Concomitant multiple sclerosis and ankylosing spondylitis: a clinical case report

Zeltina Estere[1*], Meksa Liga[2], Kadisa Anda[1,3], Karelis Guntis[1,2], Pastare Daina[1,2], Svilpe Sandra[2], Polunosika Elina[1,2], Jaunozolina Liga[4]

European Journal of Medical Case Reports
Volume 6(6):95–101
https://doi.org/10.24911/ejmcr/173-1642670323

ABSTRACT

Background: The therapy of patients with concomitant multiple sclerosis (MS) and ankylosing spondylitis (AS) is a challenge for clinicians. Secukinumab is effective in the treatment of MS. In the clinical case, we present, substantial clinical and radiological remission in the case of both autoimmune diseases was observed.

Case Presentation: A male adult was diagnosed with relapsing-remitting MS. The patient complained of severe thoraco-lumbar pain. Magnetic resonance imaging (MRI) led to a diagnosis of AS. Considering that nonsteroidal anti-inflammatory drugs were ineffective and tumor necrosis factor-α blockers are contraindicated in patients with MS, secukinumab was prescribed. MRI 8 months after initiation of therapy provided clinical stability in consideration of the two autoimmune comorbidities.

Conclusion: Secukinumab is an effective therapy for concomitant MS and AS.

Keywords: Multiple sclerosis, ankylosing spondylitis, secukinumab, autoimmune disease, case report.

Received: 20 January 2022 **Accepted:** 03 August 2022 **Type of Article:** CASE REPORT **Specialty:** Neurology

Correspondence to: Zeltina Estere
*Department of Neurology, Riga Stradiņš University, Latvia.
Email: estere.zeltina@inbox.lv
Full list of author information is available at the end of the article.

Background

Tumor necrosis factor (TNF)-α blockers are recommended as first-line biological disease modifiers for axial ankylosing spondylitis (AS). The use of TNF-α blockers in multiple sclerosis (MS) is contraindicated due to significant side effects, including nervous system demyelinating disorders [1]. Secukinumab is approved for the treatment of AS. It is effective in the treatment of MS [2].

Case Presentation

The 30-year-old patient had no significant family health history. In March 2019, he complained of numbness in the IV and V fingers of the left hand, on the lateral surface of the left forearm, and in the entire left leg. Following the persistence of symptoms for several weeks, in April 2019, he was hospitalized at Riga East University Hospital clinic "Gaiļezers" with suspected central nervous system (CNS) demyelinating disease. The patient noted that, in 2015, he experienced numbness in the left palm that lasted for a week and passed without treatment.

On neurological examination at the hospital, he showed mildly increased left leg muscle tone, slender left leg dysmetria, hypoesthesia in the left C8 segment, and below the L1 level on the left side. Mild mis stepping was noted during tandem walking.

Cerebrospinal fluid analysis showed twofold increased IgG levels and positive oligoclonal antibody chains (Table 1). Changes in glucose, folic acid, and c-ANCA were observed in blood tests (Table 2).

Contrast-enhanced magnetic resonance imaging (MRI) of the brain and spinal cord identified seven periventricular and two juxtacortical lesions. The cervical portion revealed two lesions, one of them active-gadolinium enhanced (Figure 1). Compared to a previous cerebral MRI (in 2018) and cervical MRI (in 2015), one new active lesion at the C5 vertebral level and demyelination of the left optic nerve were detected.

The patient received methylprednisolone 1 g iv for 5 days, after which condition improved.

Therapy with dimethyl fumarate was started.

During a visit in September, the patient complained of sensory disturbances and persistent thoracic and lumbar back pain of 5-6 points as measured by the numerical rating scale (NRS). The pain increased during the night and was partially eased with movement. The patient also complained of joint stiffness in the morning for 30-60 minutes.

