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RESEARCH ARTICLE

A RARE CASE OF JUVENILE MYASTHENIA GRAVIS

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Abstract

Juvenile Myasthenia Gravis is arare auto immune disorder affecting children and adolescents, characterized by ptosis, muscle weakness and fatigability, untreated patients may progress to paralysis of the respiratory muscles and the risk of aspiration, particularly at times when they have an upper respiratory tract infection. Early recognition of this disease helps avoid unnecessary testing, prevent undue parental anxiety and stop the progression of symptoms. An 18 months old girl admitted with progressive dropping of eyelids, swallowing difficulty, loss of head control and generalized fatigability. She had positive acetyl cholinesterase test. Investigation releavedelectro decrementalresponsonse in electromyography. Patient treated with oral pyridostigmine bromide and steroid resulted in improvement in muscle strength and functional ability with regularly followed in OPD.JMG requires prompt recognition and management to prevent complications. This case highlights the importance of considering JMG in children with persistent weakness and fatigue.

Introduction:-

Juvenile Myasthenia gravis (JMG) is a rare autoimmune disorder that affects children and adolescent causing muscle weakness and fatigability [1]. The incidence of Myasthenia gravis thought to be 0.5/100,000 to 3/100,000, and approximately 1% of all patients with Myasthenia gravis are children. It was first recognized by Erb in 1879.There are three main clinical forms affecting children: juvenile myasthenia gravis, congenital myasthenia and transient neonatal myasthenia.

Juvenile myasthenia gravis is an antibody-mediated disease targeting the acetylcholine receptors on the postsynaptic part of the neuromuscular junction. It is an autoimmune-mediated blockade of the acetylcholine receptors, with accompanying elevated anti acetylcholine receptor antibodies, which are thought to be produced through T-cell activation [2]. These antibodies bind to the acetylcholine receptors, leading to receptors degradation,blocking of synaptic transmission and induce local deposition of complement resultingin immune-mediated injury and disrupting the normal transmission at the neuromuscular junction leading to muscle weakness and ptosis. Anti-AchR antibodies are occasionally found in plasma of prepubertal age group.Some patients with negativeacetylcholine receptor antibody may have autoantibodies against the muscle-specific kinase.(MuSK)[3].MuSK antibodies positive myasthenia seen in female infants , toddlers having severe bulbar involvement. Diagnosis in young children can be complicated by the need to differentiate from congenital myasthenic syndromes in which some genetic mutations have been observed. Treatment commonly includes anticholinesterases drugs, corticosteroids with or without steroid-sparing agents and newer immune modulating agents. Intravenous immunoglobulin and plasmapheresis are

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effective in treatment of myasthenic crisis and before surgery.Thymectomyis most effective in patients having high titers of anti-AChR antibodies.

Background

This is a case of 18 months old girl who presented with symptoms of lower respiratory tract infections and ptosis of both upper eyelids and subsequently was diagnosed with juvenile myasthenia gravis. This case demonstrates the importance of early diagnosis and treating such patients promptly and cautiously to prevent impending grievous complications.

Discussion:-

Juvenile myasthenia gravis is rare autoimmune disorder that presents unique challenges in diagnosis and treatment. Our case report highlights several key aspect of JMG. It is a clinical diagnosis with symptoms of ptosis, limbs weakness, bulbar weakness and fatigability. JMG has 2 variants Ocular or general. Ocular MG is due to neurologic involvement is limited to ocular muscles. Approximately 80% of ocular MG progress within first 2 years to systemic involvement presenting as limb girdle and distal muscle weakness. In very young children it is very important to differentiate auto-immune myasthenia from congenital myasthenic syndromes (CMS) as the treatment options, prognosis and genetic implications are very different [4].Most CMS are transmitted as autosomal recessive traits but the slow channel syndrome is autosomal dominant. CMS usually present in the first years of childhood with variable presentations. There is often a positive family history, and diagnosis is aided primarily by electrophysiology and DNA analysis for genetic mutation and occasionally by muscle biopsy. The diagnosis of JMG requires a combination of clinical evaluation, laboratory tests like detection of anti-AChR antibodies,EMG and imaging studies(CT,MRI). In young children where anti-AChR antibodies are negative this can lead to difficulty in differentiating from CMS. False negative tests results can occur, emphasizing the need for repeated testing for anti-AChR antibodies. Patients without having antibodies to AChR or MuSK are described as having sero-negative myasthenia gravis. Sero negative MG patients are more similar to AChR seropositive patients than MuSK positive patients, both in clinical features and in response to treatment [5].

Our patient responded well to a combination of oral pyridostigmine and steroid. However,treatment responses can vary and individualized approaches are necessary.

With appropriate management, most children with JMG achieve significant improvement in muscle strength and functional ability.

