SC20

Comorbid Autoimmune Diseases in MS Patients May Influence Disease Progression

Katelyn S. Kavak[1], MS, Barbara E. Teter[1,2,3] PhD, MPH, Lynn Chouhfeh[2], MD, Bianca Weinstock-Guttman[1,2,3] MD, on behalf of the New York State Multiple Sclerosis Consortium*

and members of the New York State Multiple Sclerosis Consortium (investigators and institutions listed below)

[1.] Jacobs Neurological Institute, Department of Neurology; [2.] SUNY-UB Department of Neurology [3.] New York State Multiple Sclerosis Consortium.

OBJECTIVE

This study aims to examine the association between comorbid autoimmune diseases (AID) and Multiple Sclerosis (MS) disease progression in Relapsing-Remitting MS (RRMS) subjects.

BACKGROUND

- There is an increased occurrence of comorbid AIDs in MS subjects. This increased susceptibility is possibly due to a shared genetic or environmental background.[1]
- MS has a heterogeneous disease course. For most people, the disease begins at around 30 years of age, and is characterized by acute neurological dysfunction, followed by periods of remission, also known as a RRMS disease course. For the majority of patients, this phase is eventually followed by a phase without remission, known as Secondary Progressive MS (SPMS).[2] The time it takes to progress to the aforementioned disease stage differs from person to person.[2]
- In order to research the effect of ever having a comorbid AID on MS disease progression, we used data from the New York State Multiple Sclerosis Consortium (NYSMSC) registry. We chose a definite measure of disease worsening; clinically determined progression from RRMS to SPMS.

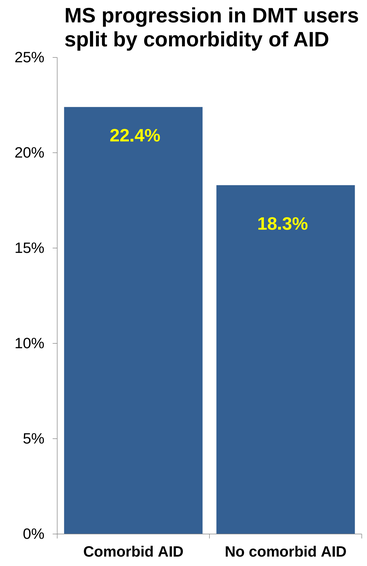
DESIGN & METHODS

- All subjects were part of the NYSMSC registry. The NYSMSC was founded in 1996 and includes 16 active centers across New York State, organized to assess demographic and clinical characteristics of MS patients attending the centers. This case-control study was based on longitudinal data (1996-2012) from the NYSMSC database.
- Subjects with clinically definite RRMS and with at least one follow up were included in the study (N=3292). There were eight types of AIDs that were reported in our database: Crohn's disease (3.7%), Irritable Bowel Syndrome (14.0%), Lupus (2.1%), Myasthenia Gravis (0.5%), Psoriasis (22.2%), Rheumatoid Arthritis (9.8%), Thyroid diseases (39.0%), and Type I Diabetes (3.1%). Subjects were considered having a comorbid AID if they ever reported having any of the above mentioned AIDs, or a combination thereof (5.6%), either at study enrollment or during a follow up.
- To determine the effects of having a comorbid AID on MS disease progression, we compared subjects who ever reported having an AID to those who did not.
- Logistic regression analyses were performed with conversion to SPMS as the outcome and comorbidity of AID as the predictor, while controlling for age at symptom onset, sex, Kurtzke Expanded Disability Status Scale (EDSS) at enrollment, enrollment year, and disease modifying therapy (DMT) use.

RESULTS

Characteristics Table – Mean (SD) and N (%)	Comorbid AID (n=762)	No comorbid AID (n=2,530)	p-value
	Total N= 3,292		
Age at MS onset (SD)	33.3 (9.8)	31.4 (8.9)	<.001
Sex, female, N (%)	639 (83.9%)	1894 (74.9%)	<.001
Race, N (%)			NS
Caucasian	716 (94.3%)	2347 (92.9%)	
African-American	31 (4.1%)	149 (5.9%)	
Other	12 (1.6%)	30 (1.2%)	
Education, N (%)			NS
< Bachelors degree	439 (58.3%)	1446 (57.8%)	
≥ Bachelors degree	314 (41.7%)	1055 (42.2%)	
DMT ever-use, N (%)	688 (90.3%)	2255 (89.1%)	NS
EDSS at enrollment	2.6 (1.6)	2.5 (1.6)	NS
EDSS at most recent follow up	3.3 (2.0)	3.0 (2.0)	<.001
MS progression, N (%)	166 (21.8%)	447 (17.7%)	.010

- The comorbid AID group was older at MS symptom onset, and had a higher percentages of females than was reported in the no-comorbid AID group. While there were no differences in EDSS scores at study enrollment, subjects with a comorbid AID had a higher score at most recent follow up compared to subjects who had no comorbid AID. There were no group differences in race, education, or DMT use.
- In unadjusted analyses, subjects in the comorbid AID group were more likely to progress to SPMS compared to those without an AID (21.8% vs 17.7%).
- After adjusting for confounders, subjects with a comorbid AID were 1.4 times as likely to progress from RRMS to SPMS than those without a comorbid AID (OR: 1.4, 1.1 - 1.7).
- Results stratified by DMT use showed that progression was significantly higher in subjects using DMT (OR: 1.4, 1.1 - 1.8), but not for those who were DMT naïve (see figure).



