EMERGENCY CASEBOOK

Case of the month: Unusual presentation of myasthenia gravis with acute respiratory failure in the emergency room

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Emerg Med J 2006;**23**:410–413. doi: 10.1136/emj.2005.030429

A 21 year old woman with no past medical history presented to the emergency room (ER) with signs and symptoms of sepsis and subsequently went into acute respiratory failure. She was found to have myasthenia gravis which was exacerbated by the infection. This report highlights the need to consider myasthenia gravis in the differential diagnosis of an otherwise unexplained respiratory failure in the critical care setting.

A 21 year old woman presented to the emergency department with fever, generalised weakness and right flank pain for three to four days. She was found to have urinary tract infection (UTI). While in the emergency room (ER) she complained of difficulty breathing. As her chest *x* ray revealed normal findings, pulmonary embolism was suspected and she was started on low molecular weight heparin.

The ER where she presented was in a hospital in a rural area so she was transferred to our tertiary care facility for further management. On examination she was found to be comfortable and not in acute distress. Her vital signs were as follows: blood pressure 135/78 mm Hg, pulse rate 120/min, respiratory rate 18 breaths/min, and temperature 98.6 ℃. On chest auscultation there were bilateral basal crackles and on palpation there was flank tenderness on the right side. The rest of the abdominal examination was normal. Her initial neurological examination was also normal with no evidence of focal neurological deficit.

Laboratory values were normal except an increased white blood cell count (21 000/cm^3) with neutrophils predominating and urine suggestive of UTI. Arterial blood gases on room air were as follows: pH 7.39, P_{CO_2} 36 mm Hg, P_{O_2} 99 mm Hg. The patient had a spiral computed tomography scan of the chest for evaluation of pulmonary embolism. There was no evidence of pulmonary embolism on the scan, but there was bilateral basal airspace disease with some atelectasis.

Within next two hours she had an sudden episode of desaturation, and she started complaining of her throat ''closing down''. She was immediately intubated and mechanically ventilated. After the intubation she was hypotensive, needing vasopressors for three to four hours. Vancomycin and imipenem–cilastatin were added to her antibiotic regimen. There was suspicion of severe sepsis, and she was started on intravenous fluids while the antibiotics were continued. Her haemodynamic measures improved with treatment, and she was afebrile within the next two days.

Next day arterial blood gases did not show any evidence of an A/a gradient. In spite of this the patient failed repeated attempts at extubation. This led us to believe that she might have some other cause of respiratory failure, either cardiac or neuromuscular, and, at this point, a more detailed history was obtained from her and her family. It transpired that prior to hospitalisation she had had symptoms of upper and lower extremity weakness for the past one month. She had also had blurred vision, and at times double vision, minimal problems with swallowing, sensation of choking on lying down, and feeling of being excessively tired by the end day for the past one and a half month. She had stopped driving her car as she was unable to change gears rapidly because of the weakness in her arms. Neurological consultation was arranged, considering the possibility of neuromuscular weakness.

The second neurological examination revealed bilateral weakness of the orbicularis oculi, deltoids, biceps, triceps, interossei, ankle dorsiflexors, and plantar flexors. Rest of the neurological examination including sensory examination was normal. Her weaning parameters were: vital capacity 500 ml, negative inspiratory force (NIF) −29 cm H_2O (normal −35 cm H_2O or less), and tidal volume 338 ml. The rapid shallow breathing index was 77. These findings suggested respiratory muscle weakness.

A diagnosis of myasthenia gravis was made on the basis of the history and examination. Neurophysiological studies and acetylcholine receptor antibodies were requested for confirmation. Electromyography studies showed significant decrement on repetitive nerve stimulation, consistent with the diagnosis of myasthenia gravis.

The patient was started on plasmapheresis along with oral steroids and azathioprine. With the first plasmapheresis treatment, her vital capacity improved from 500 ml to 1.4 l and the NIF increased to −80 cm H_2O. The next day she passed the weaning trial and was successfully extubated. She received five more plasmapheresis treatments and there was continued improvement of muscle strength during the rest of her stay in hospital. The acetylcholine receptor antibody panel was positive for binding, blocking, and modulating antibody. She was discharged after two weeks on steroid taper, azathioprine, and pyridostigmine.

At a later date she underwent a thymectomy and had an uneventful postoperative course.

DISCUSSION

Myasthenia gravis is not rare, with the prevalence of 50–125 cases per million population.[1] Respiratory muscle failure is not uncommon in this disorder. Individuals of all ages are affected, however, young women are affected most with a peak incidence in the twenties.[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. Difficulty swallowing can also be a feature as seen in our patient. She described a sensation of her ''throat closing down'' before she was intubated. Generalised weakness occurs in 85% of patients, which again is a symptom that would be difficult to attribute to a neuromuscular cause in a critical setting as in our patient.

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 crises 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] It puzzled us why we were not able to extubate our patient successfully at first. The normal A/a gradient and clinical features out of proportion with the pulmonary pathology led us to look for other causes of respiratory failure.

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.

Associated conditions, including thymic tumours and thyroid dysfunction (both hypothyroidism and hyperthyroidism) should be considered since both can exacerbate myasthenia.[2] As in our patient, infection and sepsis can exacerbate myasthenia and precipitate a myasthenic crisis.[6] 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, immunosuppression, 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 immunosuppression. 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. Although our patient had coexisting pulmonary pathology it was not severe enough to cause a major respiratory failure. In an ER/intensive care unit setting with sedation and paralytic use, a thorough neurological examination, especially of proximal muscles, may be challenging. Our patient's muscle weakness went unnoticed at the time of initial presentation. Moreover, infection is a common cause for exacerbation of myasthenia gravis as in our patient.

CONCLUSION

Myasthenia gravis can manifest as respiratory failure, and the diagnosis needs to be considered in cases of unexplained respiratory failure. Work up for other causes can be exhaustive, expensive, and hazardous if a high index of suspicion for neuromuscular causes is not maintained.

Competing interests: none declared

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Accepted for publication 5 October 2005

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