Thymectomy

Should be considered and could potentially lead a cure. Thymectomy is most effective in patients who have high titers of anti-ACh receptor antibodies in the plasma and who have been symptomatic for <2 yr but it is not effective in congenital and familial form of myasthenia gravis. Immunosuppressant drugs other than steroids have also been recommended for the long-term treatment of myasthenia gravis in adults; hopefully, investigations currently underway will elucidate its role in younger patients. These non steroidalimmunosuppresentsdrugs are often combined with a cholinesterase inhibitor and thymectomy. Both Lindner et al and Rodriguez et al determined that for best results, thymectomy should be performed within 12 months of the onset of symptoms [6,7] Intravenous immunoglobulin and plasmapheresis are reserved for refractory cases.IVIG should be tried before plasmapheresis as it is less invasive.

Case Report

An 18months old girl with normal development and without any perinatal events product of non consanguineous marriage, brought to PICU, complaining of high grade fever, cough and cold, acute exacerbation of drooping of eyelids for 2 days, breath holding episodes, breathing difficulty, generalized fatigability, poor oral intake, swallowing difficulty,loss of neck control for 1 day. Drooping of eyelids was painless, least noticeable in the morning and worsened throughout the day and partial remission with sleep. At14months of age she had similar history of cough,cold, fever, loss of neck control followed by progressive drooping of eyelids. Her parents consulted many private practitioners. Some medications in form of oral antibiotics and steroid given lead to some improvement but not completely. Ophthalmological evaluation was done and it was found to be normal .These symptoms had a variable course and fluctuation throughout the day and partial remission with sleep. There was no history of similar illness or autoimmune disorders in the family.

On physical examination, the patient was well-nourished in apparent distress, tachypneic, pulse rate was120/min, regular, rhythmic, normal in volume and no radio radial and radio femoral delay, peripheral pulse were palpable. SpO_2 was 98%, neck was hypotonic with no carotid bruits, no lymphadenopathy, swelling and thyromegaly. Chest was full of conductive sounds with no added sound bilaterally, Cardiac exam showed normal and regular heart rate with no murmurs. Abdomen was soft, non tenderwith no organomegaly or masses. There were no neurocutaneous markers or facialdysmorphism.On neurological examination GCS was10, bilateral ptosis was present, pupils were bilateral normal size and reactive to light, bilateral intact cranial nerves, Muscle bulk was normal, there was hypotonia of upper and lower limb bilateral, DTRs were not present, sensory system was intact. Routine blood investigations including electrolytes (potassium) were normal. Thyroid profile, creatine kinase and chest x-ray were found to be normal, no mass or lesion seen on CT thorax (to rule out thymoma),anticholineesterase antibodies were negative and Acetyl choline esterase test was positive. She had electro decremental response on repetitive stimulation with electromyography. Having positive EMG and acetylcholinesterase test, diagnosis of juvenile myasthenia gravis was confirmed.

Patient managed with oxygen, iv fluids, injectable antibiotics, **Acetyl cholinesterase test** done with intramuscular injection of neostigmine (0.04 mg/kg) which showed a dramatic response in form of increased distance between upper and lower eyelids, with in 20 min.(Figure1, 2) Intramuscular neostigmine continued, given every 4 hourly. Patient responded with intra muscular neostigmine, shifted to oral pyridostigmine on next day at 4mg/kg/day in 4 divided doses, oral prednisolone added at dose of 0.5mg/kg/day on next day, tapered on follow up.She responded to oral pyridostigmine and other supportive measures. Her symptoms resolved within 20 min after giving IM neostigmine and shifted on oral pyridostigmine and prednisolone. She was discharged after 3 days and advised to continue oral pyridostigmine and prednisolone (in tapering dose).She is on regular follow up and on oral pyridostigmine since 3 months.

Figure 1:-Before Neostigmine Challenge Test.

Figure 2:-After Neostigmine Challenge Test.

Conclusion:-

JMG requires prompt recognition and management to prevent complications. Despite a lack of scientifically proven treatments for juvenile myasthenia gravis, it is important that Pediatricians be able to recognize its myriad presentations, which vary widely in symptoms and severity, and be able to respond with appropriate diagnostic tests and treatments tailored to individual patient needs. Our case report highlights the importance of considering JMG in children presenting with persistentmuscle weakness and fatigue, particularly in presence of ptosis ,dysphagia and breathing difficulty. Early diagnosis and treatment of JMG can significantly impact the quality of life for affected individuals so it is essential to raise awareness among health care professionals and public to facilitate timely referral and interventions. Prognosis is good and spontaneous remissions seen in few patients withJMG and others who do not undergo total remission lifelong treatment in form of immunosuppression and thymectomy might provide a cure .Additionally multidisciplinary care involving pediatrician, neurologists and surgeons is crucial for managing complex needs of children with JMG.With respect to the case presented, daily administration of pyridostigmine bromide and steroid found to be effective in patient outcomes.

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