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A case report of cholinergic crisis evolved from myasthenia gravis due to the tumor in trigone of bladder

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Abstract

Cholinergic crisis has rarely been reported as a complication of myasthenia gravis, wherein it mainly occurs as a result of the improper accumulation of anticholinesterase agents. In this report, we present one such case. The nature of the patient's clinical manifestations suggested that the main reason for the cholinergic crisis was the abnormal accumulation of pyridostigmine bromide due to renal failure, which was secondary to a tumor in trigeon of bladder. To the best of our knowledge, this is the first report of myasthenia gravis leading to cholinergic crisis caused by acute postrenal renal failure arising from the bladder neoplasm. From our experience in this case, we suggest that renal function and whether the urinary tract is unobstructed should be closely monitored in patients with myasthenia gravis presenting with an acute onset of the signs of cholinergic crisis. In our experience, such cases may be rapidly improved temporarily with continuous renal replacement therapy, but recanalization of the urinary tract and renal function recovery is a fundamental treatment.

CASE REPORT

INTRODUCTION

Myasthenia gravis is an autoimmune disorder characterized by fatigable weakness of the skeletal muscles (Vincent *et al.* 2001). Cholinergic crisis is an emergency situation that is mainly characterized by flaccid paralysis and respiratory failure. In patients with myasthenia gravis, the condition mainly occurs due to improper administration or intake of anticholinergic agents. Pyridostigmine bromide is one of the most commonly used anticholinesterase drugs, and it is largely excreted in an unchanged form by the kidney (Meriggioli & Sanders 2009). Improper excretion of this drug due to postrenal renal failure arising from the bladder neoplasm can cause its accumulation and thereby give rise to the symptoms of cholinergic crisis.

We encountered such a case of cholinergic crisis in a patient with myasthenia gravis and herein report our findings and the treatment outcome.

CASE REPORT

A 75-year-old man presented to the emergency department of our institution with dyspnea and hoarseness since 2 hours. The patient's son reported that the patient was under treatment for myasthenia gravis,which was subsequently

confirmed by the positive result of the neostigmine test. Computed tomography (CT) examination of the thymus performed at that time showed no evidence of thymoma or thymic hyperplasia. Therefore, the patient had been advised to take tablet pyridostigmine bromide 60 mg half an hour before meals thrice daily.

Two days prior to admission at our institution, the patient developed sweating, blurred vision, and limb weakness. Assuming that these symptoms were related to the worsening of myasthenia gravis, the patient increased the frequency of pyridostigmine bromide (60 mg) to four times a day without consulting a physician. However, his condition continued to worsen, eventually leading to the presenting symptoms of dyspnea and hoarseness of voice that started after intake of the medication.

On admission, the patient appeared to be anxious and his vital signs were as follows: blood pressure, 174/100 mmHg, heart rate, 62 beats/min; respiratory rate, 20 breath cycles/min; oxygen saturation, 75% on room air; and temperature, 37.2 °C (98.9 °F). The patient had generalized sweating, foaming at the mouth, bilateral drooping of eyelids, pupils responsive, and difficulty in opening the mouth. On examination, bilateral dry and moist rales were observed in the lungs; pupils were found to be responsive but with delay of light reflex and dilatation. Further, the patient showed fasciculation of limbs and muscular hypotonia, with muscle strength of the limbs being grade 2, with absence of pathological reflexes. In view of the muscarinic symptoms, the patient was administered an intravenous injection of atropine (1.0 mg). The findings of blood gas analysis were as follows: pH, 7.31; pO_2, 48 mmHg; pCO_2, 56 mmHg; and plasma lactate, 2.1 mmol/L. These findings indicated that the patient had type II respiratory failure, and endotracheal intubation and ventilator support were promptly established. The levels of the biochemical parameters were then found to have been restored to normalcy: blood urea nitrogen, 70.11 mmol/L; serum creatinine, 1162.07 μmol/L, serum potassium, 6.4 mmol/L, serum sodium, 152.29 mmol/L; serum chlorine, 111.57 mmol/L; serum calcium, 2.16 mmol/L;

