Efficacy of interferon-β for myelin oligodendrocyte glycoprotein antibody-positive demyelinating disorder.

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【Background】

Antibody against myelin oligodendrocyte glycoprotein (MOG-Ab) can be detected in various demyelinating disorders of CNS including pediatric MS, but is rarely detected in adult MS. Interferon-β (IFNβ) may be used under diagnosis of MS, but its efficacy for MOG-Ab+ cases is not known.

【Objectives】

To evaluate the efficacy of IFNβ retrospectively in MOG-Ab+ cases.

【Material and methods】

We collected MOG-Ab+ cases with a history of previous/current IFNβ treatment, and analyzed clinical data from consecutive 3479 MOG-Ab+ samples sent to our university from July 2015 to March 2017.

【Results】

Screened for MOG-Ab in CBA: n=3479

↓

Serum MOG-Ab positive※ : n=369

↓

IFNβ in current or previous use: n=26

※in-House CBA using HEK293 cell transfected with FL-MOG (Sato DK et al. *Neurology* 2014)

Figure 1. Flowchart of study

Table 1. Clinical information of 26 cases

Median age at onset (range) years	14 (2-36)
onset < 18 years old (pediatric)	14
Male:Female (pediatric cases)	12:14 (6:8)
IFNβ1a:IFNβ1b	13:11 (used both = 2)
Observation period (month)	77 (21-238)
MOG-Ab titter	1:2048x (1:128 ～1:65536x) ※measured at remission in 8 cases
Full dose of IFNβ	13 (reduced dose in other 13 ped cases)
Use of other drugs	12 (pediatric n=7, adult n=5)
Number of relapses during IFNβ use	4 (2-22)

Table 2. Current diagnosis of 26 cases

Current clinical diagnosis	
Pediatric MS	14 (ADEM onset n=1)
NMOSD (AQP4-Ab negative)	4
MDEM	2
Rec ON	1
Other multiphasic demyelination	5

Table 3. CSF profiles of 26 cases

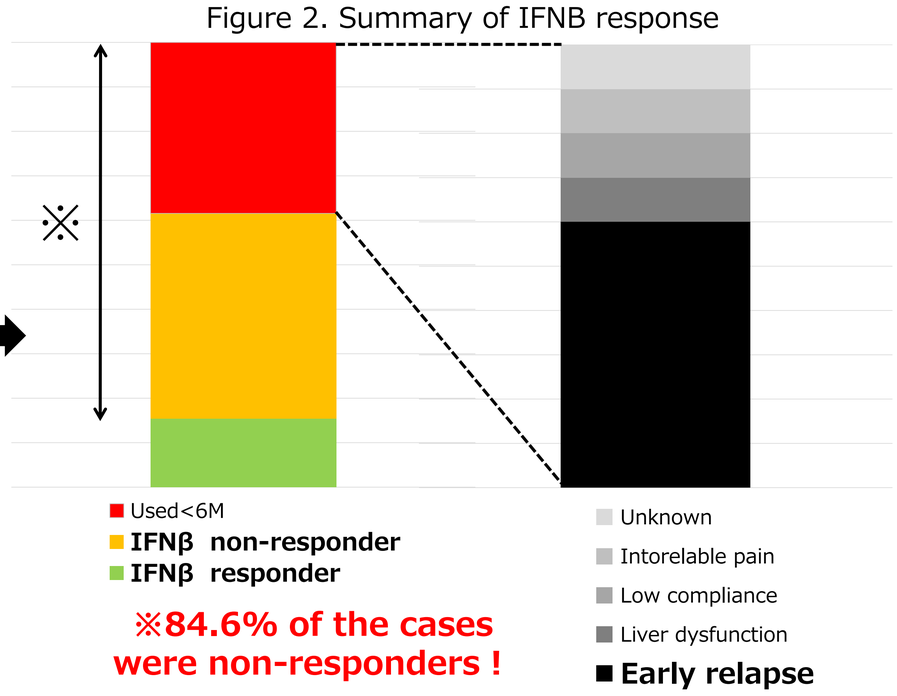
CSF profile	
Cell count in CSF (cells/mm^3)	19 (2-140)
Myelin basic protein in CSF > 100pg/μl	9/13 (69.2%)
Positive Oligoclonal IgG band	4/26(15.4%)

Criteria of IFNβ non-responder

1) Duration of full-dose therapy ≥**6 months**
2) Fully compliant on treatment
3) Fulfill at least one of the following
 a) Increase or no reduction in relapse rate, or new T2 or contrast enhancing lesions as compared with reference MRI
 or
 b) ≥ 2 confirmed relapses (clinical or MRI relapses) within a 12-month period of treatment.

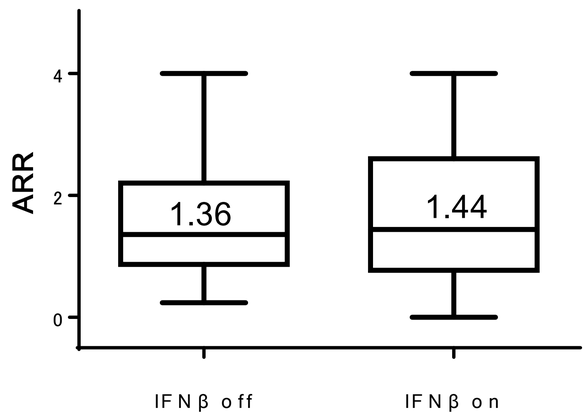
Chitnis T *MSJ* 2012

Figure 2. Summary of IFNB response



※84.6% of the cases were non-responders !

Figure 3. Comparison of ARR between IFN-on and off period



※analyzed in patients who continued IFNβ Treatment for more than 6 months.

ARR did not decrease during IFNβ Tx !

【Discussion】

・MOG-Ab+ demyelinating disease and AQP4-Ab+ NMOSD share a common cytokine profile (mainly Th17-related), while MS has Th1polorization. IFNβ is known to exacerbate AQP4-Ab+ NMOSD, and in EAE, IFNβ deteriorates Th_{17}-polarized EAE, whereas it improves Th_1-polarized EAE just like in MS.→IFNβ can deteriorate disease activity of MOG-Ab demyelinating disease.

・In some MOG-Ab+ patients, the MOG-Ab may be positive only transiently.
⇒Such patients may be relapse-free without IFNβ treatment.

・Limitations are mainly derived from the retrospective study design,
concomitant drug use (influence on the disease course?)
Efficacy was evaluated only in ARR, as EDSS requires longer follow-up
Selection bias? (only patients referred for MOG-Ab testing)
Could not evaluate MOG-Ab negative cases

【Conclusion】

IFNβ therapy is NOT recommended for MOG-Ab+ demyelinating disorders

High discontinuation rates, No evidence to support efficacy･･･

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