According to neurological examination, subacute L3 radiculopathy with neuropathic pain syndrome was diagnosed in addition to MS. The patient was recommended

Table 1. *Cerebrospinal fluid analysis.*

TEST	RESULT	REFERENCE INTERVAL
Cytosis	7 mkl	(0-6)
Mononuclear cells in absolute numbers	7 mkl	
Polymorph cells in absolute numbers	0 mkl	
Protein	0.56 g/l	(0.15-0.45)
Lactate	1.39 mmol/l	(1.10-2.40)
Glucose	3.36 mmol/l	(2.20-3.89)
Immunoglobulin G (I)	64.22 mg/l	(10-30)
Oligoclonal antibodies	Positive. Two oligoclonal immunoglobulin bands present in the CSF but absent in the serum. 12.8 g/l IgG in serum (reference interval 7-16 g/l), 55.2 mg/l IgG in the CSF (reference interval <34 mg/l)	
IgG *Borrelia burgdorferi*	Negative	

Table 2. *Blood analysis results.*

TEST	RESULT	REFERENCE INTERVAL
ANA	0.6	(0-1)
Anti-PR3 (c-ANCA)	5.6 U/ml	(0-5)
Anti-MPO (p-ANCA)	1.4 U/ml	(0-5)
ENA	0.4	(0-1)
Antibody to double-stranded DNA (anti-dsDNA)	9.7 U/ml	(0-25)
Anti-phospholipid IgG	2.2 U/ml	(0-10)
Anti-phospholipid IgM	1.6 U/ml	(0-10)
Immunoglobulin A	3.11 g/l	(0.70-4.00)
Immunoglobulin M	1.19 g/l	(0.40-2.30)
Immunoglobulin G	11.34 g/l	(7.00-16.00)
Immunoglobulin E	25.76 IU/ml	(1.50-100.00)
Anti-HCV	0.037 S/CO	S/CO < 1.0 - nonreactive
Rheumatoid factor	0.0 IU/ml	(0.00-14.00)
Glucose	9.94 mmol/l	(3.80-6.10)
Vitamin B12	366.4 pg/ml	(191.0-663.0)
Folic acid	2.42 ng/ml	(4.60-32.20)
HBsAg	0.26 S/CO	S/CO < 1.0 - nonreactive
Thyrotropic hormone	0.3796 mkIU/ml	(0.3500-4.9400)
Syphilis	0.09 S/CO	S/CO < 1.0 - nonreactive

to continue with dimethyl fumarate and to initiate pain relieving medication: etoricoxib and gabapentin.

During a follow-up visit in October, the patient complained that the night pain remained at the previous level. The patient was recommended to take gabapentin, aceclofenac, amitriptyline, and tizanidine.

In November, back pain during the day decreased, but at the night persisted. In addition, the patient complained of sacral and upper buttock pain of 6-7 points (NRS). A neurological examination showed a positive Patrick test on both sides, reduced mobility of the sacroiliac joints on both sides. The patient was recommended to switch gabapentin to pregabalin and to continue taking amitriptyline, aceclofenac. To clarify possible reasons for the consistent pain, an MRI was recommended.

In December, the MRI showed seronegative spondyloarthropathy with bone marrow edema multisegmentally in the lower frontal corners of the vertebrae, spinous processes, and in the upper segments of the thorax, posterior parts of the thoracal vertebrae, and the Th4-Th5 articulating spinouses (Figure 2). No demyelinating lesions or myelopathy were found in the thoracic spinal cord.

An MRI of the lumbar and sacral region in December showed edema of the anterior and posterior corners of lumbar vertebrae and bilaterally active sacroiliitis.

Due to the ineffectiveness of previous analgesic therapy, the patient was prescribed three intravenous infusions of dexamethasone during a follow-up visit. Significant pain relief was observed.

