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A CASE OF MYASTHENIA GRAVIS

General Medicine

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ABSTRACT

Myasthenia gravis is an acquired autoimmune disorder. It is clinically characterized by features like weakness of skeletal muscles and fatigability on exertion. The first clinical description was in 1672 by Thomas Willis. In this condition, autoantibodies are directed against the acetylcholine receptor at the neuromuscular junction of skeletal muscles. It may be considered a B-cell mediated disease. Extra-ocular muscle weakness is present in most of the patients. Progression occurs over weeks to months to severe weakness and respiratory muscle involvement. Here I report a case of Myasthenia gravis who presented with drooping of eyelids, difficulty in swallowing and difficulty in speaking for the past 3 months. The symptoms of the patient progressed to involve the respiratory muscles and the patient required mechanical ventilation. The patient was started on Azathioprine and IVIg in addition to other treatments like Methylprednisolone and Pyridostigmine. The condition of the patient stabilized and was weaned off the ventilator successfully in the next few days.

KEYWORDS

Introduction:-

In Myasthenia gravis (MG), antibodies are directed toward the acetylcholine receptor at the neuromuscular junction of skeletal muscles. This results in decreased number of nicotinic acetylcholine receptors at the motor end-plate, reduced postsynaptic membrane folds, widened synaptic cleft. Anti-AChR antibody is found in 80-90% of patients with MG. This has been proven with passive transfer experiments. MG may be considered a B cell-mediated disease. T-cell mediated immunity also has some influence. Thymic hyperplasia and thymomas are recognized in myasthenic patients. Here I report a case of Myasthenia gravis who was treated successfully[1].

Case report:-

The patient being reported here is a married male aged 88 years. He is farmer by occupation and is a right-handed person. He was admitted with chief complaints of-

Drooping of the eyelids for the past 3 months
Difficulty in chewing for the past 3 months
Difficulty in swallowing for the past 3 months
Difficulty in speaking for the past 3 months
Dyspnoea for the past 3 days

Patient was alright 3 months back when he started having drooping of the eyelids which was more in the evenings and increased in severity as the day progressed. Towards the end of the day the drooping was so severe that it was difficult to keep the eyelids open. At this time the patient also had diplopia. There was improvement in the complaints whenever the patient took rest and after sleep.

Patients had difficulty in chewing which was more after chewing hard substances and was in the form that the strength of mastication decreased with number of attempts.

Patient also complained of difficulty in swallowing. This was more to liquids. Swallowing became difficult after the initial few vigorous attempts. There was nasal regurgitation of liquids. These also improved after taking rest. But later on i.e., 3 days before presentation, the patient had started having breathlessness. To start with 3 days back, the patient experienced breathlessness even on walking for some distance. It later progressed and patient became more breathless. In the next one day patient felt breathless even at rest. There was no history of orthopnoea or PND. There was also an associated complaints of generalised weakness. There was no history of fever or any history of limb weakness. Patient needed assisted ventilation in the form of BiPAP due to hypoventilation and CO2 retention. The patient was able to maintain saturation on this. Then one day later, the patient had to be intubated and started on invasive ventilation. There was no history of bladder/bowel disturbance. Ther was no history of any sensory involvement. There was no history of any involuntary movements. There was no history of any other cranial nerve involvement. There was no past history of similar complaints. Family history showed nothing significant. Personal history showed that the patient is vegetarian. Habits are normal. Patient is a reformed smoker.

On general physical examination, patient was conscious, cooperative, well oriented to time, place and person. Built of the patient was asthenic. Patient was afebrile, PR – 92/min, regular, other parameters normal. Respiratory rate of 28/min, abdominothoracic. BP – 130/80 mm Hg. No pallor, icterus, cyanosis, clubbing, lymphadenopathy, edema. JVP was not raised. Single breath count decreased on repititive testing. CNS examination showed that higher mental function was normal. Speech - Slurring of speech on prolonged talk was present.

