



Clinical and demographic features of LRP4 positive myasthenia gravis

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Background

- 80-90 % of generalized MG patients are Ach R Ab+ , and 7 % are Musk positive.
- 50 % of ocular MG are Ach R Ab+
- 9-18% of double seronegative patients are LRP 4 positive⁽¹⁾
- There is limited literature looking at the clinical presentation of this group of patients.

Objective

- To study the demographic, clinical features of LRP4-positive myasthenia gravis (MG) patients compared to triple seronegative patients.

Design & Methods

- KUMC is a site for the "Characterization of Agrin/LRP4 Antibody-Positive Myasthenia gravis" study (R01 NS090083-Lin Mei –Augusta University, Augusta, GA, United States)
 - RNS/ Single fiber positive EMG is inclusion criteria for this study
 - We obtained permission to access and report our site data
 - Majority of the data is collected from this study. Some data collected from commercial testing
- IRB approval for exempt study was obtained
- A retrospective chart review was performed
- The information on LRP4 positive patients was compared to the negative patients

Results

Double seronegative MG pts N=28

	LRP 4 +	Triple seronegative
Number of patients	4	24
Age of onset (mean)	55.8±7.4	59.7±15.8
Female/Male	2/2	12/12
RNS+	2	4
Single fiber EMG +	2	19
Thymoma	0	0

Results

	LRP 4 + (N=4)	Triple seronegative (N=24)
MGFA class I at the onset	3 (75%)	14 (58%)
MGFA class II at the onset	1 (25 %)	10 (42%)
Worst MGFA score during disease course (Nadir)	MGFA I - 3 MGFA II -1	MGFA I-8 MGFA II-14 MGFA III-2
Ocular symptoms at the onset	4	18
Generalized symptoms at the onset	-	5
Shortness of breath at the onset	-	1

Results : LRP4+

Age	Gender	Age of onset	Prior treatment	Current medication
60	M	56	Prednisone;Cellcept; Pyridostigmine	Cellcept
57	F	47	Pyridostigmine;IVIG; Prednisone; Pyridostigmine	Pyridostigmine
68	M	65	Prednisone; Pyridostigmine	None
57	F	55	Prednisone; Pyridostigmine	Prednisone

Literature Review

Study	No. of patients with LRP4+/total double SN	Mean age of onset	Female	MGFA I/II grade at onset	Worse MGFA	Thymoma
Pevzner , 2012	8/15 12/25	46.5	4	6 mod to severe	-	Not reported
Zisimopoulou, 2014	119/635	34.9	85	97	-	Thymoma-0/42 Hyperplasia-31%
Marino, 2015	8/55	7- Early onset (<50)	7	6	2	1
Nikolic, 2016	8	46.6 ±9.9	5	8	3	-
Our study	4/28	55.8±7.4	2	4	-	None

Literature Review

Study	No. of patients	Response to Pyridostigmine	Response to Prednisone	No of patients required immune therapy
Pevzner ,2012	13	12/13	-	12
Zisimopoulou,2014	119	47/52	35/39	60
Marino,2015	8	No data	7	5
Nikolic, 2016	8	-	6	4
Our study	4	4	4	1

Discussion

Literature review

- Mean age described in literature is late 30's to late 40's.
- More common in women than men (Michael Rivner, 2018)
- Most cases are described as mild to moderate, and the ocular muscles are usually involved
- Symptoms similar to AChR positive patients however usually symptoms are milder
- These patients respond to conventional MG treatment modalities
- Incidence of thymoma is less in these patients

Discussion

Our study

- 15 % of DSNMG patients were positive for LRP 4 .
- Our LRP4 patients presented with mild (ocular) symptoms similar to literature .
- MGFA grades were low at onset and remained same throughout the course.
- None of our patients had thymectomy.
- Our patients required mostly single immunosuppressive medications.
- We had equal number of female and male patients unlike literature where more females were reported.

Limitations

- 1) Single site
- 2) Low number of subjects (rare disease)
- 3) This mainly included mainly MG patients with either RNS or single fiber EMG positive

Conclusion

- While the clinical characteristics of more LRP4 positive cases need to be determined in a larger cohort, it is possible that majority of them constitute pure ocular symptoms based on our observation
- Compared to triple seronegative group:
 - Disease course is usually mild
 - Single immunosuppressive therapy may be sufficient for management of these patients suggesting good response to medications
 - Thymoma may be less common

Thank you

- We would like to thank principal investigator for allowing us to present our site data.