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Bulbar Myasthenia Gravis With Hyperthyroidism - A Case Report

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ABSTRACT

Myasthenia gravis is a disease of skeletal muscle acetylcholine receptors. The underlying defect is reduction in the number of available Acetyl Choline Receptors at neuromuscular junction. The postsynaptic folds are flattened or simplified. As a result the patients experience Myasthenic Fatigue. Here the patient had presented with ptosis and dysphagia. On further history and examination, the patient was found to be a case of Bulbar Myasthenia Gravis and turned out to be having coexistent hyperthyroidism.

KEYWORDS

Bulbar myasthenia gravis
Hyperthyroidism

CASE REPORT

- 50 year old male, manual labourer, chronic smoker and occasional alcoholic, with Type 2 diabetes mellitus on irregular treatment for past 1 year, got admitted with saliva drooling.

- Informant was his wife. She gave history of

  -Increasing fatiguability—3 to 4 months

  -Blurring of vision and inability to open eyes completely –consulted many doctors for that without any improvement.

  -Pain in the nape of neck, occipital headache

  -Slurring of speech

  -Difficulty in chewing, swallowing food, swallowing saliva and history of aspiration of solid food and fluids.

  -All symptoms increased for past 1 month. On further enquiry, No history of emotional lability, fever, difficulty in breathing, deviation of angle of mouth, weakness of the trunk or limbs, bowel and bladdder involvement, difficulty in sensing smell, loss of taste sensation, any chronic drug intake, connective tissue disorders.

- Patient was a mixed diet consumer.
- Patient has two children.
  -No h / o similar illness in family members
- On examination – Conscious
  Comfortable in sitting position

  On lying down,he developed difficulty in breathing

  Moderately built and poorly nourished

  No pallor/icterus/cyanosis/clubbing/pedal edema

  No neurocutaneous markers/markers of HIV/ markers of TB

  Skin, hair, nails-normal

  Vitals : PR-98/min, regular, equally felt in all peripheral vessels.

  BP :130/80 mm Hg measured in right upper limb in supine posture.

  RR : 18/min, abdominothoracic, regular.

- CVS - S1 , S2+,No murmurs.
- RS - Normal vesicular breath sounds heard on all lung areas No added sounds
- P/A – Soft , no organomegaly
- CNS –Slurring of speech, nasal twang to the voice present suggestive of palatal muscle weakness

Asymmetrical ptosis of bilateral eyes more on right side

Extra ocular movements decreased in all directions

Muscles of mastication were wasted bilaterally

Jaw jerk-Brisk

Wrinkling of forehead had decreased bilaterally

Complete apposition of eyelids was not possible

Blowing of cheeks was decreased bilaterally

Nasolabial fold was equally prominent on both sides

Mandible depression was impaired
Nasal regurgitation, Nasal twang-present
Uvula slight deviation to left
Movement of posterior pharyngeal wall, palatal reflex, palatal movement were reduced
Shrugging of shoulder -decreased
Cant protrude tongue completely
Small tongue
Reduced movement of tongue against cheek

Spinomotor system examination revealed no abnormalities. There was generalized muscle wasting. No muscle fasciculations or fibrillations
Tone was normal in all four limbs
Power- 5/5 in all four limbs
Reflexes –Superficial-present bilaterally
Deep tendon-brisk bilaterally
No sensory involvement
No abnormal movements
Gait-normal
No autonomic system involvement.
No cerebellar signs, menigeal signs
Skull and spine -normal
Cardiovascular system/Respiratory system/Gastrointestinal system examination revealed no abnormalities.

