Isolated respiratory failure caused by myasthenia gravis

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ABSTRACT

Isolated respiratory failure due to myasthenia gravis that selectively involved the respiratory muscles alone is extremely rare and difficult to diagnose. We reported herein, a 46 year old patient who presented with acute respiratory failure, 4 weeks after thymoma resection. The respiratory failure was due to myasthenia gravis that selectively affected the respiratory muscles only without having any peripheral signs. The initial response to therapy with pyridostigmine was unexpectedly complicated with severe bradycardia that made insertion of permanent pacemaker essential, before further therapy.

Keywords: Respiratory failure, myasthenia gravis, thymoma.

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It is well known that myasthenia gravis can cause respiratory muscle weakness that leads to respiratory failure as part of generalized skeletal muscle involvement. Isolated involvement of respiratory muscles alone in the absence of other peripheral signs of myasthenia gravis is an unusual presentation. Extensive midline search from 1966 to date revealed only 2 cases that have been reported. We believe to the best of our knowledge, that this is the first case to be reported in Saudi Arabia and Asia.

Case Report. A 46 year old nonsmoker gentleman who works as a computer programmer presented to the emergency room of King Abdulaziz University Hospital (KAUH) with acute respiratory distress that was preceded by a 6 day history of flu like illness, fever, and non productive cough. On examination he was tachypneic, with respiratory rate of 32/minute. His temperature was 38.5°C, and blood pressure was 100/60 mmHg. Pulse rate was 100 beats per minute. The examination of respiratory system, showed recently healed right thoracotomy scar, and decreased breath sounds and bilateral scattered rhonchi. There were no signs of consolidation or hyper-inflation. Examination of cardiovascular system, and abdomen was unremarkable. Neurological examination showed no weakness of the limbs or ocular muscles. Tendon reflexes, superficial and deep sensations were normal. He rapidly deteriorated, and developed respiratory arrest for which he was intubated, and placed on mechanical ventilation in the intensive care unit (ICU). Preliminary results showed, white blood cell count 18.5 x 103/mm³, neutrophil 86%, hemoglobin 15.2g/dl, platelet count was normal. His Electrolytes, urea, creatinine, blood sugar, cardiac enzymes, and liver function tests were normal. Arterial blood gases on 3 liters of oxygen/minute showed, pH 7.25, PCO₂ 97.5 mmHg, PO₂ 57 mmHg. His ECG showed left anterior hemiblock. Chest radiograph showed right sided pleural thickening, partially resected 6th rib posteriorly, and normal lung parenchyma. Empirical therapy with IV cefuroxime, and nebulized bronchodilators, was started with presumptive diagnosis of acute respiratory failure due to chest infection. Subsequently sputum and

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blood cultures were negative for micro-organisms but *Klebsiella pneumonia* was isolated from urinary culture, that was sensitive to cefuroxime. On the 2nd day in ICU, fever subsided, and he became fully awake, but he was unable to use his respiratory muscles, and the measurements of his tidal volumes (VT) and vital capacity (VC) while on mechanical ventilation were markedly reduced (VT 0.05 L, VC 0.15 L). In a search for the cause of his acute respiratory failure, and after exclusion of the common causes of respiratory failure such as pneumonia, acute exacerbation of chronic obstructive pulmonary disease, left ventricular failure), myasthenia gravis (despite the absence of its peripheral signs) was thought to be the most likely diagnosis because of the well known association of thymoma with myasthenia gravis. So edrophonium hydrochloride test was performed but it turned out to be negative. Electromyography was highly suggestive of myasthenia gravis as it showed positive decremental response test with significant reduction of the evoked response after tetanization compared to the initial response. So a trial of pyridostigmine 60 mg QID, and prednisone 60 mg OD, was started. On the 3rd day in ICU, pyridostigmine was discontinued as the patient developed severe bradycardia (pulse rate dropped to less than 40 beats/minute). On the 6th day in ICU, lung mechanics were the same, so a permanent pacemaker was inserted (Figure 1) and pyridostigmine was restarted. On the 8th day in ICU respiratory muscles regained almost normal power, and then the measurements of lung mechanics showed significant improvement of VT, and VC up to 0.450 L, and 0.840 L. On the 10th day in ICU, weaning off ventilator and extubation took place. On the 12th day in ICU, the result of acetyl choline receptors antibodies was found to be significantly elevated (2.23 nmol/l), normal (<0.25 nmol/l). Subsequently, he made an eventual recovery and was discharged on pyridostigmine and steroid therapy.