DISCUSSION

- This study is the first to research the effects of a large array of comorbid AIDs on MS disease progression. Results of our study are in line with other studies reporting adverse effects of comorbidities on various disorders. [3,4,5]
- The increased susceptibility MS patients have to other AIDs might also be due to the effects of DMT use, as others have reported an increased susceptibility to thyroid issues in MS patients after interferon treatment. [6,7]
- Subjects in the comorbid AID group were older at MS symptom onset, a finding previously observed by others. [8] Our results remained significant after adding this as a confounder.
- Causality cannot be assumed in this study and it has to be considered that subjects with a comorbid AID might be different from those without a comorbid AID. Subjects with a more severe form of RRMS may have a higher prevalence of medication use, which may not necessarily stop disease progression but might induce AID. Others suggest that subjects with MS and a comorbid AID are similar to those without a comorbid AID. [9]
- Future studies are needed to replicate these results (preferably in a longitudinal setting). It would be of interest to investigate whether treating the AID comorbidity would improve MS disease course.

CONCLUSION

- Results of this study suggest that having a comorbid AID significantly increases the odds of disease progression in subjects with MS. Interestingly, these outcomes could only be observed in subjects using DMT.

NYSMSC

Bianca Weinstock-Guttman, SUNY-UB Dept. of Neurology & Jacobs Neurological Institute, Buffalo NY; ♦ Andrew Goodman, University of Rochester, Dept. of Neurology, Rochester, NY; ♦ Burk Jubelt, SUNY-Upstate Medical University, Dept. of Neurology, Syracuse, NY ♦ Patricia Coyle and Lauren Krupp, SUNY-Stony Brook Dept. of Neurology, Stony Brook, NY; ♦ Alfred Frontera and Mustafa Khan, Kingston Neurological Associates, Kingston, NY; ♦ Brian Apatoff, Judith Jaffe MS Care Ctr, Dept. of Neurology Cornell Medical Ctr, NY, NY; ♦ Malcolm Gottesman, Winthrop University Hospital, Mineola, NY; ♦ Joseph Herbert and Ilya Kister, Langone Medical MS Comprehensive Care at NYU School of Medicine, NY, NY; ♦ Richard Holub, Neurological Associates of Albany, Albany, NY; ♦ Neil Lava, Matthew Murnane, Krupa Pandey, Albany Medical College, Dept. of Neurology, Albany, NY; ♦ Michael Lenihan, Adirondack Neurology, Glen Falls, NY; ♦ Aaron Miller, Maimonides Medical Center ♦ Aaron Miller and Fred Lublin, Corrine Goldsmith Dickinson Ctr, Mt. Sinai School of Medicine, Dept. Neurology, NY, NY; ♦ Allan Perel, Alpha Neurology MS Care Center, Staten Island University Hospital, Staten Island, NY; ♦ Mark Tullman, Columbia University, NY, NY; ♦ David Snyder, New York Hospital of Queens, Flushing, NY; ♦ Keith Edwards, Empire Neurology MS Care Center of NE NY, Latham, NY.

REFERENCES

1. Marrie, R. A., Horwitz, R. I., *et al. Neuroepidemiology* **36**, 85–90 (2011).
2. Confavreux, C., Vukusic, S., *et al. The New England journal of medicine* **343**, 1430–8 (2000).
3. Marrie, R. A. *et al. Neurology* **74**, 1041–7 (2010).
4. Armstrong, A. W., *et al. Dermatology (Basel, Switzerland)* **225**, 121–6 (2012).
5. Doraiswamy, P. M., Leon, J., *et al. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences* **57**, M173–M177 (2002).
6. Caraccio, N. *et al. The Journal of clinical endocrinology and metabolism* **90**, 4133–7 (2005).
7. Karni, A. & Abramsky, O. *Neurology* **53**, 883–5 (1999).
8. Marrie, R. A., Horwitz, R. I., *et al. Acta neurologica Scandinavica* **124**, 135–41 (2011).
9. Tourbah, A. *et al. Archives of neurology* **55**, 517–21 (1998).

This study was funded by Genzyme