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

Sirs,

We read with great interest the letter by Ciccia *et al*., recently published (1). As our Colleagues, we managed a patient affected by ankylosing spondylitis (AS) and multiple sclerosis (MS), but treated with a higher dosage of secukinumab.

Our 40-year-old man patient was affected by AS since 2005 and treated over the years with TNF-inhibitor (TNFi): firstly etanercept, interrupted for recurrent infections, then adalimumab, suspended for inefficacy and appearance of dorsal spinal pain. MRI showed myelitis in the D2-D3 metameres and meanwhile central nervous system (CNS) MRI showed an area of hyperintensity to T2 sequences in the paratrigon area. Thus, MS was diagnosed and copaxone therapy was started, with a good clinical response. The management of the rheumatological disease was therefore mandatory: the patient's assessment was a BASDAI of 7.33 and an ASDAS-CRP of 3.3. Given the concomitant diagnosis of MS, treatment with IL-17A inhibitor (IL17A-i), secukinumab 150 mg monthly was started. After an initial good response, an exacerbation of AS occurred after 9 months of treatment. An increasing of secukinumab dosage from 150 mg to 300 mg every 4 weeks, as an off-label dosage, was started after obtaining the local Ethics Committee consent. The patient's clinical condition rapidly improved and currently, after 6 and still 18 months, a low disease activity (BASDAI 2.5 and ASDAS-CRP 1.5) was achieved associated with MS stability.

Our clinical case has similarities with the one described by Ciccia *et al*.: MS occurrence after several years of TNFi treatment and MS remission during IL17A-i use.

Considering the first point, it is now known that high levels of TNF are found in both active MS lesions biopsies and in cerebrospinal fluid, configuring MS development as autoimmune inflammatory reaction of CNS in which TNF lead to demyelination (2). Being CNS an immune-privileged site, due to the presence of the blood-brain barrier (BBB), TNFi are unable to enter the CNS, meanwhile they can penetrate the joint and bowel tissues: this results in an overall reduction of TNF in the body but relatively unchanged brain TNF levels, with consequent up-regulation of CNS TNF expression and exacerbation of TNF-mediated demyelination (2).

On the other hand, a recent study by Setiadi *et al*. (3), underlined also by Ciccia *et al*., namely that CNS cells might contribute to local IL-17A production, by inducing release of additional cytokines and chemokines, that recruit new inflammatory cells. Particularly, high CSF IL-17A levels in relapsing-remitting MS patients were demonstrated, correlated with CSF/serum albumin quotient, a measure of BBB dysfunction: both IL-17A and IL-6 reduced tight junction (TJ)-associated genes expression and disrupted integrity in BBB cells, promoting proinflammatory cytokines passage (3). This would explain why trials involving secukinumab treatment in MS patients are succeeding and rheumatological patients treated with this molecule are not experiencing re-exacerbations of neurological disease (4).

With regard to differences between the two clinical cases, we would like to stress the need for treatment with secukinumab 300 mg in off-label. Actually, Setiadi findings were valid only for IL-17A but not for IL-17F, so new molecules directed against other IL-17, such as the F portion (5), entering in the treatment armamentarium, are not likely to give the same results as secukinumab, especially in benefiting MS. Moreover, secukinumab 300 mg showed an excellent safety profile (6), with the development of severe adverse reactions in less than 2% of total treated patients. At the same time, secukinumab retention rate proved to be high (7), making us conclude that 300 mg dosage every 4 weeks in off-label could be considered safe and effective also in AS patients.

G.L. FONTI[1], *MD*
M.S. CHIMENTI[1], *MD, PhD*
E. GRECO[1], *MD*
L. BOFFA[2], *MD*
P. CONIGLIARO[1], *MD, PhD*
P. TRIGGIANESE[1], *MD, PhD*
R. PERRICONE[1], *MD*

[1]Rheumatology, Allergology and Clinical Immunology, Department of Systems Medicine, University of Rome Tor Vergata; [2]Department of Neurosciences, MS Centre, Tor Vergata University, Rome, Italy.

Please address correspondence to:
Giulia Lavinia Fonti,
Rheumatology, Allergology and Clinical Immunology,
Department of Systems Medicine,
University of Rome Tor Vergata,
viale Oxford 81,
00133 Roma, Italy.
E-mail: glfonti@hotmail.it

Competing interests: none declared.

References

1. MACALUSO F, GUGGINO G, MAURO D, RIZZO C, BIGNONE R, CICCIA F: Safety and efficacy of secukinumab treatment in a patient with ankylosing spondylitis and concomitant multiple sclerosis. *Clin Exp Rheumatol* 2019; 37: 1096.
2. KALTSONOUDIS E, VOULGARI PV, KONITSIOTIS S, DROSOS AA: Demyelination and other neurological adverse events after anti-TNF therapy. *Autoimmun Rev* 2014; 13: 54-8.
3. SETIADI AF, ABBAS AR, JEET S *et al*.: IL-17A is associated with the breakdown of the blood-brain barrier in relapsing-remitting multiple sclerosis. *J Neuroimmunol* 2019; 332: 147-54.
4. CORTESE A, LUCCHETTI R, ALTOBELLI A *et al*.: Secukinumab may be a valid treatment option in patients with CNS demyelination and concurrent ankylosing spondylitis: Report of two clinical cases. *Mult Scler Relat Disord* 2019; 35:193-195.
5. TORGUTALP M, PODDUBNYY D: Emerging treatment options for spondyloarthritis. *Best Pract Res Clin Rheumatol* 2018; 32: 472-84.
6. DEODHAR A, MEASE PJ, MCINNES IB *et al*.: Long-term safety of secukinumab in patients with moderate-to-severe plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis: integrated pooled clinical trial and post-marketing surveillance data. *Arthritis Res Ther* 2019; 21: 111.
7. FAVALLI E, MARCHESONI A, BALDUZZI S *et al*.: Effectiveness and Retention Rate of secukinumab for Psoriatic Arthritis and Axial Spondyloarthritis: Real- life Data from the Italian LORHEN Registry [abstract]. *Arthritis Rheumatol* 2019; 71 (suppl 10).