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General Medicine

AN UNUSUAL PRESENTATION OF MYASTHENIA GRAVIS

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ABSTRACT Myasthenia gravis is often complicated by respiratory failure, known as a myasthenic crisis. However, most of the patients who develop respiratory symptoms do so during the late course of disease and have other neurological signs and symptoms. However, in some patients respiratory failure is the initial presenting symptom. We report the case of a 28-year-old gentleman with MG who presented with respiratory failure and proximal muscle weakness of the upper limbs as his first presenting symptom. As this patient was not responding to plasma exchange or iv immunoglobulin but to Inj.Rituximab.

KEYWORDS : Myasthenia gravis, Respiratory failure, Proximal muscle weakness, Rituximab

CASE REPORT:

A 28 year old gentleman with no comorbids presented to the emergency room with complaints of gradual progressive weakness of both upper limbs since 1 week and shortness of breath since 2 days. He had similar complaints 2 months back for which he was treated in an outside hospital as cervico -brachial neuropathy and spasmodic bronchitis with BIPAP support, antibiotics and other supportive measures with which he recovered.

On examination he was found to be comfortable and not in acute distress. His vital signs were as follows: blood pressure 138/90 mm Hg, pulse rate 184/min, respiratory rate 32 breaths/min, and temperature 98.6 °C. On chest auscultation there were bilateral basal crackles and on palpation abdomen was soft with no tenderness. His neurological examination showed weakness of both upper limb proximal muscles (Right > left). In view of respiratory distress he was kept on BIPAP with which his saturation was maintaining.

Laboratory values were normal except an increased white blood cell count (21,065/cm^3) with neutrophils predominating and blood cultures growing Acinetobacter. ABG repeated next day in the ICU showed gradual increase in CO2 retention and his weakness was progressively increasing. In view of respiratory muscle weakness, CO2 retention he was intubated and mechanically ventilated. After the intubation he was hypotensive, needing vasopressors for 3 days. There was suspicion of severe sepsis, and he was started on intravenous fluids while the antibiotics were continued. His hemodynamic measures improved with treatment, and he was afebrile within the next two days. His chest X-ray showed left lobar pneumonia for which pulmonologist inputs were obtained and the orders were carried out. MRI brain plain and cervical spine was done which were essentially normal . In spite of repeated attempts for extubation it could not be done. This led us to believe that he might have some other cause of respiratory failure, either cardiac or neuromuscular. He also had blurred vision, and at times double vision, minimal problems with swallowing. Neurological consultation was arranged, considering the possibility of neuromuscular weakness.

The second neurological examination revealed bilateral weakness of the deltoids, biceps and triceps. Rest of the neurological examination including sensory examination was normal. Neostigmine challenge test was done and had a subjective betterment of respiratory efforts after 1mg of neostigmine but the proximal muscle weakness remained persistent.

A diagnosis of myasthenia gravis was made on the basis of the history and examination. Neurophysiological studies and acetylcholine receptor and anti MUSK antibodies were requested for confirmation. NCS was normal in upper limbs and RNS showed features of possible post synaptic NMJ effect. NCS cannot be completed in lower limbs as he was feeling restless. While the acetylcholine receptor antibody was negative and anti MUSK antibodies turned out to be positive.

The patient was started on plasmapheresis along with pyridostigmine and azathioprine. With the first plasmapheresis treatment, his vital capacity improved. Following 5 cycles of plasma exchange he passed the weaning trial and was successfully extubated. There was continued improvement of muscle strength during the rest of his stay in hospital. Weaning from the ventilator failed over the next 2 weeks; therefore, a tracheostomy was performed. However, the patient was eventually successfully weaned from the ventilator in 2 more weeks and was discharged with T piece (overnight BIPAP), azathioprine, and pyridostigmine.

3 days later he was brought again to the ER with complaints of restlessness, shortness of breath and upper limb weakness (proximal). His routine investigations revealed neutrophilic leukocytosis. On examination, airway was patent, tachypneic with respiratory rate of 30/min, pulse rate-110/min, BP-140/80mm/hg and SpO2-98% at room air. CNS examination showed decreased power in both upper limbs (proximal muscle weakness) and both lower limbs were normal, exaggerated deep tendon reflexes, normal sensory system and plantar flexor. In view of his respiratory efforts, he was kept on Bipap (12/6) and his saturations was maintaining. In view of his persistent weakness he was started on IV immunoglobulin for 5 days with IV steroids following which his proximal muscle weakness and respiratory muscle involvement dint recover. Finally patient and the attenders were explained about the need for Rituximab and it was started. His upper limb power gradually became normal in 3 days time. While his respiratory muscle paralysis was also better requiring only overnight BIPAP at the time of discharge. He was discharged with azathioprine, oral steroids, biphasic insulin and other supportive measures.