Table -1 Basic investigations

HEMOGLOBIN	8.6 g/dl
TOTAL COUNT,DC	4700 P68,L30,E2
ESR	48 mm in first hour
SGOT/PT	42/36
UREA/CREATININE	7/1.0 mg/dl
RBS,SERUM SODIUM/ POTASSIUM	86mg/dl, 136/4.4 meq/l
CHEST XRAY PA VIEW	NORMAL
ECG	NORMAL SINUS RYTHM
ROUTINE URINE EXAMINATION	ALBUMIN NIL,SUGAR NIL, NO DEPOSITS
PERIPHERAL SMEAR	MICROCYTIC HYPOCHROMIC ANAEMIA
HIV,HBS Ag, ANTI HCV ANTIGEN	NEGATIVE
CREATINE PHOSPHOKINASE	56 U/L
RHEUMATOID FACTOR	NEGATIVE
THYROID FUNCTION TEST	T3-1.2ng/ml T4-13.89ng/ml TSH-<0.39ng/ml

- USG ABDOMEN AND PELVIS –NORMAL
- USG NECK-NORMAL
- ECHO – NORMAL
- MRI BRAIN-NORMAL
- RNS-ORBICULARIS OCULI DECREMENTAL PATTERN,10-15%
- CT THORAX-NORMAL
- PULMONARY FUNCTION TESTFT-MILD RE STRICTIVE PATTERN
- VIDEO LARYNGOSCOPY-LIMITED MOVEMENT OF BILATERAL SOFT PALATE;NO MASS LESION
- ANTI NUCLEAR ANTIBODY –NEGATIVE
- MANTOUX TEST-NEGATIVE
- ACETYLCHOLINE RECEPTOR ANTIBODY-6.95nmol/l
- ANTI TPO ANTIBODY-Negative

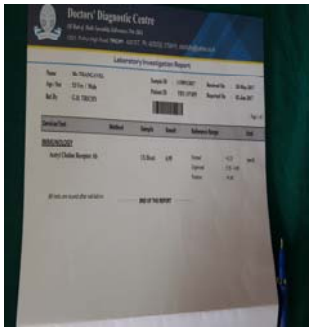
FIGURE1. AT THE TIME OF ADMISSION

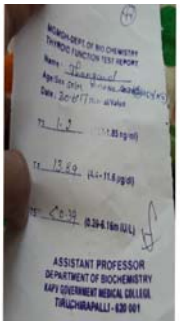
FIGURE 2.IN THE MORNING AND IN THE EVENING-Ptosis increases in the evening

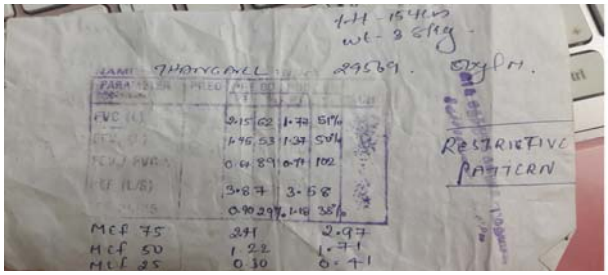
FIGURE 3.AFTER ICE PACK TEST-Ptosis disappeared

FIGURE 4. AFTER CONTINUOUS EYE CLOSURE-Ptosis increased

FIGURE 5







He was treated with antibiotics, Prednisolone, Neostigmine. Patient improved in a month and was discharged.

DISCUSSION

Myasthenia gravis is an auto immune disease of skeletal muscle acetylcholine receptors.

- The underlying defect is reduction in the number of available AChRs at NMJ and postsynaptic folds are flattened or simplified

- It occurs at any age and can involve either sex. Male to female ratio is 2:3. It usually begins insidiously, in the second and third decades in women and fourth to sixth decades in men. Exacerbation occurs in pregnancy or before menstruation. Patients complains of specific muscle weakness, not generalized fatigue Ptosis or diplopia may be initial symptoms in 65% of patients. Oropharyngeal muscle weakness causing difficulty in swallowing and talking can be the initial symptoms in 17% of patients. Limb weakness as the presenting symptom in only 10% of cases.