Cranial Nerves examination showed -

I Normal
II Normal
III, IV, VI Diplopia, Nystagmus, Ptosis was present on repeated use.
V Drooping of jaw was present after a few clenches of teeth
VII Smile of the patient was altered
VIII Normal
IX, X Nasal twang to voice was present

Weakness was present on repeated stimulation of posterior pharyngeal wall
Nasal regurgitation of liquids was present
XI Normal
XII Weakness was present on repeated testing

Motor system examination showed -

No wasting
Tone was normal

Proximal muscle weakness of upper limbs was present. (Forward arm abduction time was 3 minutes)

No involuntary movements were present
Coordination was normal
Gait was normal

Reflexes –

DTRs were normal
Superficial reflexes were normal
Sensory system was normal
No signs of meningeal irritation were present
CVS – S1, S2 heard, RS – b/l NVBS, P/A – Normal.

Differential Diagnosis was kepr as-

1.Myasthenia Gravis with crisis
2.Eaton-Lambert Myasthenic Syndrome
3.Basilar Artery Thrombosis
4.Brainstem Gliomas
5.Cavernous Sinus Syndromes
6.Multiple Sclerosis

7. Neurosarcoidosis
8. Botulism
9. Drug induced myasthenia-like syndrome
10. Mitochondrial myopathies
11. Oculopharyngeal Muscular Dystrophy

Investigations done showed –
Hb 11.9 gm%
TLC 7200/cu.mm
P62/L32/M3/E3
Platelet ct 1.54 lac/cu.mm

PBF Normal
Viral markers Negative
Urine R,M Normal RBS 157 mg%
RFT Normal
LFT Normal
Sr Na 146 mEq/L
Sr K 3.3 mEq/L
FLP Normal
ESR 10 mm 1st hr
ABG showed CO2 retention which improved after assisted ventilation
FT3 2.24 (low)
FT4 1.01 (normal)
TSH 0.464 (low)
CXR(PA) WNL
ECG WNL
RA factor Negative.
CT Chest and Neck Normal.

Edrophonium Test was positive
NCV – showed a decremental response of >10% on repeated stimuli. This was consistent with a disease of neuromuscular junction.
MRI Brain –
Areas of gliosis right anterior basifrontal region
Few tiny white matter hyperintensities
Cortical and periventricular ischaemic damage
Anti-Acetylcholine Rc Ab – Positive
24.01 nmol/L
Neg <0.25
Pos >0.40

ANA – Positive.
Final diagnosis was Myasthenia gravis Class IV.
Treatment given was steroids i.e., Inj Hydrocortisone, Inj Methylprednisolone,Anticholinesterase drug tab Pyridostigmine, Tab Azathioprine, IVIg.

Mechanical ventilation was given from which the patient was successfully weaned off with the treatment given. Patient was on BiPAP and the CO2 retention had improved initially. After increasing the dose of pyridostigmine and after starting azathioprine and IVIg, the condition of the patient had stabilized.

Discussion:-
Frequency of the condition shows an annual incidence in US of 2/1,000,000 persons. Worldwide prevalence is 1/10,000 persons. There has been a recent decrease in mortality rate due to advances in the treatment. It is 3-4% (can be as high as 30-40%). Risk factors the disease include age > 40 years, short history of disease, presence of thymoma, female sex. Mean age of onset is males-42years, females-28years. Myasthenia gravis is characterized by fluctuating weakness increased by exertion. Weakness increases during the day and improves with rest. Extraocular muscle weakness - ptosis is present initially in 50% of patients and during the course of disease in 90% of patients. Head extension and flexion weakness may be present. Weakness may be worse in proximal muscles. Progression of disease from mild to more severe occurs over weeks to months. It usually spreads from ocular to facial to bulbar to truncal and limb muscles. Often, symptoms may remain limited to EOM and eyelid muscles for years. The disease remains ocular in 16% of patients. Most remissions with treatment occur within the first three years. On basic physical examination, one should do muscle strength testing, recognize patients who may develop respiratory failure (i.e. difficult breathing), sensory examination and DTR's tested which are normal. Facial muscle weakness is almost always present. Bulbar muscle weakness causing palatal muscles weakness and "Nasal voice", nasal regurgitation. Chewing may become difficult, severe jaw weakness may cause jaw to hang open, swallowing may be difficult and aspiration may occur with fluids—coughing and choking while drinking occurs. Upper limbs weakness is more common than lower limbs. Weakness of the *intercostal muscles* and the *diaghram* may result in CO2 retention due to hypoventilation which may cause a neuromuscular emergency. Weakness of *pharyngeal muscles* may collapse the upper airway. Co-existing autoimmune diseases may be associated like hyperth yroidism, rheumatoid arthritis, scleroderma, lupus. AChR antibodies are found in 90% of patients developing MG secondary to penicillamine exposure[2].