DISCUSSION:

MG is an autoimmune disorder. In about two thirds of patients, extrinsic ocular muscle abnormalities present as the initial symptoms or bulbar weakness may also be the initial symptoms. The symptoms usually progress to include the limb muscles [1]. Respiratory failure can be a complication during the late course of MG in about 3 to 8% of cases, known as a myasthenic crisis [2] .

Clinical features are fatigue and weakness in the muscles, but reflexes are usually retained. Weakness increases with repeated muscle use and is attenuated by rest and sleep. The cranial muscles are involved early and the presentation is more of diplopia and ptosis. Here in our patient he had ptosis, upper limb proximal muscle weakness and respiratory failure.

Physical findings can vary in myasthenia as the muscle weakness tends to be more when the muscles are stressed. Muscle strength improves with rest, so the initial physical examination may not reveal any neurological deficit as in our patient. The important factor that distinguishes the disorder from other neuropathies is that sensation and reflexes are preserved. Vital capacity, timed forward abduction, and muscle dynamometry can be used as objective tools to diagnose and assess the disease activity.

Respiratory muscle involvement in myasthenia gravis can be of two types: myasthenic and cholinergic crises. The term myasthenic crisis is used to described muscle weakness because of decreased neuromuscular transmission at the synapse. In contrast, cholinergic crisis occurs because of excessive depolarisation at the neuromuscular junction. Myasthenic crisis can occur as a result of infection, decreased anticholinergic medication, use of aminoglycoside antibiotics, and postoperative stress. There has been a recent report of fluoroquinolones exacerbating myasthenic weakness[3]

Gracey *et al*[4] described their two year experience with 288 patients with myasthenia. Of these, 22 (7.6%) developed respiratory failure needing mechanical ventilation. For unassisted ventilation the following parameters were necessary: vital capacity 15 ml/kg and negative inspiratory force −100 cm H_2O. It has been described that early detection of respiratory muscle involvement can be difficult because of a normal breathing pattern and sometime selective affection of the diaphragmatic and intercostals muscles.

The basic pathophysiology of myasthenia gravis involves a decrease in the number of acetylcholine receptors at a neuromuscular junction where vesicles containing acetylcholine are released. Acetylcholinesterase in the clefts rapidly hydrolyses the acetylcholine and terminates its action on the muscle. Drugs such as edrophonium act by increasing the concentration of acetylcholine at the neuromuscular junction. It is now accepted that the changes in myasthenia are due to an antibody−mediated process.

Diagnostic tests are needed to confirm clinical suspicion, including anticholinesterase test, repetitive nerve stimulation test, and acetylcholine receptor antibody test. Edrophonium is the drug of choice for the anticholinesterase test because of its rapid onset and short half−life (few minutes). The test is considered positive if there is considerable improvement in muscle strength. In the repetitive nerve stimulation test, electricity is delivered to the nerve, and action potentials are recorded on the surface of the muscle. The test is considered positive if there is decremental response of 15%.5 Acetylcholine receptor antibody testing is done with an radioimmunoassay and is positive in 85% of patients with generalised myasthenia gravis. About 10% of patients with generalized myasthenia gravis do not have detectable antibodies to acetylcholine receptors or muscle specific kinase (MuSK) (double seronegative myasthenia), so neurophysiological tests and a positive response to therapy secure the diagnosis like in our case.

Associated conditions, including thymic tumours and thyroid dysfunction (both hypothyroidism and hyperthyroidism) should be considered since both can exacerbate myasthenia.6 . Infection and sepsis can exacerbate myasthenia and precipitate a myasthenic crisis. Other differential diagnoses that should be considered are Lambert–Eaton syndrome, drug induced myasthenia, botulinism, and intracranial lesions.

Current treatment options for myasthenia gravis include anticholinesterase agents, surgical thymectomy, immunosupression, and short term but fast acting therapies such as plasma exchange and intravenous immunoglobulin. In general anticholinesterase agents are used as the first line agents along with surgical thymectomy or immunosupression. Contemporary opinion is to carry out thymectomy in all patients who have attained puberty and are under 60 years of age even if they do not have a thymoma.

This case report raises many interesting points. It highlights the importance of considering neuromuscular disorders in cases of unexplained respiratory failure in an acute setting. And the case is more interesting just because he improved completely only with rituximab but not with anticholinesterase agents, immunosupression, or plasma exchange and intravenous immunoglobulin. In an ER/intensive care unit setting with sedation and paralytic use, a thorough neurological examination, especially of proximal muscles, may be challenging. Moreover, infection is a common cause for exacerbation of myasthenia gravis as in our patient.

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