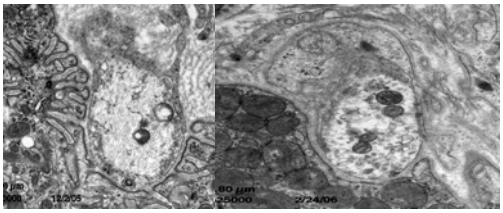
- The AChR Abs reduce number of available receptors by

  1. Accelerated turn over of AChR by a mechanism involving cross linking and rapid endocytosis of the receptors

  2. Damage to the post synaptic muscle membrane by the antibody in collabration with the complement

  3. Blockade of the active site of AChR

FIGURE 6



FEATURES OF MYASTHENIA GRAVIS

The amount of Ach released per impulse normally declines on repeated activity termed PRESYNAPTIC RUNDOWN

The decreased efficiency of neuromuscular transmission along with normal RUN DOWN, only a fewer and fewer muscle fibres activated by successive impulses resulting in MYASTHENIC FATIGUE

CLASSIFICATION

MG FOUNDATION OF AMERICAN CLASSIFICATION

I. Ocular alone
II. Mild weakness of other muscle+/- ocular

a. Predominantly limb/axial muscles or both+/- oropharyngeal muscles

b. Predominantly oropharyngeal/respiratory muscle or both+/-axial/limb muscles

III. Moderate weakness-a & b

IV. Severe weakness-a & b

V. Need for invasive ventilatory support except when used during routine post operative management

MODIFIED OSSERMAN SCALE

I. Ocular only
II. Ocular +generalised
III. Generalised +Myasthenic crisis
IV. Acute myasthenic crisis

DIAGNOSIS

- Clinical features-Dysphagia, Dysarthria, Diplopia, Ptosis, Dyspnoea

  Weakness in characteristic distribution; proximal lims, neck extensors, generalized

  Fluctuation and Fatigue-worse with repeated activity, improved with rest

- Laboratory testing-AntiAChR Radio immunoassay-85% positive in generalised Myasthenia Gravis and 50% positive in Ocular Myasthenia gravis. Definite diagnosis, if positive. Negative result doesn't rule out Myasthenia gravis.40% of those with negative AChR antibody assay have positive AntiMusk antibody positive.

Repetitive Nerve Stimulation-Decrement of >15% at 3Hz,highly probable

Single fibre Electromyography-Blocking and jitter with normal fibre density; confirmatory but not specific

Edrophonium chloride-2mg+8mg IV: Highly probable if unequivocally positive

For ocular and cranial Myasthenia Gravis-Exclude intracranial lesions by CT or MRI brain

- SIGNIFICANCE OF ANTIBODY TITRE

The AChR Ab titre varies widely among patients with similar degrees of weakness.

The amount of Ab in the serum does not predict the severity of the disease in individual patients .Treatment induced fall in Ab level shows clinical improvement; rise of titre results in exacerbations. The Ab level may be low at onset on MG and gradually become elevated in late stage. Worthwhile to repeat test if initial values are normal.

The Presence of AChR Antibody is not diagnostic for MG, also present in:

Systemic lupus erythematosus
Inflammatory neuropathy
Amyotrophic lateral sclerosis
Rheumatoid arthritis in patients taking D-penicillamine
In cases of thymoma without Myasthenia Gravis

- Antibody negative Myasthenia Gravis

1. Ab to lrp4-no commercial test is available for assay
2. Ab to agrin –a protein released from motor nerves which binds to lrp4
   Interfere with clustering of AChRs in NMJ
3. Anti striational Ab-react with epitopes on the muscle protein titin & ryanodine
   receptors present in almost all with thymoma&>50yrs.
   These antibody titres have prognostic significance
4. AntiSM Ab-84% with thymoma<4oyrs

- OCULAR MYASTHENIA GRAVIS

Ocular myasthenia – if progressing to generalized MG usually does so within the first 3 years after onset. fluctuating, asymmetric external ophthalmoplegia with ptosis and weak eye closure is virtually diagnostic of myasthenia. Combined patterns of weakness of the extra-ocular muscles, levator palpebrae superioris, and orbicularis oculi are highly indicative of myasthenia. Ocular features represent a combination of paresis and secondary central compensatory mechanisms.