At the rheumatologist's visit in January 2020, according to the Assessment of Spondyloarthritis International

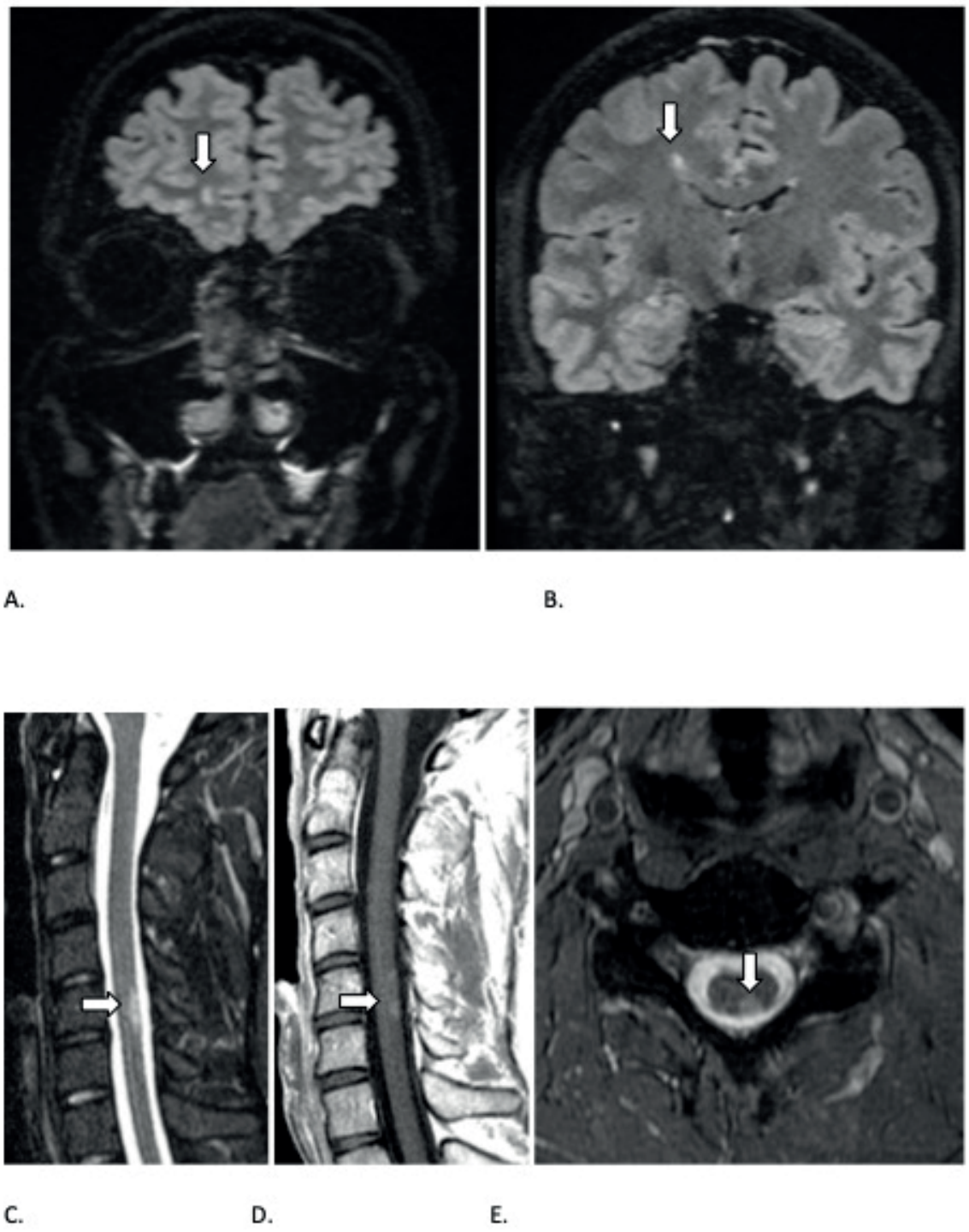

Figure 1. *MRI of the brain and the spinal cord, T2 FLAIR 3D, STIR sag., T1 sag+C, T2 ax. A typical juxtacortical lesion in the right frontal lobe (A), a typical periventricular lesion (B), and a segmental gadolinium-enhanced lesion in the cervical part of the spinal cord (C, D, and E) that is compatible with demyelinating disease.*

