Follow-up of three patients with multiple sclerosis developing IFN beta-induced atypical hemolytic uremic syndrome and treated with Eculizumab.

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Background

The atypical hemolytic uremic syndrome (aHUS) is a rare complicance of INF-beta (IFNB) therapy. It can lead to renal failure due to the dysregulation of the pathway of complement, endothelial damage and intravascular thrombosis. Eculizumab is a monoclonal antibody acting as a terminal complement inhibitor, approved for paroxysmal nocturnal hemoglobinuria and aHUS, currently under investigation in neuromyelitis optica, a B cell-mediated autoimmune disease.

Objective

To describe three relapsing-remitting multiple sclerosis (RRMS) patients who developed an aHUS under INFB treatment. Over the follow-up, the patients underwent a complete neurological assessment including EDSS and brain MRI at yearly intervals.

Case Reports

•Patient 1 was a 32 years old female, treated with INFB subcutaneously (Rebif®44 mcg) since 2002. In December 2013 she developed an aHUS: INFB was interrupted and she was treated with plasmapheresis , therefore with Eculizumab, with remission of the aHUS. After 4 years, under Eculizumab therapy, we documented neither further relapses nor disability increase, one new T2 lesion at MRI.

•Patient 2 was a 46 years old female, treated with INFB (Betaferon®) since 1996. In April 2011 she developed an aHUS and suspended IFNB. After hemodialysis, plasmapheresis and steroid therapy, Eculizumab was introduced and is still ongoing. Hematological values normalized, but she had to continue hemodialysis. After 6 years under Eculizumab her neurological status remained stable, without any new relapses and disability increase, the MRI scans showed a new lesion in T2.

•Patient 3 was a 37 years old male, in therapy INFB-1a subcutaneously (Rebif®44 mcg) since 2006. In May 2015 he developed an aHUS. INFB was interrupted and he started plasmapheresis, then Eculizumab with remission of the aHUS. After one month from Eculizumab initiation, he experienced a mild sensory-motor attack, followed by complete recovery. After 2 years, there was no evidence of clinical disease activity, brain MRI showed a new T2 lesion.

Conclusions

Our MS cases add to previous knowledge of this rare but harmful complication of IFNB treatment. Furthermore, over a follow-up period of 2-6 years with Eculizumab treatment the patients' neurological status remained clinically stable and there was only modest increment of T2 lesion load at MRI. Gathering further follow-up information of other similar MS cases described in the literature may be of interest, particularly in light of the renewed focus on B-cell role in the pathogenesis of MS.

	Patient 1	Patient 2	Patient 3
Age	32	46	37
Sex	F	F	M
Treatment before aHUS	Rebif®44 mcg	Betaferon®	Rebif®44 mcg
Relapses at last follow up	0	0	1
New T2 lesion at last follow-up	1	1	1
Years of follow up	6	4	2

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