Treatment Refractory Ocular Symptoms in Myasthenia Gravis: Clinical and Therapeutic Profile CK Symposium

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Background

- Most MG patients develop ocular symptoms over the course of the disease
- Despite many therapeutic options available for management of MG, some patients remain resistant to standard therapies
- Limited literature is available regarding management of refractory ocular symptoms

Objectives:

To review clinical characteristics of patients with treatment resistant ocular symptoms in myasthenia gravis (MG)

Methods:

- Retrospective chart review after IRB approval
- Neuromuscular Research Database at KUMC
- Information on MG patients with ocular symptoms between January 2013 and December 2017 was obtained and reviewed
- Treatment resistance was defined as persistent diplopia or ptosis despite adequate trial of prednisone and at least one additional immunosuppressive agent
- Demographic, clinical, diagnostic and therapeutic information were extracted from the charts

Results: Demographics

Treatment resistant group

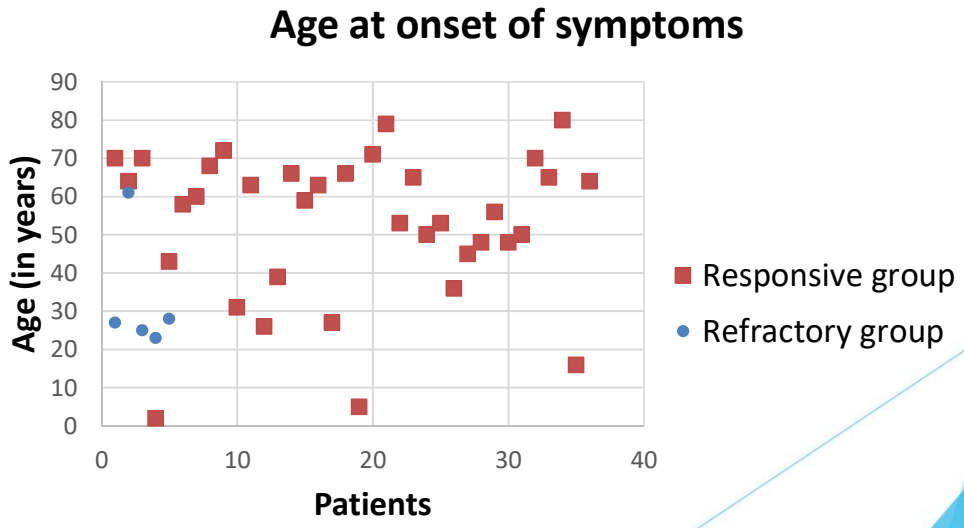
- Patients with treatment resistant ocular symptoms with acetylcholine receptor antibody positive MG : 5
- Gender: F:M=3:2
- Age at symptoms onset

  Mean=32, Median=27

Treatment responsive group

- Patients with treatment responsive ocular symptoms: 36
- Gender: F:M=12:24
- Age at onset of symptoms:

  Mean=52, Median=59



Results: Symptoms

1) In the refractory group 3/5 patients had ocular symptoms at the onset of disease and 2 of these patients progressed to have generalized disease

2) In the responsive group 34/36 patients had ocular symptoms at onset of disease and 8 progressed to have generalized disease

Presence of other autoimmune diseases

Treatment refractory group:

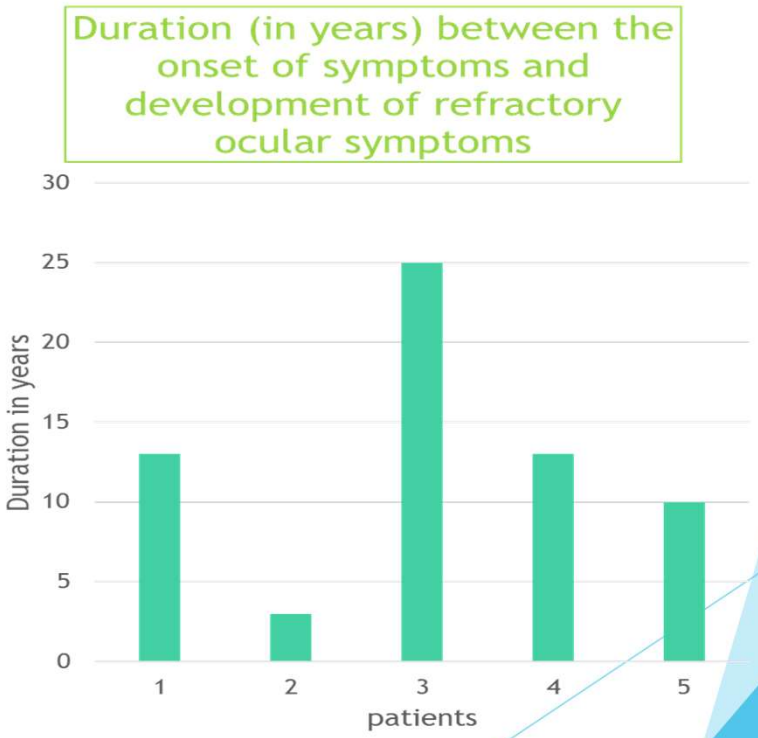
- Two patients had positive thyroid peroxidase and thyroglobulin antibodies
- One patient was diagnosed with type 1 DM

Treatment responsive group:

- Two had psoriasis
- Two had mixed connective tissue disease
- One had Hashimoto's thyroiditis

Results: Symptoms

The median time between the onset of symptoms and development of refractory ocular symptoms was 13 years (range of 3 to 25)



Results:
Diagnostic testing

1) In the refractory group all patients had positive AChR Ab

2) In the responsive group
    1) 21/36 had AChR Ab positive
    2) 1 MUSK positive
    3) Rest diagnosed with RNS and SFEMG

Results:

Interval between symptom onset and starting high dose steroids

- All patients in both groups were initially managed with pyridostigmine
- Most of these patients were started on high dose steroids within 6 months of the symptom onset

	Treatment refractory group Total N: 5	Treatment responsive group Total N: 36
Soon after symptom onset	3	7
3-6 months after the onset	1	27
2-8 years after the onset	1	2

Results:

Refractory group

Other immunomodulators used in the refractory group were:

1) Cellcept (2 patients)
2) Imuran (1 patient)
3) Cyclosporine (1 patient)
4) IVIG (4 patients)
5) PLEX (3 patients)
6) Thymectomy (1 patient)

- 3/5 patients in the refractory group required ICU admission for exacerbation

Responsive group

Patients in the treatment responsive group were treated with

1) Cellcept (5 patients)
2) Imuran (2 patients)
3) Methotrexate (2 patients)
4) IVIG (3 patients)
5) PLEX (3 patients)
6) Thymectomy (3 patients)

- 5/36 patients in the responsive group required hospital admission for exacerbation

Discussion – Ocular Symptoms Response to Treatment

- Benatar's group showed that treatment failure for ocular MG was 17% in the prednisone group (1/6 patients)
- Kupersmith et al reported that 27% of OMG patients treated with steroids (13/48) had refractory ocular symptoms
- Our study showed that ocular symptoms were refractory in 12% of the patients (5/41), all treated with prednisone and additional immunomodulatory therapy.

Discussion – Progression to Generalized MG

- Progression to generalized MG in myasthenia patients treated with prednisone was variable in the literature.
- Mittal et al showed that 38 patients with ocular myasthenia treated with prednisone and none of them progressed to generalized MG
- Monsul et al reported that 3/27 (11%) patients with ocular MG treated with prednisone developed generalized MG
- In our study, 27% of the patients with ocular onset developed generalized MG in spite of prednisone treatment.

Conclusion

- MG patients with treatment refractory ocular symptoms were mostly younger at symptom onset
- Duration between the onset of MG to the development of refractory ocular symptoms was variable
- Starting steroid therapy early was effective in resolving the ocular symptoms in most patients but a subgroup progressed to have refractory ocular symptoms
- More patients in the refractory group generalized compared to the responsive group

Questions & Discussion

THANKS

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