Coexistence Of Myasthenia Gravis And Myotonic Dystrophy In A Thyrotoxicosis Patient
E Karagoz, I Midi, T Tanridag

Citation

Abstract
A 28 year old previously healthy female presented with a four month history of difficulty of swallowing and drinking liquids and proximal weakness with fluctuation. At her physical examination, she had bilateral exophtalmus which were compatible with hyperthyroidism. Her facial appearance, distribution of weakness without atrophy and presence of reflex myotonia, quadriparesis, and decreased gag reflex resulted in clinical diagnosis of myasthenia gravis and myotonic dystrophy. Her medical and family history was unrevealing. Her acetylcholine receptor antibody was negative, her laboratory was normal except thyroid hormone tests, but on needle electromyography, myotonic discharges were observed and repetitive nerve stimulation was positive, and she was responsive to anticholinesterase medication. It is well known that myasthenia gravis may be seen with thyrotoxicosis and also overlapped with other autoimmune diseases. The objective of this report is to discuss the unique coexistence of two distinct neuromuscular diseases in the same patient with an overlapped disease.

INTRODUCTION
Myotonic dystrophy (MyD) is an autosomal dominant disorder with highly variable clinical manifestations: affected patients may be asymptomatic, have minimal features ( e.g. cataract and asymptomatic myotonia ) or show moderately severe facial and distal limb muscle wasting and weakness, or be very severe congenital cases with hypotonia, respiratory insufficiency, dysphagia, talipes and mental retardation. Myasthenia gravis ( MG ) is an autoimmune disorder causing postsynaptic impairment of neuromuscular transmission. Ocular, bulbar, or proximal limb muscles are most frequently affected, and weakness worsens during exercise. We report the coexistence of these two disorders in a patient since this coexistence is extremely rare.

CASE REPORT
Twenty-eight year old woman presented at our neurology outpatient clinics with difficulty chewing, swallowing, dysarthric speech, fatigue and palpitation for about 4 months. She first noticed hoarseness in her voice and had difficulty drinking liquids. Symptoms progressively worsened and restricted her daily life. Her symptoms worsened at the end of the day and after moderate exercise. Two months later she was referred to a ear-nose-throat unit of another institution for evaluation to rule out achalasia or postcricoid tumor. On physical examination, thyroid gland was palpable. Then, she was investigated for hyperthyroidism and thyroid hormone levels was as follows; T3: 602 pg/ml ( N: 80-200 ), T4: 30 ng/dl ( N: 4,5-12 ), TSH: < 0.002. Thyroid sintigraphy showed bilateral diffuse adenomatous hyperplasia. Treatment for hyperthyroidism was initiated and she was put on propylthiouracil 3x2 tb and propranolol 2x1/2 tb. Eusophagogastroduodenoscopy was informative other than chronic eusophagitis. Thorax CT revealed a upper mediastinal enlargement and reported as thymic hyperplasia or thymoma. Under treatment, her symptoms didn't improve then, she was referred to our institution to rule out any thymoma or thymic hyperplasia. The medical history was unremarkable. She had grown up without any major health problem and was not hypotonic. Family history was non-contributory for any muscle disease.

When she was admitted to our hospital, she was anxious, and sweating. She complained of difficulty swallowing, drinking liquids, hoarseness in her voice, fatigue, heat intolerance, and sweating. She had slight bilateral ptosis with exophthalmus but without ophthalmoparesis ( orbicularis oculi 3-4/5 on Medical Research Council scale), bilateral facial weakness ( orbicularis oris 3/5 on Medical Research Council scale), decreased gag reflex, bilateral sternocleidomastoid and trapezius muscle weakness (4-5/5 on Medical Research Council scale ), quadriparesis ( deltoid, biceps, triceps 4-5/5, wrist flexors and extensors, finger
Coexistence Of Myasthenia Gravis And Myotonic Dystrophy In A Thyrotoxicosis Patient

flexors and extensors 4/5, gluteus maximus, medius, minimus, adductor, quadriceps femoris, biceps femoris 4-5/5, plantar flexors and extensors, finger flexors and extensors 4/5 on Medical Research Council scale. But there was not any observable and measurable proximal or distal muscle atrophy. Deep tendon reflexes were symmetrical and normactive and plantar responses were flexor. She had difficulty performing hand grip. At the bedside examination, temporal hallowing, and atrophy of masseter and sternocleidomastoid muscles were noticed but there was, however, no pseudohypertrophy of the calves. When she was asked to make a handgrip, she presented clinical myotonia (difficulty releasing hand grip). With repeated opening and closing of her hand resulted in faster release. When she was asked specifically, she did not report any periodic generalized paralysis attacks.