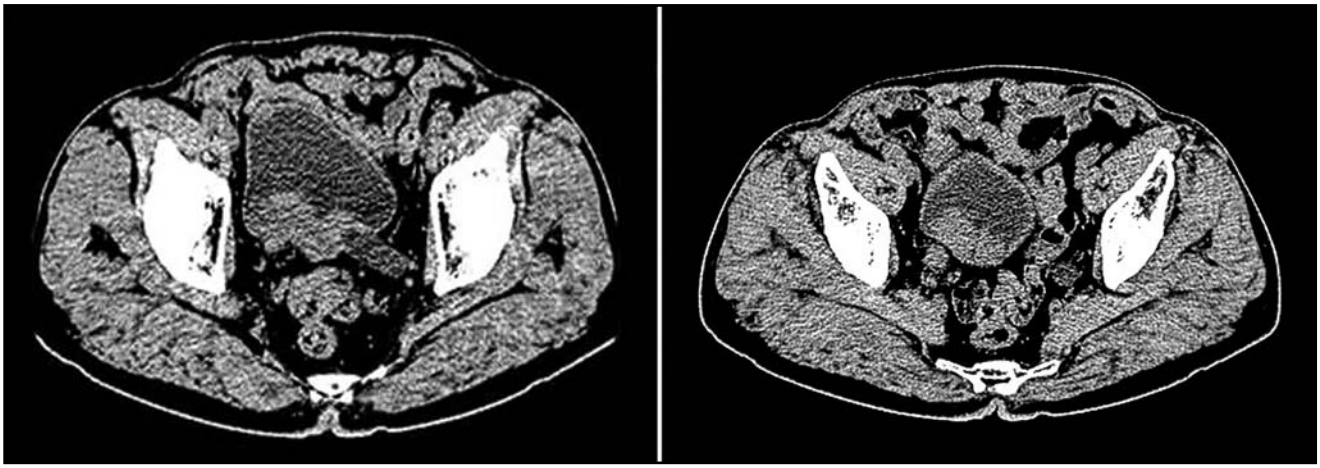

Fig. 1 Computed tomography images of the patient indicating urinary obstruction: Bladder neoplasm present in the trigone, with invasion of the lower segment of the ureter and obstruction of the left ureteral orifice.

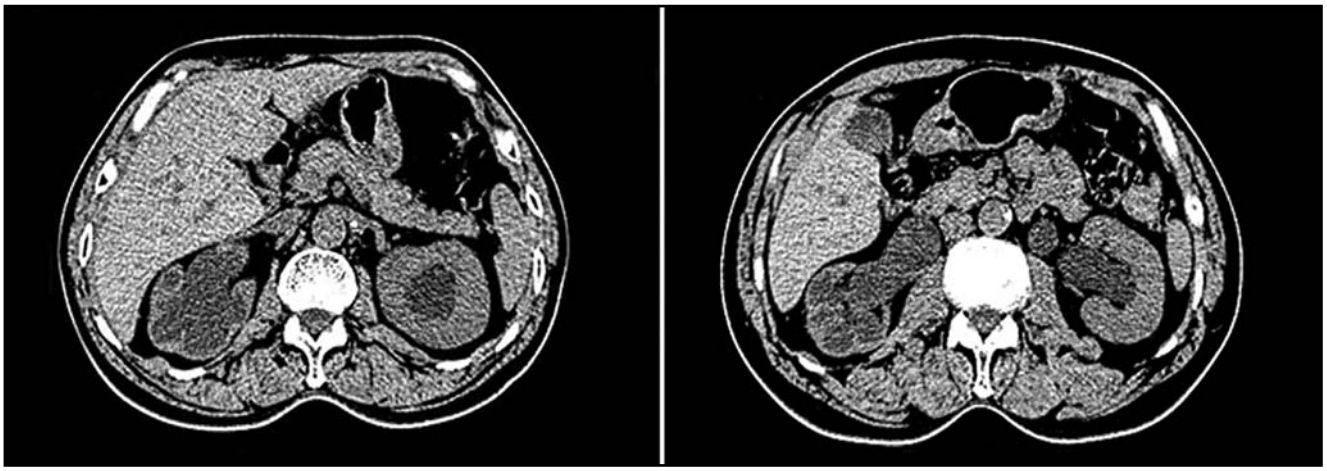

Fig. 2 Computed tomography images of the patient indicating acute postrenal renal failure: Bilateral hydronephrosis and hydroureter, with atrophy of the right renal cortex.