Modified Osserman Scale
Class I Ocular only
Class II Ocular + generalised symptoms
Class III Generalised symptoms + myasthenic crisis
Class IV Acute myasthenic crisis
On Lab studies,

Anti-acetylcholine receptor antibody
- Positive in 74%
- 80% in generalized myasthenia
- 50% of patients with pure ocular myasthenia
- Anti-striated muscle (MuSK)
- Present in 84% of patients with thymoma who are younger than 40 years.
- Imaging studies
- Chest x-ray
- nPlain anteroposterior and lateral views may identify a thymoma as an anterior mediastinal mass

Chest CT scan is mandatory to identify thymoma
MRI of the brain and orbits may help to rule out other causes of cranial nerve deficits but should not be used routinely

Electrodiagnostic studies that can be done include-
Repetitive nerve stimulation
Single fiber electromyography (SFEMG)
Edrophonium (Tensilon test)
Patients with MG have low numbers of AChR at the NMJ
Ach released from the motor nerve terminal is metabolized by Acetylcholine esterase

Edrophonium is a short acting Acetylcholine Esterase **Inhibitor** that improves muscle weakness

Evaluate weakness (i.e. ptosis and opthalmoplegia) before and after administration.

Treatment modalities that are available are-
AChE inhibitors
Immunomodulating therapies
Plasmapheresis
Thymectomy
Important in treatment, especially if thymoma is present
AChE inhibitor
Pyridostigmine bromide

- Starts working in 30-60 minutes and lasts 3-6 hours
- Individualize dose
- Adult dose:
- 60-960mg/d PO
- 2mg IV/IM q2-4h
- Immunomodulating therapies
- Prednisone
- Most commonly used corticosteroid in US
- Significant improvement is often seen after a decreased antibody titer which is usually 1-4 months
- No single dose regimen is accepted
- Some start low and go high
- Others start high dose to achieve a quicker response
- Clearance may be decreased by estrogens or digoxin
- Patients taking concurrent diuretics should be monitored for hypokalemia

Hydrocortisone
Azathioprine
Cyclosporine
Plasmapheresis
IVIg

Rituximab
Surgery

Diet - Patients may experience difficulty chewing and swallowing due to oropharyngeal weakness

If dysphagia develops, liquids should be thickened.
Thickened liquids decrease risk for aspiration

Activity
- Patients should be advised to be as active as possible but should rest frequently and avoid sustained activity
- Educate patients about fluctuating nature of weakness and exercise induced fatigability.

Complications-
Respiratory failure
Dysphagia
Complications secondary to drug treatment

- Long term steroid use
- Osteoporosis, cataracts, hyperglycemia, HTN
- Gastritis, peptic ulcer disease
- Pneumocystis carinii infection[3].

Conclusion:-
Myasthenia gravis is a rare entity to be encountered in daily practice. A high degree of suspicion along with recognition of the mild form of the symptoms occuring initially in the disease is important for the diagnosis to be made. The patients initially may present with only ocular symptoms which may remain static for many months and all of sudden due to some secondary inciting or aggravating agent it may progress very fast and the patients may require life saving measures like mechanical ventilation. There are also many modalities of treatment which are available now in the form of drugs which is helping these patients to fight this dreaded disease.Immunomodulators and IVIg are some of these.

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