Complete blood count, sodium, potassium, serum creatinin, blood urea nitrogen, liver function tests, serum creatin kinase, lactate dehydrogenase were normal. She was hyperthyroid with hormone titers (T3: 206 pg/ml, T4: 18,9 ng/dl and TSH: < 0.002 ). Anti-AChR antibody titer was normal ( less than 0.5 nmol/l ).

Edrophonium test 1 mg administered intravenously did not produce any change in her clinical findings. Her routine motor and sensory nerve conduction studies were normal. Concentric needle EMG of biceps brachii, abductor pollicis brevis, tibialis anterior, medial gastrocnemius, and rectus femoris muscles demonstrated characteristic dive bomber sounds together with myotonic discharges suggesting muscle fiber irritability (figure 1). Initial motor unit action potential of accessory nerve was normal.

**Figure 1**
Figure 1: myotonic discharges

A single train of repetitive nerve stimulation (3-5 Hz) was performed at rest on accessory nerve (upper trapezius) showed typical marked decrement response (figure 2). She was asked to elevate her shoulder strongly against resistance for 10 seconds (short exercise test), posttetanic exhaustion was observed.

**Figure 2**
Figure 2: Decrement response with repetitive nerve stimulation

Her clinical and electrophysiological diagnosis was compatible with seronegative myasthenia gravis. She was started on anticholinesterase medication physostigmine and her proximal weakness, and difficulty swallowing and drinking liquids were improved. She was, then, started on daily peroral methylprednisolone treatment and monthly intravenous immun globulin and prepared for thymectomy.

**DISCUSSION**
There is a definite link between myasthenia gravis and a number of diseases that are believed to be related to immunological disturbances, and thymoma is a well-known association with myasthenia gravis.

Prevalence of MG is 0,5 to 14,2 per 100000, and the prevalence of MyD is 1-10 Per 100000, with probable underestimation because mildly affected individuals escape detection. The chance of MG and MyD to occur in a single individual is a rare situation, assuming that the combination of the two diseases is detected by chance alone. This combination has been reported in 13 year old female patients, and 32 year-old female who had coexistent MG and MyD, 16 month-old female with MG whose mother and grandmother had MyD, and a child with MG whose mother had a “myotonic syndrome”.

Our patient, the combination of ptosis, bilateral facial weakness, decreased gag reflex, normal deep tendon reflexes, and proximal muscle weakness of bilateral upper and lower extremities, coupled with positive response to repetitive nerve stimulation and anticholinesterase treatment and low titre of acetylcholine receptor antibody confirmed the diagnosis of seronegative MG (Osserman Class IIA according to Osserman classification). Evidence for MyD included typical distal distribution of weakness, presence of
facial features and neck muscle weakness, presence of reflex
myotonia and myotonic discharges on electromyography.

The autoimmune etiology of myasthenia gravis is well
established, such as pernicious anemia, systemic lupus
erthematous, sarcoidosis, Sjögren's syndrome, scleroderma, dermatomyositis, ulcerative colitis, pemphigus,
Eaton-Lambert myasthenic syndrome, autoimmune
hemolytic anemia, pure red cell aplasia, pancytopenia,
Guillain Barré syndrome, neuromyotonia, Addison's disease,
and multiple sclerosis. This association has been shown
also with autoimmune and nonautoimmune thyroid disease.
Epidemiological studies showed that autoimmune thyroid
disease occur in approximately 5-10% of MG patients. It
was reported that MG associated with autoimmune thyroid
disease has a mild clinical expression, with preferential
ocular involvement and lower frequency of thymic disease
and AChR antibody. Our patient presented with bulbar
symptoms. But when first seen in another institution, she
was diagnosed as hyperthyroid. Her physical examination
revealed a hypertrophic thyroid gland without any nodule.
Her hormone titers were elevated and TSH was suppressed.
Her thyroid syfmtigraphy showed diffuse adenomatous
thyroid hyperplasia.