Society diagnostic criteria [3], a diagnosis of AS, axial form, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) = 4.4 (high), Bath Ankylosing Spondylitis Functional Index (BASFI) = 1.8, Ankylosing Spondylitis Disease Activity Score containing C reactive protein (ASDAS - CRP) = 3.64 (very high), bilateral sacroiliitis, stage III was determined, based on chronic inflammatory back pain and active bilateral sacroiliitis seen on MRI. Due to the axial form of the disease, comorbidity of MS, and ineffectiveness of various previously used nonsteroidal anti-inflammatory drugs (NSAIDs), the initiation of the interleukin 17 (IL-17) blocker secukinumab was recommended. As a temporary therapy, three infusions of methylprednisolone followed by methylprednisolone orally for 20 days, with gradual withdrawal, were administered.

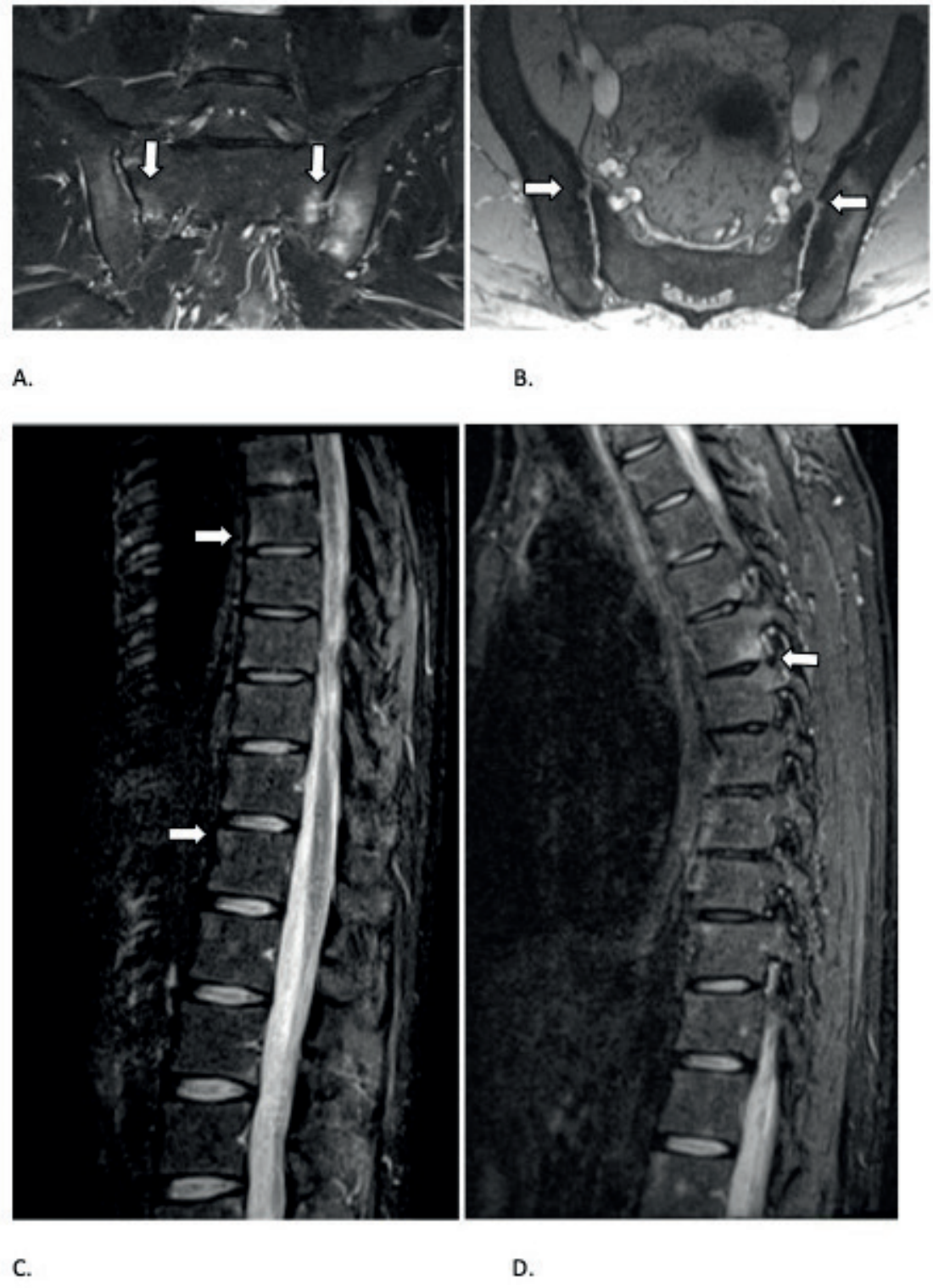

Figure 2. *MRI thoracal spine and sacroiliac joints TRIM sag and cor., T2 me 2D ax. Bilateral sacroiliitis with bone marrow edema (picture A), subchondral erosions (picture B) and multisegmental bone marrow edema at the anterior and dorsal corners of the vertebrae (picture C and D) as a sign of early, active spondylitis.*

During a follow-up visit in January 2020, the patient complained of gripping pain in the lower back of 6-7 points (NRS), and difficulty moving the back, especially in the morning, as well as a week-long tingling in the chest. In addition to the previous neurological conditions, examination revealed hyperesthesia at the level of Th3-Th7. Blood analyses showed an increased CRP of 18 mg/l. The rheumatologist's decision to choose secukinumab for the treatment of AS was supported, as the use of TNF-α inhibitors is contraindicated for the treatment of AS in this case.

In May, following an ordinance by a council of rheumatologists with support from the National Health Service,

secukinumab 150 mg was initiated once weekly subcutaneously for 5 weeks.

In May, a control MRI was performed. In addition to the previously described MS lesions, a demyelination of the right optic nerve without nerve atrophy was detected. There was no radiological progression of the focal lesions of the brain and spinal cord.

