

Lipoprotein receptor-related protein 4 (LRP4) antibody positive myasthenia gravis in North Sardinia.

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Introduction

Antibodies against low-density lipoprotein receptor related protein (LRP4Ab) have recently been detected in AchRAb and MuSKAb seronegative myasthenia gravis (MG) patients with a highly variable prevalence, from 3 to 54%, depending on different methods and origin countries of the tested population (1). Two recent studies of Italian MG patients showed a frequency of 14,5% and 21,2% respectively (2,3). We determined the prevalence of LRP4Ab in a cohort of Sardinian definite MG patients and studied their clinical features.

Case Series and Methods

Sera of 58 consecutive and consenting Sardinian MG patients were collected from January 1, 2012 to June 30, 2014 and tested by AchRAb and MuSKAb RIA and LRP4Ab cell based assay. The diagnosis of MG was based on the clinical presentation together with positive electrophysiological results and/or unequivocal positive response to acetylcholinesterase (AChE) inhibitors and to immunosuppressive therapies. Onset and maximal MGFA grading system together with all performed treatments were considered for clinical evaluation.

Results

Five out of 30 AchRAb and MuSKAb double seronegative MG patients were LRP4Ab positive (16,6%); one of these had double positivity for LRP4Ab and AchRAb. Twenty-five MG patients were triple-seronegative (AchRAb-, MuSKAb-, LRP4Ab-). Individuals with LRP4Ab were showed to have a form with intermediate severity of illness between the triple seronegative (a milder form in our case series) and the AchRAb positive patients (more severe). In spite of this difference, immunosuppressive treatments were used with similar frequency in LRP4Ab and AchRAb patients. Individuals with MuSKAb MG were more probable to have an onset with bulbar involvement and to reach higher grades of MGFA.

Discussion and Conclusions

Frequency of LRP4Ab MG in our Sardinian cohort is similar to Italian data (14,5% and 21,2%) obtained with cell based assay. Clinical features of LRP4Ab MG are similar to AchRAb MG, as already described (3,4). Clinical data about MuSKAb and AchRAb MG patients do not differ significantly from other case series (3,4). Triple seronegative MG appears to be the most prevalent form in our case series, contrary to data in literature (4). Some patients probably have low affinity or low concentration antibodies against AchR or MuSK no detected by radioimmunoassay. Cell based assay needs to be performed also for these antibodies.

Bibliografia

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LRP4 – Ab +
Patients

sex	Age of onset	Follow-up (years)	MGFA (onset-max.)	Immunosuppressive therapy (yes/no)
M	44	8	I	yes
M	66	0,6	II B – III B	yes
F	39	2	I - IIA	no
F	28	4	IIA	yes
F	54	2	IIA - IIIB	no

	Ach-R Ab +	MuSK Ab +	LRP 4 Ab +	Triple seronegative
Number of patients	19	9	5	25
Sex/M:F	3:16	2:7	2:3	10:15
Age of onset	47,68 ± 20,82	49,1 ± 17	46,2 ± 13,5	46,28 ± 20,21
MGFA MGFA maximum ≥ III	12/19 (63%)	6/9 (66,6%)	2/5 (40%)	7/25 (28%)
Follow up	13,37 ± 13,26	7,44 ± 5,4	3,33 ± 7,8	9,21 ± 5,28
Immunosuppressive therapy	57,9%	89%	60%	32%