Multiple Sclerosis and non specific demyelination after treatment with Tumor necrosis factor alpha blockers

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Objective: Document clinical and radiological features of patients who developed a demyelinating disorder such as multiple sclerosis (MS) after the use of tumor necrosis factor alpha blockers (TNFα).

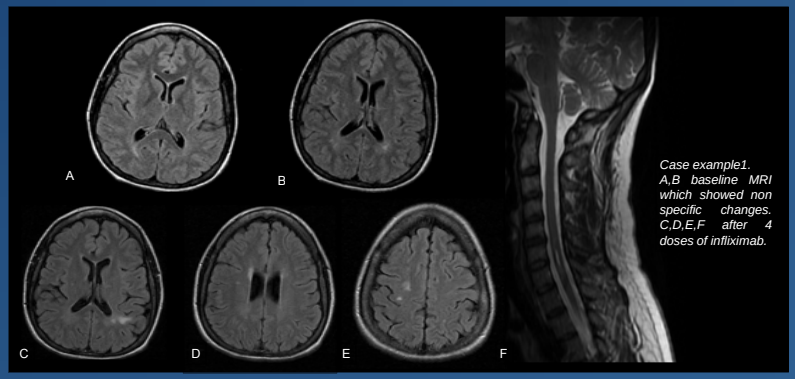
Background: TNFα blockers (infliximab, etanercept, adalimumab, golimumab) are biologic drugs that slow the progression of inflammatory conditions. They have been associated with lymphoma, lupus like syndrome, opportunistic infections, blood dyscrasias and central nervous system (CNS) demyelination.

Methods: Case series of patients who developed CNS demyelination after the use of TNFα blockers for various indications. Brain and spinal cord MRIs were evaluated for fulfillment of McDonald and Barkhof criteria.

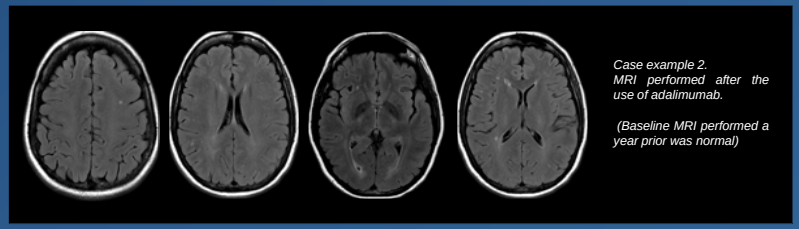
Results: A total of 12 patients were included, 11 female. Median age of 41.7 years. Five patients received infliximab; 3 adalimumab; 3 etanercept and one received etanercept and golimumab. Duration of treatment on TNFα blockers ranged from 2 months to 5 years. 3 patients were on treatment for Crohn's disease, 3 for RA, 3 for psoriasis, 1 for Behcet's, 1 for uveitis and 1 for mixed connective tissue disorder. Demographic characteristics are presented in table 1. All patients had white matter brain lesions, 7 also had also spinal cord involvement. Enhancing lesions were present in 66% . Ten out of the 12 patients fulfilled McDonald and Barkhof diagnostic criteria for MS and were placed on treatment (7 on Copaxone, 2 on Rebif , 1 on Betaseron). One patient worsened despite treatment and was placed on Tysabri. Two patients developed demyelinating lesions which did not fulfill MS diagnostic criteria. CSF analysis was performed in 7 patients results are presented in table 2.

Table 1. Demographics	
Median age	41.7
Female	11
Race Caucasian African American	 11 1
Adalimumab	3
Infliximab	5
Etanercept	3
Etanercept and golimumab	1
Treatment duration	2 m to 5 y

Table 2. MRI findings	patients (n)
Demyelinating lesions	12
Mc Donald Criteria	10
Barkhof Criteria	10
Enhancing lesions	8
Spinal cord lesions Cervical Thoracic	 7 3
Abnormal CSF Findings	7
Increased IgG index	4
Increase IgG synthesis rate	4
Oligoclonal bands	3



Case example1, A,B baseline MRI which showed non specific changes. C,D,E,F after 4 doses of infliximab.



Case example 2. MRI performed after the use of adalimumab.

(Baseline MRI performed a year prior was normal)

Conclusion: TNFα blockers are an effective treatment for inflammatory conditions. However these medications can induce autoimmunity. Cases of systemic lupus erythematous have been previously documented. It is unclear if these medications worsen or cause demyelination. The occurrence of other immune mediated inflammatory diseases has been linked to the observation that removal of TNF may result in an increased activity of T and B cells that react with autoantigens and foreign antigens. It is not uncommon for autoimmune disorders to coexist. Therefore, we strongly recommend brain MRI prior to initiating therapy with TNFα blockers.

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