One month before this presentation, he underwent mediastinal mass resection. Preoperatively his chest CT scan showed a large well defined rounded anterior mediastinal mass that was occupying most of the right hemithorax (Figure 2). The macroscopic findings of the resected mass showed an oval shaped well-defined solid tumor measuring 16 x 12 x 10cm, and weighing 1.2 kg. Microscopically the findings were consistent with benign thymoma. One week postoperatively he was discharged, and remained healthy for 3 weeks till this current presentation with respiratory failure and arrest. Currently he is on pyridostigmine and steroid therapy and regularly seen at the out patient clinic.

**Discussion.** It is well known in myasthenia gravis that generalized muscle weakness may occur in up to 85% of affected patients. Isolated involvement of a group of muscles in myasthenia gravis may occur in 15% of patients and mainly affects the extra ocular, and eye lid muscles. Respiratory muscle involvement that causes respiratory failure usually occurs as a part of generalized muscles weakness. Selective involvement of respiratory muscles alone in the absence of peripheral signs is extremely rare. In a retrospective study by Gracey et al. on 22 patients with myasthenia gravis that required mechanical ventilation; only 4 presented with respiratory failure due to involvement of respiratory muscles. All of them had generalized muscle weakness beside their respiratory failure due to respiratory muscle involvement. Dushay et al. has reported the 1st case of myasthenia gravis that presented with respiratory failure due to selective involvement of respiratory muscles. There was no peripheral neuromuscular involvement, and edrophonium hydrochloride test was negative. In contrast to our patient, their patient showed lack of response to pyridostigmine, corticosteroid therapy, and extubation took place only after plasmapheresis. Mier et al. has also reported a similar patient who developed isolated...
respiratory failure due to undiagnosed myasthenia gravis, that occurred after surgical removal of recurrent thymoma. However, their patient presented initially with ptosis due to ocular myasthenia that was initially undetected. The diagnosis of myasthenia gravis was only reached by exclusion of the common causes of type 2 respiratory failure. The following differential diagnoses were initially considered: 1) chronic obstructive pulmonary disease (but he never smoked, his preoperative spirometry and chest radiograph showed no evidence of airflow obstruction), 2) Severe pneumonia (but there was no clinical or radiological findings of it), 3) phrenic nerve paralysis secondary to thymoma resection (but if this is the case, the diaphragmatic weakness would have been seen immediate post operatively and would have not been improved on anticholinesterase and steroid therapy), 4) Guillain Barre syndrome (but there was no evidence of proximal and distal muscle paralysis), 5) Lamber-Eaton myasthenic syndrome (but the proximal muscles, and tendon reflexes were normal), 6) Drug overdose (but there was no clinical evidence of drug abuse, and he became awake on the 2nd day while ventilatory muscles remained paralyzed for one more week). 7) Botulism (but the pupils were normal and in contrary to myasthenia gravis there was reduction rather than an increase in the evoked response amplitude of peripheral muscles). So myasthenia gravis, despite the absence of its peripheral sings was considered to be the most likely diagnosis. The association of thymoma with myasthenia gravis that occurs in up to 40% of patients has also strengthened this diagnosis. Failure of edrophonium hydrochloride to show any significant improvement of the tidal volume and vital capacity while the patient on a mechanical ventilator has been reported in similar way to our patient. The possible explanation of negative response may be either due to use of a small dose of edrophonium hydrochloride or the effect may pass unnoticed because of short duration of action. The decision to use pyridostigmine at therapeutic doses of 60 mg QID was taken empirically, and unexpectedly was complicated with severe bradycardia that occurred even after lowering the doses up to 30 mg TID. The occurrence of this complication was extremely unusual, and may be due to the presence of the conduction defect that was aggravated by the effect of anti cholinesterase therapy rather than to cholinergic crisis. In this patient, electromyography of the peripheral muscles was positive for myasthenia gravis, as the evoked response amplitude decreased to 40% when compared with initial response. Normally it is considered positive when the amplitude decreases more than 15%, however it may be negative in the presence of myasthenia gravis and it is not specific. When pyridostigmine was resumed after pacemaker insertion, the power of the respiratory muscle has improved quickly, and extubation took place on the 3rd day of therapy. Myasthenia gravis was also confirmed when high levels of acetyl choline receptor antibodies were received after extubation. Acetyl choline receptor antibodies are highly specific, but a high level doesn't correlate with disease activity, and up to 20% of myasthenia patients may have negative antibodies.

In conclusion, in patients with respiratory failure of unknown etiology, myasthenia gravis should always be considered even in the absence of its peripheral signs or in the presence of a negative edrophonium hydrochloride test.

References