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REFRACTORY MYASTHENIA GRAVIS;
PATIENT ON RITUXIMAB WITH ACUTE RESPIRATORY FAILURE: A CASE REPORT

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ABSTRACT… Myasthenia gravis (MG) is prototypical neurological autoimmune disorder, characterized by limb and occulo-bulbular fragility. Our case study will facilitate the practitioners as well as the scientific community to consider other therapy plans with patients presented with acute respiratory failure due to the use of rituximab.A 25-year-old man presented with acute respiratory failure This case reporte sheds light on the importance of differential diagnoses of refractory myasthenia gravis for inexplicable acute respiratory failure upon rituximab treatment. The case study demonstrates the problems associated with use of rituximab in refractory myasthenia gravis. It can cause acute respiratory failure among the patients with relapse specially. Our case study will facilitate the practitioners as well as the scientific community to consider other therapy plans with patients presented with acute respiratory failure due to the use of rituximab.

Key words: Rituximab, Myasthenia gravis, Respiratory failure

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INTRODUCTION

Myasthenia gravis (MG) is prototypical neurological autoimmune disorder, characterized by limb and occulo-bulbular fragility[1,2]. It is usually treated by a number of immune-modulating therapies. MG usually presents with generalized, oropharyngeal, or ocular symptoms. About 50% of MG presents with ocular symptoms (e.g. diplopia, ptosis). Approximately 15-20% of patients' experiences myasthenic crisis in the first two years of diagnoses that necessitates mechanical ventilation[2,3,5].

CASE PRSENTATION

A 25 year old man was presented with fever, generalized body fragility, bilateral phasis, fatigue and right side pain from the last two weeks. He also complained about obstruction in his trachea and difficulty in breathing at night. His chest examination and radiological findings revealed no pulmonary embolism and all other reports were clear.

He was agitated and confused at the time of admission. He showed symptoms of underlying anxiety and depression due to his respiratory distress. His vital signs included: body temperature 101°C, pulse rate 120/min, respiratory rate 16 breaths/min, and blood pressure 140/80 mm Hg. The computed tomography scan (CT scan) of chest revealed normal trachea and bronchi. Normal lung parenchyma. No mass lesion in hila, no pleural effusion and pleural thickness, no alveolar or nodular shadows were seen. Sections through the abdomen were remarkable. In-fact it was a normal CT report. Flank tenderness was observed on palpation on the left side of his chest auscultation. His initial clinical investigation showed no focal neurological deficit and thus appeared normal to the staff.

Laboratory values showed normal result with hemoglobin (13.4g/dl), TLC (5100/Cmm), neutrophils (45%), eosinophils (3%), Mast cells (2%) and a platelet count of 197000/Cmm. But after one hour he started complaining about his throat choking down. He was then mechanically ventilated and intubated. The following day, no A/a gradient was marked by arterial blood gases. But still failure of extubation led us to the point that his respiratory distress may be due to any infection or any other causative agents such as

neuromuscular or of cardiac origin. So an Electro Cardio Graph (ECG) was done and few other neurological tests were performed. The ECG was normal. A further inquiry from the relatives revealed that the patient, prior to hospitalization, complained about fatigue, blurred vision, lower and upper extremity weakness.

So further neurological investigation (NCS/EMG) was done. The NCS was done using surface electrodes. DML was 3.5ms (Amplitude was 4.1 mV, velocity was 61.8m/s) while SLP was 3,5ms, (Amplitude was 18 mV, velocity was 50 m/s). LT of accessory nerve demonstrated DML of 1.92ms and amplitude of 7mV. RNS accessory nerve stimulation recorded at trapezoidal LT side revealed decrement on first stimulation to be -18%. Upon second and third stimulation of one min and 10 second exercise demonstrated a value of -24% and 3% respectively.EMG was done using concentric needle electrodes. LT Deltoid and LT FDI showed normal potentials, pattern and recruitment. Significant decrement upon stimulation, after one minute exercise was consistent with the diagnoses of MG. Rest of the neuralinspection was normal.