serum phosphorus, 1.25 mmol/L; carbon dioxide combining power, 15.19 mmol/L; and serum cholinesterase, 1358 U/L. On the basis of these findings, we arrived at a group provisional diagnosis of myasthenia gravis, cholinergic crisis, acute renal failure, electrolyte disturbance, and acid-base imbalance. Accordingly, the patient was treated with continuous venovenous hemofiltration (CVVH) as continuous renal replacement therapy (CRRT) after obtaining consent from the patient's family members. Additionally, we performed a bedside color Doppler sonography to identify the cause of renal failure. The findings of the scan revealed the presence of bilateral hydronephrosis, hydroureter, space-occupying lesions in the trigone region of the bladder, and bilateral involvement of the ureteral orifices. Therefore, we consulted a urologist who concurred with the treatment and recommended abdominal computed tomography (CT) examination once the patient's condition had stabilized. Twenty-two hours after initiating CRRT treatment and ventilator support, the patient was able to breathe spontaneously; the muscular strength and eyelid movement were restored to normalcy; and the muscarinic manifestations had subsided. One hour later, mechanical ventilation and CRRT treatment were discontinued; thereafter, the results of blood gas analysis and the levels of the blood biochemical parameters were nearly retrieved. Considering these findings, we believed that the cholinergic crisis and the acute renal failure were reversed. The patient now underwent plain abdominal CT examination, which revealed the presence of a neoplasm in the trigone region of the bladder, with invasion of the lower segment of the right ureter, obstruction of the left ureteral orifice (Figure 1),bilateral hydronephrosis and hydroureter, and atrophy of the right renal cortex (Figure 2). On consultation, the urologist deemed the patient too weak to undergo emergency operation and therefore performed percutaneous nephrostomy under guidance of color Doppler sonography. The urinary outflow collected via the inserted drainage tubes was 1500 mL. Ten days later , the patient underwent laparoscopic radical cystectomy and creation of ileal orthotopic neobladder. Pathology revealed trigone urothelial carcinoma. Two weeks after surgery, the patient was discharged at an improved health condition. The patient continues to be regularly followed up and has shown further improvement.

DISCUSSION

Cholinergic crisis is a complication of myasthenia gravis that involves acute respiratory failure, requiring hospitalization in an intensive care unit and, frequently, ventilator support (Grob *et al.* 2008). On the other hand, cholinergic crisis is caused by overdosing of a cholinesterase inhibitor and is characterized by a marked decrease in serum acetylcholinesterase (AChE) levels and parasympathetic symptoms such as sweating, salivation, miosis, bradycardia, diarrhea, and circulatory failure (Kariyone *et al.* 2010).

This patient had the mild generalized form (Osserman classification type IIA) of myasthenia gravis as well as the adverse effects of long-term oral anticholinesterase administration. Despite being under regular medication, the patient developed dyspnea and dysarthria, in addition to other muscarinic manifestations such as sweating and blurred vision. Blood examination revealed extremely low serum levels of cholinesterase. Put together, these findings were indicative of cholinergic crisis. In addition, blood and ultrasonography examinations revealed that the patient had acute renal insufficiency due to urinary tract obstruction. Since the patient was taking pyridostigmine bromide, which is known to be largely excreted unchanged by the kidney (Meriggioli & Sanders 2009), we speculated that the cholinergic crisis may have been caused by the abnormal accumulation of the drug secondary to the acute postrenal renal failure. Confirming our diagnosis, all the signs and symptoms of cholinergic crisis subsided once renal function was restored after hemofiltration.

Although numerous cases of cholinergic crisis have been reported thus far, we believe that ours is the first case of myasthenia gravis progressing to cholinergic crisis due to the accumulation of anticholinesterase agents after acute postrenal renal failure arising from a neoplasm in the trigone of the bladder. Our experience in this case indicates that it is necessary to closely monitor the renal function and check if the urinary tract is unobstructed in patients with myasthenia gravis receiving cholinesterase inhibitors who suddenly manifest symptoms of cholinergic crisis. In addition, in such cases, the patient's blood levels of anticholinesterase agents should also be determined, if possible. Continuous renal replacement therapy appears to yield satisfactory outcomes temporarily in this case, but recanalization of the urinary tract and renal function recovery is a fundamental treatment.

Conflicts of interest statement: *We declare that we have no conflict of interest.*

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