in the CNS by Th17 cells, MAIT cells and γδ-T cells negatively affects the functions of microglia, astrocytes, oligodendrocytes, neurons, neural precursor cells and endothelial cells. AS is a chronic inflammatory disease in which Th17 cells, MAIT cells and γδ-T cells play a pathogenetic role (5). Encouraging clinical data with the anti-IL-17A antibody secukinumab have been recently published in a small proof of concept study in multiple sclerosis patients (6). Here we provide the first demonstration of the clinical efficacy of secukinumab on neurological manifestations in a patient with concomitant AS and multiple sclerosis. According to recently published studies (7), the control of multiple sclerosis with absence of disease activity at one year has a high positive predictive value for absence of progression at seven years. Considering this information, IL-17A blockade may become an alternative option at least for AS patients for whom TNF blockers are not indicated.

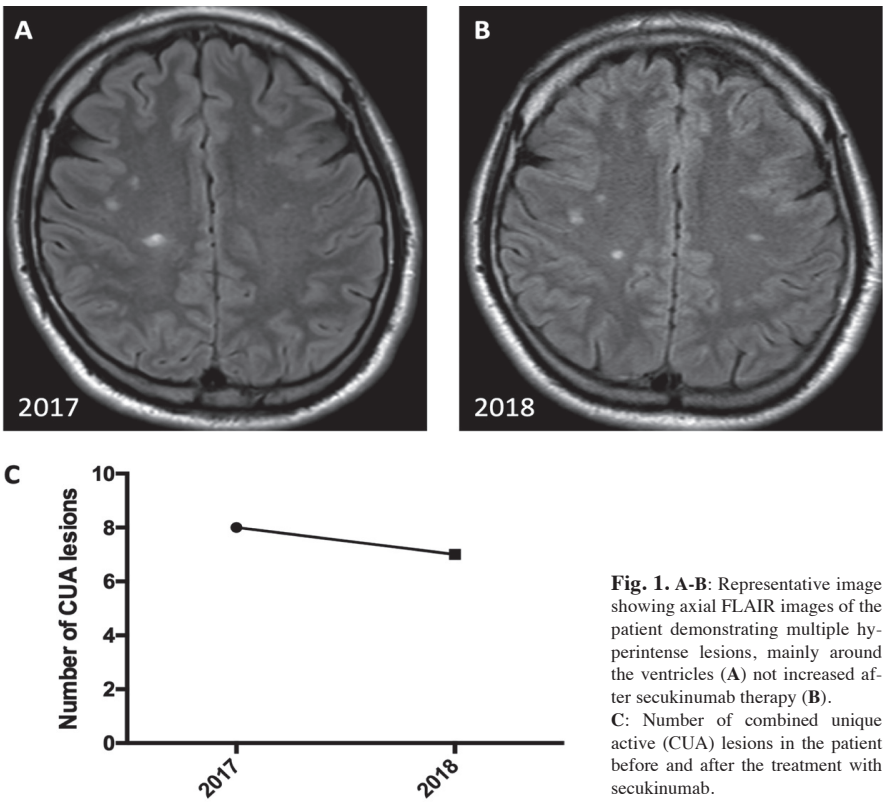

Fig. 1. A-B: Representative image showing axial FLAIR images of the patient demonstrating multiple hyperintense lesions, mainly around the ventricles (**A**) not increased after secukinumab therapy (**B**).
C: Number of combined unique active (CUA) lesions in the patient before and after the treatment with secukinumab.

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