So a clinical diagnoses of MGrelapse was madeand intravenous loading dose of Ig of 400 mg/kg was administered daily for 5 days, with a maintenance dose of 400 mg/kg every week. But yet again the patient was admitted with acute respiratory failure after two weeks. His chief complaints included fever, dyspnoea, dry cough, wheezing and skin rash. Through evidence based medicine, we established that it was due to the use of rituximab (RTX). His condition was aggravated by RTX on the basis of the clinical examination and history. Immediately RTX was tapered off from the pharmacotherapy plan. The patient was then on prednisolone and azathioprine. That significantly improved the symptoms of the disease and quality of life of the patient.TheNIF increased to −70 cm H_2O while the vital capacity of the patient was significantly improved from 450 ml to 1.2 L. He was counseled for his underlying depression and anxiety due to MG along with respiratory trauma he suffered lately.

DISCUSSION

Clinical features of refractory MG includes generalized body fragility and fatigue and weakness. Ptosis and diplopia on the other hand are due to the anomaly of cranial muscles. Muscle attenuation escalates with incessant muscle usage and are weakened by sleep and rest. The diagnostic tests for MG are very necessary to clear the mist and dilemma of the disease. Whereas the refractory/relapse of MG make it even more difficult to diagnose. Different diagnostic tests that are available are: acetylcholine-receptor-antibody test, repetitive-nerve-stimulation test, anticholinesterase test. The therapies of MG includes: corticosteroids, thymectomy, azathioprine, mycophenolatemofetil, methotrexate, cyclo-phosphamide, intravenous immunoglobulin (IVIg) and rarely plasmapheresis is used. These drugs can carry high risk of potential side effects. On the other hand, rituximab (a chimeric IgG) demonstrates good response and substantial benefit for refractory/relapsing MG. It appears to be having effective and promising clinical response for the treatment of MG, with good tolerability[1,2,4].

However a recent review[1] indicated pulmonary toxicity to be caused by rituximab. By the laboratory, clinical, radiological, epidemiological and histo-pathological evaluation of RTX-associated interstitial-lung disease was done. In which out of 121 cases, 18 cases were fatal. Onset from last rituximab infusion until development of symptoms was 30 days. (0-158 days) and a median of 15 days. (IQR=7-31 days).Whereas few patients (n=9) showed hyper-acute onset within hours whereas some took weeks to months. Unusual radiological findings with diffuse bilateral lung infiltrates were seen in all the patients. All cases included hypoxemia and with obstructive ventilator pattern.

Theoveralltoxicityandtolerabilityprofileofrituximab doesn't appears to be fatal with relatively rare adverse events and estimated incidence of 0.01-0.03%[2]. Still practitioners are required to situate the patients under observation while prescribing rituximab. If the patientdevelopsradiological

changes or respiratory symptoms then rituximab should be stopped and CSs should be prescribed instead[1,3,5].

This case study demonstrates few important aspects of refractory MG and use of RTX as a drug of choice. It highlights comparably rare side effects of rituximabin unexplained respiratory failure among patients with MG relapse. The patients presented with respiratory failure misled the physicians with pulmonary disorders. Moreover, extensive clinical and neurological investigations as well as past medical history must be scrutinized imminently with patients of acute respiratory failure.

CONCLUSIONS

The patients with refractory MG can experience acute respiratory failure due to the use of rituximab. The diagnoses of asthmatic patients or COPD can be well-thought-out regarding unexplained respiratory-failure. If neuromuscular causes are not there, then other non-neurological causative agents should be considered before establishing any pharmacotherapy plan of patients with refractory MG.

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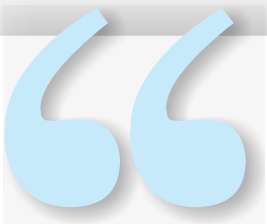

"Opportunities are like sunrises.
If you wait too long,
you miss them."

William Arthur Ward