During a visit in October, the patient denied any new neurological complaints or sensory disturbances, noted that he did not have any more back pain. Due to the good response, it was recommended that the secukinumab therapy be continued under the supervision of the rheumatologist. Further follow-up with the neurologist and control MRI ought to be conducted once a year.

In January 2021, an MRI of the brain, optic nerves, and spinal cord was compared to the MRI from May 2020, no new MS lesions were found. Investigation found convincing regression of the previously described vertebral inflammation.

Discussion

MS is a chronic autoimmune neurodegenerative disease of the CNS characterized by multiple sites of inflammation, demyelination [4]. AS is a chronic inflammatory disease characterized by inflammatory changes mainly in the sacroiliac joints and spine [2]. A possible association between the two diseases has been noted relatively recently. The concomitant development of both diseases limits the choice of remedies, and the treatment of such patients is difficult [5].

The mechanisms of pathogenesis of AS have not been fully identified, but it has been observed that the inflammatory site contains an elevated amount of the inflammatory cytokine TNF-α, strongly connected to local tissue inflammation, erosion, and bone destruction.

Initially, an inflammatory process is observed, in which the infiltration of immune cells, such as T and B lymphocytes, TNF-α overexpression, play a major role. Lymphocytes, T helper cells, Th17 cells secrete the inflammatory cytokine IL-17 and activate synovial fibroblasts and chondrocytes [6]. The most common sites of inflammation are the sacroiliac joints, peripheral entheses. Inflammation results in cartilage erosion, damage to the subchondral bone, later fibroblast infiltration, connective tissue formation. As a result, fusion of the vertebrae and sacroileacal joints can be observed.

In the pathogenesis of MS, inflammatory process activation is also observed. When immune cells cross the blood-brain barrier, immune cell infiltration into the CNS occurs [7].

