An Unusual Early Onset Myopathy

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ABSTRACT

EM is a 28 year old right handed male with scoliosis, sinus tachycardia (on metoprolol) and anxiety (on escitalopram) who presented to the neuromuscular clinic for 2nd opinion on progressively worsening weakness over the past 6 months in his arms, legs and neck. He has difficulty climbing up stairs and reports difficulty holding glasses of water. Two months ago, he noticed numbness in his right hand. He denies inability getting out of a chair and weakness changing with temperature. Brief neurological exam showed bilateral ptosis, bilateral upgaze paralysis, impaired abduction on the left, impaired adduction on the right, bilateral sternocleidomastoid and neck flexion weakness (4/5), generalized weakness (right deltoids and supraspinatus 3/5, right biceps, triceps and wrist extension 4+/5, right interossei 3/5, left biceps, triceps, wrist extension, 4+/5, left wrist flexion 4/5, left supraspinatus and deltoid 3/5, right proximal lower extremity 4/5, right distal lower extremity 5/5, left iliopsoas 4+/5, remaining left lower extremity 5/5), normal brachioradialis, biceps, triceps, patellar and ankle reflexes bilaterally, decreased sensation in right hand, normal cerebellar testing with a slightly waddling based gait. Previous workup included an electromyogram (EMG) and nerve conduction studies (NCS) that showed low amplitude polyphasic units in the right arm but was otherwise reported as normal. He also had an MRI brain and cervical spine without contrast that were reportedly normal. Repeat EMG/NCS in our lab showed findings consistent with myopathy. Acylcarnitine, amino acids, ammonia, lactate dehydrogenase, organic acids, pyruvic acid and free Invitae neuromuscular panel were sent off.

INTRODUCTION

Congenital myasthenic syndromes (CMS) are a group of disorders affecting the neuromuscular junction (NMJ). These patients typically present in the neonatal period to early childhood with fatigable ocular, bulbar and limb girdle weakness. The amount of weakness in each region is variable. There have been several genes associated with CMS, however around 40% of patients remain undiagnosed. Recognized genes include *DOK7, RAPSN, LRP4, COLQ, CHRNA1, CHRND, CHRNE, AGRN, GFPT1,* and *SCN4A*. *COLQ* represent Collagen Q, a protein responsible for anchoring and concentrating acetylcholine esterase (AChE) at the NMJ. Here, its expression is restricted to the extracellular matrix and thus accessible to auto antibodies.

Electrographically, CMS is diagnosed with an abnormal decrement on low frequency repetitive nerve stimulation or increased jitter on single fiber EMG. However, these findings are similar to that of myasthenia gravis. A unique feature of CMS is a single nerve stimulus can be seen in endplate AChE deficiency or slow channel CMS but not myasthenia gravis. Genetic testing is confirmatory.

COLQ can also be found in patients with an end plate myopathy. Hereditary myopathy and CMS should be considered in these cases.

RESULTS

SNC

Nerve / Sites	Rec. Site	Onset Lat ms	Peak Lat ms	NP Amp µV	Distance mm	Velocity m/s	Temp. °C
R Median - Digit II (Antidromic)							
Wrist	Dig II	2.0	2.7	74.8	130	66	33.9
R Sural - Ankle (Calf)							
Calf	Ankle	2.6	3.5	44.1	140	54	29.4

Sensory NCS Normal Limits:

Nerve	Onset Latency <ms	Peak Latency < ms	Amplitude > µV	CV > meters/sec
Median	3.4	3.5	15	49
Ulnar	3.0	3.1	10	49
Radial	1.8	2.7	15	49
Sural	4.0	4.5	5	39
Superficial Peroneal	4.0	4.5	5	39

Needle EMG Examination:
The study was performed with a disposable monopolar/concentric needle electrode. Fibrillations and fasciculation activity is graded from none (0) to continuous (4+). The configuration and recruitment pattern of motor unit action potentials under voluntary control, if not normal, are described.

