Neuroinflammatory events after anti-TNFα therapy

We have read with interest the article by Kopp et al that has been published recently in the Annals of the Rheumatic Diseases. The article deals with the risk of neuroinflammatory events (NIEs) in patients with inflammatory arthritides (IA), receiving tumour necrosis factor alpha (TNFα) inhibitors. Their cases were identified from the nationwide registries of Sweden and Denmark, in a prospective observational study. The authors found an increased risk of NIEs after anti-TNFα therapy in patients with spondyloarthopathies (SpAs) as compared with those not receiving TNF blockers, while no consistent and significant risk of NIEs after anti-TNFα treatment in rheumatoid arthritis (RA) patients. They concluded that the risk profile of NIEs in patients receiving TNFα inhibitors differs among patients with different IA which has an impact on decision-making in clinical practice.

In a prospective imaging and electrophysiological study of our clinic, patients with RA and SpAs who were eligible for anti-TNFα therapy had been investigated, during the period May 2009 to December 2011. Before starting anti-TNFα therapy all patients had a full physical examination and a detailed neurological evaluation. In addition, all had brain and spinal spin MRI and neurophysiological studies with nerve conduction velocity and needle electromyography (EMG) of the upper and lower extremities. Patients with severe and uncontrolled hypertension, diabetes mellitus, dyslipidaemia, history of atherosclerotic events, heart arrhythmias, B12 and iron deficiency as well as patients with a history of head and cervical spine injury had been excluded from the study. From a cohort of 101 patients, 24 had been excluded. From the remained 77, there were 36 with RA and 41 with SpA (24 psoriatic arthritis (PsA) and 17 ankylosing spondylitis (AS)). Before the onset of therapy one patient with AS complained for numbness of the left arm and dizziness. The neurological evaluation, as well as brain and cervical spine MRI and neurophysiological studies, showed no abnormalities and the patient received anti-TNFα therapy. On the other hand, two patients without any objective clinical manifestations never received anti-TNFα therapy because their brain MRI showed pathological findings compatible with multiple sclerosis (MS) (figure 1A). These two patients with brain MRI and suggestive findings of MS but without MS symptoms are classified as having radiological isolated syndrome (RIS) which is considered to be a preclinical MS syndrome. Finally, 75 patients received anti-TNFα therapy. All patients were naïve to TNFα inhibitors except one patient with PsA who was switched from etanercept (ETN) to infliximab (INF) due to primary inadequate response. During follow-up (mean period 18 months) three patients manifested NIEs. More specifically: the patient with PsA who switched from ETN to INF developed clinical symptoms and signs compatible with MS after a period of 8 months. The findings were confirmed by MRI and electrophysiological studies. One patient with RA treated with adalimumab (ADA) developed optic neuritis after 9 months of treatment. Finally, another patient with AS and Crohn’s disease receiving INF developed sensorimotor peripheral neuropathy after 24 months of INF treatment. The estimated rate of NIEs in our study was 4% (3/75). But, if we also calculate the incidental MRI findings of RIS in those two additional patients, the estimated rate of NIEs arises to 6.66% (5/75) leading to a p value of <0.00001 (significant at p<0.05). This means, that we may treat a clinically asymptomatic patient (RIS patient) with an anti-TNFα agent and as a consequence, the patient may finally develop a NIE.

We believe that the autoimmune phenomena like NIEs that develop during anti-TNFα therapy, are agent-dependent and not disease-dependent meaning that these are a class-effect phenomenon. Indeed, new autoimmune NIEs have been described. Two patients with RA, one receiving ETN and another treated with ADA developed myasthenia gravis syndrome. Thus, in patients which are candidates for anti-TNFα therapy, in order to avoid NIEs a detailed neurological evaluation is mandatory. In addition, a close follow-up and an appropriate monitoring with MRI and EMG are also essential when indicated.

Evrípidis Kaltonoudís, Eleftherios Pelechas, Paraskevi V Voulgari, Alexandros A Drosos

Internal Medicine, Division of Rheumatology, University of Ioannina Faculty of Medicine, Ioannina, Greece

Correspondence to Professor Alexandros A Drosos, Internal Medicine, Division of Rheumatology, University of Ioannina Faculty of Medicine, Ioannina 45110, Greece; adrosos@cc.uoi.gr

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ORCID iD
Alexandros A Drosos http://orcid.org/0000-0002-2232-0326

Figure 1 Sagittal fluid-attenuated inversion recovery scans demonstrating (A) ovoid hyperintense lesions in the deep periventricular white matter (thin arrows) and (B) bilateral diffuse hyperintense signal in the periventricular white matter of the parietal and occipital lobes (thick arrows).
REFERENCES