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CENTRAL NERVOUS SYSTEM (CNS) INFLAMMATORY DEMYELINATION WITH TNF- α INHIBITORS

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BACKGROUND

In recent years, with tumor necrosis factor- α (TNF- α) inhibitors playing a central role in the treatment of several inflammatory diseases, new studies are demonstrating an association between them and central nervous system (CNS) demyelinating events. Particularly in patients who have an autoimmune disease, it is still elusive whether TNF- α blockage acts like a trigger, causing inflammation or an exacerbation of aberrant inflammatory pathways that already exist in these conditions again.

CASE REPORT

A 48-year-old man, with a previous diagnosis of type I enteropathic arthropathy, HLA-B27 positive, with axial and peripheral involvement, secondary to an ulcerative colitis diagnosed in 1994. No family history of autoimmune diseases. He started anti TNF- α treatment in 2007 due to poor disease control (intestinal and musculoskeletal) with only conventional synthetic disease-modifying anti-rheumatic drugs. He used infliximab for the first nine years, changed to certolizumab in 2015, due to secondary non-response. In February 2019, he presented progressive tetraparesis, urinary incontinence and numbness in the lower limbs. It was performed a neuroaxis MRI with findings compatible with demyelinating disease (Figs. 1 and 2). Investigation for anti-aquaporin 4 was negative. Certolizumab was discontinued, he was treated with intravenous methylprednisolone 1 g daily for 5 days and it was started immunosuppression with cyclophosphamide 1 g (0.5 g/m²) monthly. He had partial resolution of his symptoms. Two months later, he complained of blurred vision and worsening of previous deficits, thus treatment with intravenous glucocorticoid was repeated. Since then, he had two more exacerbations with residual deficits upon recovery, characterizing a relapsing-remitting multiple sclerosis pattern. Although the recent neuroaxis MRI did not show gadolinium enhancing brain lesions, suggesting a possible neurologic improvement with cyclophosphamide, due to worsening of musculoskeletal symptoms, its use had to be discontinued. Tofacitinib (an oral Janus kinase inhibitor) was selected for treatment. Despite the fact that there is limited data and clinical experience on its use, recent studies suggest it might be a future therapeutic option for both conditions.

Figure 1. Multiple periventricular T2 lesions consistent with CNS demyelination on sagittal T2/FLAIR brain MRI.

Figure 2. Contrast enhancement of the cervical cord on sagittal T2 post gadolinium cervical spine MRI.

CONCLUSION

Recent studies found that exposure to TNF- inhibitors in patients with autoimmune diseases appear to be associated with increased risk for inflammatory demyelinating CNS events. Systematic and long-term follow-up of affected patients might shed light to unanswered questions and help distinguish which patients will safely benefit from anti TNF- treatment for their inflammatory disease.