MG and MyD have contrasting clinical features, and differ
in their pathophysiology, response to Edrophonium,
immunology, and their genetic characteristics. Decrements
are not uncommon with repetitive nerve stimulation with slow
(3 Hz) and faster frequencies (10 Hz) in myotonic
dystrophies. Therefore, an amplitude decrement alone may
not be enough to prove the presence of myasthenia in our
case. Our patient, however, showed diurnal fluctuation of
her weakness, ptosis and difficulty swallowing and drinking
 liquids which responded to the anticholinesterase
medication, steroid, intravenous immunoglobulin and
thyrmectomy. These clinical feature cannot be expected in
myotonic dystrophy, and consequently the concomitant
occurrence of MyD and MG is reliably supported.

Hyperirritable muscle fibers act as source generator of
myotonic discharges that are in the form of either a positive
wave or a brief spike potential. Neuromuscular
transmission abnormality has not been demonstrated.
Although anticholinesterase agents have been reported to
aggravate myotonic dystrophy and myotonia congenita, our
patient was responsive to pyridostigmine, and we did not
observe any deterioration in her clinical status when started
on treatment.

About 10% of patients with generalized myasthenia gravis
(MG) do not have detectable serum antibodies to
acetylcholine receptor (AChR) on conventional
radioimmunoassay. Our patient's anti AChR antibody was
obtained and found to be within normal limits and she was
accepted as seronegative MG (SNMG). Her presenting
symptoms were dysarthria (nasal speech), facial weakness,
swallowing difficulties caused by weakness of both tongue
and pharyngeal muscles. But, except mild bilateral ptosis,
opthalmoparesis was not observed and she did not notice
any diplopia . She did not report any respiratory crisis attack
or difficulty in respiration. Neck extensor muscle weakness
was not observed in neurologic examination, and weakness
were predominantly distal. She was responsive to oral
pyridostigmine, her symptoms improved.

Coexistence both diseases has been previously described in
only 5 cases. Our case has a specialty that she has also
hyperthyroidism which is an other combination with MG.

MG and MyD have specific clinical and laboratory features
that permit appropriate diagnosis individually, they present
with some common features that can make the
differentiation of the diseases difficult. Although this
combination is very rare, it is necessary to search MG
patients in detail.

References
1. Meola J. Myotonic dystrophies. Curr Opin Neurol
330: 1797-1810.
3. Treves TA, Rocca WA, Meneghini F. Epidemiology of
myasthenia gravis. In Anderson DW, Schoenberg DG (eds).
Neuroepidemiology: A Tribute to Bruce Schoenberg.
unusual myotonic and myopathic phenotype and no CTG
expansion ( proximal myotonic myopathy ) : a challenge for
future molecular studies. Neuromusc Disord 1996; 6:
143-150.
5. Schon R.T. Myasthenia gravis and myotonic dystrophy in
6. de los Angeles Avaria M, Kleinsteuber K, Novoa F,
Fauendez P, Carvallo P. Myotonic
dystrophy in a female with myasthenia gravis. Pediatr
Neurol. 2007;36:421-3.
7. Maytal J, Spiro AJ, Sinnar S, Moshe SL. The coexistence
of myasthenia gravis and
myotonic dystrophy in one family.Neuropediatrics.
1987;18:8-10.
of myasthenia gravis in a patient with congenital myotonia. J
Neurol Sci 1982; 57: 83-88
9. Osserman KE. Myasthenia gravis. New York: Grune and
Stratton, 1953, 80.
10. Engel AG. Acquired autoimmune myasthenia gravis. In
Engel AG, Franzini-Armstrong C (eds): Myology. New
Author Information

ET Karagoz
Department of Neurology, Marmara University Hospital

I. Midi
Department of Neurology, Marmara University Hospital

T. Tanridag
Department of Neurology, Marmara University Hospital