The involvement of Th17 cells is observed in the pathogenesis of both MS and AS, which, when choosing a Th17 cell blocking therapy, creates an opportunity to potentially influence the pathogenesis of both diseases.

In the axial form of AS, the first drugs to be prescribed are NSAIDs, but the effect of NSAIDs may be insufficient [8]. According to the recent AS treatment recommendations, biological disease-modifying antirheumatic drugs are preferred for patients who have high disease activity despite previous treatment [9].

As the major inflammatory cytokine in the pathogenesis of AS is TNF-α, TNF-α blockers are recommended as first-line biological disease modifiers for axial disease. The use of TNF-α blockers in MS is contraindicated because they may promote MS progression [1,2].

Secukinumab is recommended as an alternative treatment for AS [2]. Secukinumab is a human IgG1κ immunoglobulin monoclonal antibody that binds to and inhibits IL-17A. Mononuclear blood and cerebrospinal fluid cells in MS patients express IL-17A [10]. Secukinumab inhibits its binding to the IL-17 receptor, thereby inhibiting the release of inflammatory cytokines and chemokines, reducing the inflammatory picture in many autoimmune diseases. The use of the drug reduces clinical symptoms, CRP levels in blood tests, and the radiological picture of inflammation seen on MRI [11]. A randomized, double-blind, placebo-controlled study showed that the efficacy of secukinumab was superior to placebo after only 6 weeks of treatment [12]. Secukinumab is the first inhibitor of IL-17A to be approved for the treatment of AS. It is the first known target drug to be approved as an alternative to TNF-α inhibitors. It should be used when TNF-α inhibitors are ineffective or contraindicated.

When planning therapy for patients with concomitant AS and MS, it is important to ensure that AS therapy will also be effective in the treatment of MS. The first evidence that the IL-17 blocker secukinumab is also effective in the treatment of MS was found in 2010, in a randomized study of 73 patients. The results indicated the efficacy of secukinumab treatment in reducing contrast enhancing lesions [13].

Several case reports of secukinumab treatment in patients with concomitant MS and AS or psoriatic arthritis have been published [14,15]. Iulia Georgiana et al. [5] in the article *AS and MS: a surprising parallel* concluded that the pathogenetic relationship between AS and MS had not yet been fully explained and, therefore, each such clinical case should be recorded and published. MS and AS on their own each pose a challenge for doctors, but the coexistence of the two diseases in one patient requires further research and evidence.

In our presented clinical case, the patient's general condition improved upon the initiation of secukinumab, and no new neurological complaints were observed in the dynamics. The remission of the inflammatory process of AS was also observed, and overall clinical stability was achieved, demonstrating the efficacy of secukinumab in both MS and AS.

We presented a rare clinical case in which MS co-morbid with AS was successfully and very quickly diagnosed, and a safe and specific therapy was initiated early, resulting in stabilization of the patient's clinical condition (Figure 3).