EMG Summary Table											
	Spontaneous					MUAP				Recruitment	
Muscle	IA	Fib	PSW	Fasc	Other	Poly	Amp	Dur.	Rate	Pattern	Effort
R. Tibialis anterior	Normal	0	0	0	None	Moderate	Normal	Normal	Normal	Normal	Normal
R. Gastrocnemius (Medial head)	Normal	0	0	0	None	Few	Normal	Normal	Normal	Normal	Normal
R. Vastus lateralis	Normal	0	0	0	None	Moderate	Normal	Some units with dec. dur.	Normal	Early	Normal
R. Iliopsoas	Normal	0	0	0	None	Moderate	Normal	Some units with decr. Dur.	Normal	Early	Normal
R. First dorsal interosseous	Normal	0	0	0	None	Moderate	Normal	Normal	Normal	Early	Normal
R. Deltoid	Normal	0	0	0	None	Moderate	Normal	Decr	Normal	Early	Normal

Repetitive Stimulation:

Ulnar.R

baseline 1
1
08:03:41
5 stimuli at 2Hz

Nerve Potential Number	Amplitude Val. mV	Amplitude Decr. %	Area Val. mVms	Area Decr. %
1	8.47	0	65.00	0
2	7.75	9	52.20	20
3	7.30	14	46.10	29
4	7.11	16	43.50	33
5	7.16	15	43.10	34

baseline 2
2
08:04:00
5 stimuli at 2Hz

1	8.29	0	60.80	0
2	7.61	8	49.40	19
3	7.29	12	43.90	28
4	7.08	15	42.00	31
5	7.15	14	41.30	32

immediate post 1 min. ex.
3
08:06:04
5 stimuli at 2Hz

1	8.20	0	41.70	0
2	8.14	1	40.00	4
3	7.92	3	38.90	7
4	7.79	5	38.90	7
5	7.81	5	38.90	7

1 min. post 1 min. ex.
4
08:07:04
5 stimuli at 2Hz

1	9.78	0	52.90	0
2	8.78	10	45.40	14
3	8.05	18	40.90	23
4	7.80	20	39.10	26
5	7.90	19	38.70	27

2 min. post 1 min. ex.
5
08:08:04
5 stimuli at 2Hz

1	9.10	0	54.10	0
2	8.38	8	46.90	13
3	7.65	16	41.30	24
4	7.39	19	39.70	27
5	7.39	19	38.80	28

4 min. post 1 min. ex.
7
08:10:04
5 stimuli at 2Hz

1	9.62	0	53.90	0
2	8.47	12	45.30	16
3	7.70	20	39.50	27
4	7.41	23	37.20	31
5	7.29	24	35.60	34

5 min. post 1 min. ex.
8
08:11:03
5 stimuli at 2Hz

1	8.53	0	46.80	0
2	7.59	11	39.20	16
3	7.05	17	35.20	25
4	6.79	20	33.40	29
5	6.86	20	32.60	30

Facial.R

baseline 1
1
08:16:54
5 stimuli at 2Hz

1	2.17	0	12.80	0
2	1.86	14	11.50	10
3	1.53	29	10.60	17
4	1.44	34	10.20	20
5	1.40	35	10.30	20

baseline 2
2
08:17:23
5 stimuli at 2Hz

1	2.27	0	12.60	0
2	1.96	14	11.10	12
3	1.67	26	10.00	21
4	1.57	31	9.68	23
5	1.54	32	9.77	22

immediate post 1 min. ex.
3
08:19:05
5 stimuli at 2Hz

1	2.40	0	12.10	0
2	2.04	15	10.80	11
3	1.73	28	9.87	18
4	1.69	30	9.60	21
5	1.66	31	9.66	20

DISCUSSION

Our patient presented with a late onset myopathic disorder. Certain features of the exam were consistent with NMJ disorder (ptosis, upgaze paralysis, and neck flexion weakness), however, the diffuse weakness was concerning for a myopathic process. Initial and repeat electromyography were consistent with a myopathy. Invitae neuromuscular panel was ordered to further evaluate hereditary myopathies and came back positive for *COLQ* CMS. Based on this finding, repetitive nerve stimulation testing of the ulnar nerve at the adductor digiti minimi and facial nerve at the nasalis were performed and showed >10% decrement at 2 Hz stimulation, thus confirming the diagnosis of CMS. He was then started on a beta agonist.

In a patient with this type of eye findings, RNS should be considered to evaluated for a neuromuscular disorder.

REFERENCES

Katarzyna, et al. Collagen Q – A potential target for autoantibodies in myasthenia gravis. Journal of the Neurological Sciences 348 (2015) 241–244

Kao, et al. Congenital myasthenic syndromes in adult neurology clinic: a long road to diagnosis and therapy. Neurology® 2018;91:e1770-e1777. doi:10.1212/WNL.0000000000006478

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