Secukinumab treatment for ankylosing spondylitis and concomitant Huntington's disease: real-world experience

Sirs,

We would like to comment on an article which has recently appeared in your journal by Macaluso *et al*. with our experience with secukinumab in ankylosing spondylitis and accompanying Huntington's chorea to contribute to the treatment of rheumatological diseases complicated by neurological diseases (1).

Huntington's disease is a slowly progressive neurodegenerative disorder that typically manifests itself between the ages of 35 and 45. It causes cognitive and behavioural impairment and is inherited in an autosomal dominant pattern (2). There is currently no treatment for this disease because its molecular pathogenesis is not fully understood (3). TNF-alpha is a cytokine released by activated monocytes, macrophages and T lymphocytes that plays a key role in inflammation. Excessive production of TNF-alpha has been observed in rheumatic diseases such as rheumatoid arthritis and ankylosing spondylitis, and in neurological diseases such as multiple sclerosis. TNF-alpha was found in abundance in the synovial fluid and cerebrospinal fluid of these patient groups (4). Some studies have shown that anti-TNF therapy can exacerbate existing neurological symptoms and even lead to de novo demyelination (5). As a result of these findings, anti-TNF agents are generally avoided in the treatment of neurological diseases and have been reported to potentially worsen the clinical course of multiple sclerosis (6).

On the other hand, secukinumab is a biologic targeting interleukin-17, which plays an important role in the pathological processes of rheumatological diseases. It was first approved for the treatment of plaque psoriasis and psoriatic arthritis in 2015, and then for ankylosing spondylitis in 2016 (7). Importantly, secukinumab has been reported as a safe option in studies related to neurological disease and other specific organ toxicities (8). Several studies in the literature have aimed to assess the safety of secukinumab using demyelination models. One of these studies demonstrated the anti-inflammatory, antioxidant and neuroprotective effects of secukinumab (9). In fact, several studies have shown that IL-17 blockers can reduce magnetic resonance imaging findings associated with multiple sclerosis.

This letter to the editor describes our experience with the use of secukinumab in a 55-year-old male patient diagnosed with ankylosing spondylitis and concomitant Huntington's chorea. The patient had been under our care for six years for ankylosing spondylitis, during which time he had been treated with indometazine and sulfasalazine. During a routine follow-up, we noticed that the patient had choreic movements and cognitive impairment. Upon further investigation, we learned that the patient's daughter and mother had also exhibited similar movements. The patient was subsequently diagnosed with HD by the neurology department and was managed in a multidisciplinary approach involving neurology and rheumatology. As the patient's acute phase reactants increased, his pain worsened and his spinal mobility progressively decreased during follow-up, the possibility of biological therapy was considered. Due to the patient's concomitant neurodegenerative disease, the use of anti-TNF therapy was considered inappropriate. Therefore, we decided to initiate anti-IL-17 treatment, specifically secukinumab, after obtaining approval from the neurology department. The patient has now been on secukinumab for two years and there has been no worsening of his HD symptoms. In addition, his ankylosing spondylitis remains stable and his acute phase reactants are consistently within the normal range.

IL-17 is produced by T helper 17 cells and astrocytes and oligodendrocytes in the central nervous system. Elevated levels of IL-17 have been associated with autoimmune diseases. IL-17 activates inflammatory pathways by stimulating microglia and astrocytes, and contributes to neurodegenerative disease pathways through neutrophil recruitment and chemokine production (10). Blockade of interleukin 17 seems appropriate for suppressing inflammation by inhibiting these mechanisms.

Treatment of rheumatic diseases should be individualised, taking into account any comorbidities. In the management of ankylosing spondylitis in the presence of concomitant neurodegenerative disease, particular caution should be exercised when considering anti-TNF therapy (11). On the other hand, secukinumab is increasingly being used to treat ankylosing spondylitis in patients with co-existing neurological conditions (12). Blocking IL-17 may have the potential to improve neurodegenerative processes. Based on our clinic's experience, we believe that IL-17 blockers could be a viable alternative for the treatment of ankylosing spondylitis in the presence of concomitant neurological disease.

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