Ocular signs:

SIGNS OF FATIGUE
Levator palpabrae superioris Lid twitch-COGAN'S SIGN Ptosis after sustained up-gaze Lid nystagmus after sustained up-gaze Orbicularis Oculi Afternoon Ectropion Peek sign
Extra ocular muscles Saccadic slowing or truncation with repeated saccades Intrasaccadic fatigue Rapid small saccade Gaze evoked nystagmus after sustained gaze Quiver eye movements
Improvement with sleep test

SIGNS OF ADAPTATION	SIGNS OF VARIABILITY
Levator palpabrae Enhanced ptosis Lid retraction contralateral to optic eye	Levator palpabrae Lid hopping
Extraocular muscles Hypermetric small saccades Dissociated gaze-evoked Nystagmus	Extraocular muscles Saccadic jitter

SIGNS OF COMBINED WEAKNESS AND ADAPTATION
Levator palpabrae Lid retraction with COGAN'S lid twitch sign
Extra ocular muscles Saccadic Hypermetria fter Edrophonium

DISORDERS ASSOCIATED WITH MYASTHENIA GRAVIS AND RECOMMENDED LABORATORY TESTS

Auto immune disorders-Hashimoto's thyroiditis, Grave's disease, SLE, Rheumatoid arthritis, Skin disorders

Conditions exacerbate Myasthenia Gravis-Hyperthyroidism, Hypothyroidism, Pregnancy, Respiratory tract infection, drugs like betablockers, Pencillamine, Botulinum toxin, Aminoglycosides, Quinolones, Macrolides

Disorders interfering with therapy-TB, Diabetes, Peptic ulcer,, GI bleeding, Hypertension, Asthma, Obesity, Osteoporosis

Investigations-CT/MRI of chest, ANA, Antithyroid antibodies, TFT, PPD skin tests, Fasting blood glucose,HbA1C,Pulmonary function Tests, Bone densitometry

TREATMENT

1. Choline esterase inhibitors

Mestinon (Pyridostigmine bromide) first choice, dose 30-60 mg q 6-8 h/daily;not>120mg q4- 6h/day

Prostigmine (Neostigmine bromide) 7.5 – 15.0 mg q 6-8 h/ daily

No fixed dosage schedule.

2. Immunosuppression

a. Immediate improvement-IVIG(2gm/kg over 5 days)/ plasmapheresis (5 exchange over 10-14day period)

b. Intermediate term-3 to 4months

Glucocorticoid+cyclosporine/tacrolimus

c. Long term benefit-Azathioprine/mycophenolate mofetil (1-1.5gm bd)

d. With antiMuSK Ab-Rituximab (375mg/m2 iv in 4weekly infusions or 1 gm iv on 2 occasions 2weeks apart)

3. Thymectomy

4. Glucocorticoid-DOSE:Prednisone 60 to 80 mg/day given until sustained improvement (usually 2 weeks) then alternate days beginning with 100-120 mg tapered over months to lowest dose necessary (usually less than 20 mg alternate days)

Given as a single dose to minimize side effect-start with lower doses to avoid early weakening.

In myasthenic crisis,

- If the weakness of respiration persists give respiratory assistance
- May be due to excess ACHE medications-cholinergic crisis, if so stop drugs
- In intercurrent infection, start antibiotic early, along with respiratory support preferably non invasive bilevel positive airway pressure and pulmonary physiotherapy
- Treat fever or infection as in an IMMUNOCOMPROMISED patient

CONCLUSION

Myasthenia gravis can present as generalized or localized weakness simulating Upper motor neuron disorders. It can be associated with other autoimmune or non auto immune disorders which can ultimately influence the prognosis of the patient.

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