2019		
March	• Complaining of numbness in the IV and V fingers of the left hand, on the lateral surface of the left forearm, and in the entire left leg	
April	• Hospitalized at Riga East University Hospital clinic "Gaiļezers" with suspected CNS demyelinating disease • Twofold increased IgG levels and positive oligoclonal antibody chains in cerebrospinal fluid analysis • Seven periventricular, two juxtacortical brain lesions and two lesions in cervical spinal cord, one of them with contrast enhancement	• Received methylprednisolone 1 g iv for 5 days
June	• The diagnosis of MS, cerebrospinal form, relapsing-remitting course (G35.0), EDSS 2.0	• Dimethyl fumarate was started
September	• Complained of sensory disturbances and persistent thoracic and lumbar back pain of 5-6 points as measured by the NRS, joint stiffness in the morning for 30-60 minutes	• Was recommended to continue with dimethyl fumarate, and • Pain relieving medication: etoricoxib, gabapentin
October	• Complained that the night pain remained at the previous level	• Was recommended to take gabapentin, aceclofenac, amitriptyline, tizanidine
November	• Complained of sacral and upper buttock pain of 6-7 points (NRS) • Positive Patrick test on both sides, reduced mobility of the sacroiliac joints on both sides	• Was recommended to switch gabapentin to pregabalin and • To continue taking amitriptyline, aceclofenac
December	• The MRI showed seronegative spondyloarthropathy. No demyelinating flesions or myelopathy were found in the thoracic spinal cord	• Three intravenous infusions of dexamethasone. Significant pain relief was observed
2020		
January	• A diagnosis of AS, axial form, BASDAI = 4.4 (high), BASFI = 1.8, ASDAS (CRP) = 3.64 (very high), bilateral sacroiliitis, stage III was determined	• The initiation of the IL-17 blocker secukinumab • As a temporary therapy, three infusions of methylprednisolone followed by methylprednisolone orally for 20 days, with gradual withdrawal
Follow-up visit in January	• Complained of gripping pain in the lower back of 6-7 points (NRS), and difficulty moving the back, especially in the morning, as well as a week-long tingling in the chest. In addition to the previous neurological conditions, examination revealed hyperesthesia at the level of Th3-Th7. Blood analyses showed an increased CRO of 18 mg/l	• The rheumatologist's decision to choose secukinumab for the treatment of AS was supported
May	• A control MRI • No radiological progression of the focal lesions of the brain and spinal cord	• Secukinumab 150 mg was initiated once weekly subcutaneously for 5 weeks
October	• No new neurological complaints or sensory disturbances, no more back pain	• Was recommended that secukinumab therapy be continued under the supervision of the rheumatologist
2021		
January	• An MRI of the brain, optic nerves, and spinal cord was compared to the MRI from May 2020, no new MS lesions were found • Convincing regression of the previously described vertebral inflammation	

Figure 3. *Timeline.*

Conclusion

AS and MS are chronic autoimmune, inflammatory diseases that are rarely associated. Biological drugs are used to treat both diseases, but the use of TNF-α blockers, which are widely used in the treatment of AS, is contraindicated in MS patients. The role of the inflammatory cytokine IL-17 in the pathogenesis of AS and MS has been described, which explains the possible efficacy of the IL-17 blocker secukinumab in the successful treatment of both diseases. The clinical case presented by us actualized the relationship between AS and MS and demonstrates the importance of effective cooperation between specialists in improving patient health.

What is new?

TNF-α blockers are recommended as first-line biological disease modifiers for axial AS. The use of TNF-α blockers in MS is contraindicated due to significant side effects, including nervous system demyelinating disorders. Secukinumab is approved for the treatment of AS. It has been shown to be effective in the treatment of MS.

List of Abbreviations

CNS	Central nervous system
IL-17	Interleukin 17
MRI	Magnetic resonance imaging
MS	Multiple sclerosis
NRS	Numerical rating scale
NSAID	Nonsteroidal anti-inflammatory drug
TNF-α	Tumor necrosis factor alpha

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Funding

There are none funding sources, during the article submission process.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

Author details

Zeltina Estere[1*], Meksa Liga[2], Kadisa Anda[1,3], Karelis Guntis[1,2], Pastare Daina[1,2], Svilpe Sandra[2], Polunosika Elina[1,2], Jaunozolina Liga[4]

1. Faculty of Medicine and Healthcare, Riga Stradins University, Latvia.
2. Neurology and Neurosurgery department, Riga East University Hospital clinic "Gaiļezers", Latvia.
3. Internal Diseases department, Riga East University Hospital clinic "Gaiļezers", Latvia.
4. Radiology department, Riga East University Hospital clinic "Gaiļezers", Latvia.

References

1. Kemanetzoglou E, Andreadou E. CNS demyelination with TNF-α blockers. Curr Neurol Neurosci Rep. 2017;17(4):36. https://doi.10.1007/s11910-017-0742-1
2. Zhu W, He X, Cheng K, Zhang L, Chen D, Wang X, et al. Ankylosing spondylitis: etiolo-gy, pathogenesis, and treatments. Bone Res. 2019;7:22. https://doi.10.1038/s41413-019-0057-8
3. Rudwaleit M, van der Heijde D, Landewé R, Akkoc N, Brandt J, Chou CT, et al.The assessment of spondyloarthritis international society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. Ann Rheum Dis. 2011;70(1):25–31. https://doi.10.1136/ard.2010.133645
4. Ghasemi N, Razavi S, Nikzad E. Multiple sclerosis: pathogenesis, symptoms, diagno-ses and cell-based therapy. Cell J. 2017;19(1):1–10.
5. Iulia Georgiana S, Daniel A, Bogdan I, Cristian Dinu P. Ankylosing spondylitis and multiple sclerosis: a surprising parallel. Rom J Neurol. 2014;13(3):93–102.
6. Koenders MI, van den Berg WB. Secukinumab for rheumatology: development and its potential place in therapy. Drug Des Devel Ther. 2016;10:2069–80. https://doi.10.2147/DDDT.S105263
7. Volpe E, Battistini L, Borsellino G. Advances in T Helper 17 cell biology: pathogenic role and potential pherapy in multiple sclerosis. Mediators Inflamm. 2015;2015:475158. https://doi.10.1155/2015/475158
8. Khan MA. Ankylosing spondylitis: introductory comments on its diagnosis and treatment. Ann Rheum Dis. 2002;61(Suppl 3):iii3–7. https://doi.10.1136/ard.61.suppl_3.iii3
9. van Der Heijde D, Ramiro S, Landewé R, Baraliakos X, Van Den Bosch F, Sepriano A, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloar-thritis. Ann Rheum Dis. 2017;76(6):978. https://doi.10.1136/annrheumdis-2016-210770
10. Cortese A, Lucchetti R, Altobelli A, Conte A, Primavera M, Valesini G, et al. Secuki-numab 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;35:193–5. https://doi.10.1016/j.msard.2019.08.006
11. Blair HA. Secukinumab: a review in ankylosing spondylitis. Drugs. 2019;79(4):433–43. https://doi.10.1007/s40265-019-01075-3
12. Baeten D, Baraliakos X, Braun J, Sieper J, Emery P, van der Heijde D, et al. Anti-interleukin-17A monoclonal antibody secukinumab in treatment of ankylosing spondylitis: a randomised, double-blind, placebo-controlled trial. Lancet. 2013;382(9906):1705–13. https://doi.10.1016/S0140-6736(13)61134-4
13. Havrdová E, Belova A, Goloborodko A, Tisserant A, Wright A, Wallstroem E, et al. Ac-tivity of secukinumab, an anti-IL-17A antibody, on brain lesions in RRMS: results from a randomized, proof-of-concept study. J Neurol. 2016;263(7):1287–95. https://doi.10.1007/s00415-016-8128-x
14. Di Tullio F, Odorici G, Lasagni C, Capobianco M, Conti A, Mandel VD. Combination treatment with secukinumab and dimethyl fumarate in a patient with psoriasis and recent diagnosis of multiple sclerosis. Dermatol Ther. 2020;33(6):e13943. https://doi.10.1111/dth.13943
15. Nisar MK. Combining secukinumab and fingolimod to successfully treat ankylosing spondylitis and multiple sclerosis-a novel approach. Biologicals. 2019;60:93–4. https://doi.10.1016/j.biologicals.2019.06.002

Summary of the case

1	**Patient (gender, age)**	Male, 30
2	**Final diagnosis**	AS with concomitant MS
3	**Symptoms**	Thoraco-lumbar back pain, joint stiffness
4	**Medications**	Methylprednisolone, dimethyl fumarate, etoricoxib, gabapentin, aceclofenac, amitriptyline, tizanidine, pregabalin, dexamethasone, secukinumab
5	**Clinical procedure**	MRI
6	**Specialty**	Neurology, Rheumatology