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Case Report

Noninvasive ventilator prevents intubation in thyrotoxic hypokalemic periodic paralysis-associated respiratory failure: A case report and literature review

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Abstract

Thyrotoxic periodic paralysis (TPP) is a rare complication of hyperthyroidism, often presents with limb muscle paralysis, hypokalemia with elevated-free T3, T4, and low thyroid-stimulating hormone (TSH). We herein reported an unusual presentation of TPP with acute hypercapnic respiratory failure. A 28-year-old female had complaints of nausea and vomiting. Laboratory investigations showed a serum potassium level of 1.2 mEq/L. Thyroid function test revealed the TSH level of 0.021 μlU/mL and free T4 at 2.01 ng/dL. She suddenly suffered from dyspnea and drowsiness. Acute hypercapnic respiratory failure with CO_2 retention was found. Noninvasive ventilation was used. Rapid correction of hypokalemia and administration of propylthiouracil, propranolol, and 5% Lugol's solution were performed. After the normalization of potassium levels, the patient's respiratory pattern stabilized and noninvasive ventilator (NIV) use was discontinued. Respiratory failure is an unusual but lethal complication of TPP. Rapid correction of hypokalemia and temporarily NIV can successfully avoid endotracheal intubation for respiratory failure.

Keywords: *Acute respiratory failure, Hypokalemia, Noninvasive ventilator, Thyrotoxicosis periodic paralysis*

Introduction

Thyrotoxic periodic paralysis (TPP) is a rare but serious complication of hyperthyroidism, characterized by the sudden onset of hypokalemia and muscle paralysis [1]. In Asia, the incidence of TPP is approximately 1.8%, whereas it is only 0.1% in Western countries [2]. Hyperthyroidism occurs more frequently in women, but TPP has a higher prevalence among men [1,2].

TPP usually occurs after the second decade of life [2]. Precipitating factors for TPP include infection, intense exercise, high-carbohydrate intake, alcohol consumption, and use of β2-adrenergic drugs [3]. These precipitating factors can be identified in about one-third of patients [3]. Prodromal symptoms include general weakness, stiffness, and cramps a few hours to days before paralysis [2]. The onset of weakness often occurs in the proximal muscles of the lower extremities and may progress to all the four limbs [2]. The severity of paralysis varies from mild weakness to complete paralysis [2]. Urinary, gastrointestinal, and respiratory systems usually remain unaffected [2]. Typical presentation through laboratory testing is characterized by extremely low-serum potassium levels (average 2.0 mEq/L), with the degree of muscle weakness often correlating with the level of serum potassium [2].

Although the typical TPP presentation involves muscle weakness of the limbs and respiratory tract is often sparing, we herein report an unusual case of TPP complicated with acute hypercapnic respiratory failure. Previously, there were few case reports about TPP with respiratory failure, but all these reported cases were treated by endotracheal intubation with an invasive mechanical ventilator [4-6]. The current case report is the first case report that described the successful management of noninvasive ventilator (NIV) to treat respiratory failure. Avoidance of endotracheal intubation can decrease the complications of intubation and invasive mechanical ventilator. We, therefore, suggest that such patients with respiratory failure should undergo a trial

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of NIV with the rapid correction of hypokalemia to avoid endotracheal intubation.

Case report

The patient described in this case report is a 28-year-old female who smoked and had a medical history of gastritis and gastroesophageal reflux disease. She also had hyperthyroidism but was not compliant to antithyroid drug treatment. Recently, she experienced immense work stress and also consumed considerable amounts of coffee. She then suffered from nausea, vomiting, epigastric burning sensation, and poor appetite for 2 weeks. Due to persistent nausea, vomiting, malaise, and shortness of breath, she visited our emergency department. Her initial respiratory rate was 29 breaths/min; pulse rate was 120 beats/min; and blood pressure was 123/71 mmHg. Her laboratory investigations showed serum potassium level of only 1.2 mEq/L and sodium 136 mEq/L. Other laboratory data and whole blood test results are shown in Table 1. For tachypnea, oxygen supply with O_2 nasal cannula at 3 L/min was administered, and arterial blood gas analysis showed a pH of 7.25, $PaCO_2$ 22 mmHg, PaO_2 116 mmHg, and HCO_3^- 9.6 mmol/L. Her chest X-ray [Figure 1] revealed infiltration in the right lower lung, consequently leading to the diagnosis of pneumonia. Her electrocardiogram [ECG, Figure 2a] showed sinus tachycardia with flattening and inversion of T-wave, ST depression, prominent U-waves, T and U fusion, and long QU. The patient had no history of diuretic abuse and no family history of hypokalemia. Thyroid function test was performed owing to her history of hyperthyroidism; test results revealed a thyroid-stimulating hormone (TSH) level of 0.021 μlU/mL (reference range: 0.35–5.5 μIU/mL) and free thyroxine (T4) level of 2.01 ng/dL (reference range: 0.89–1.76 ng/dL). The initial diagnosis was thyrotoxicosis with severe hypokalemia. She was immediately transferred to the intensive care unit (ICU) for the risk of arrhythmia due to severe hypokalemia.

Table 1: Laboratory data on arrival

	Measured data	Normal range
Potassium (mEq/L)	1.2	3.3-4.5
Sodium (mEq/L)	136	135-145
Chloride (mEq/L)	127	98-107
Creatinine (mg/dL)	0.8	0.5-0.9
Albumin (g/dL)	2.2	3.4-4.8
Magnesium (mg/dL)	2.2	1.6-2.3
Hemoglobin (g/dL)	11.5	12-16
Total leukocyte count (10^9/L)	7.7	3.5-11
Neutrophils (%)	66	40-75
Thyroid-stimulating hormone (μlU/mL)	0.021	0.35-5.5
Free thyroxine (ng/dL)	2.01	0.89-1.76
Antithyroid peroxidase antibody (U/mL)	2615.5	<60

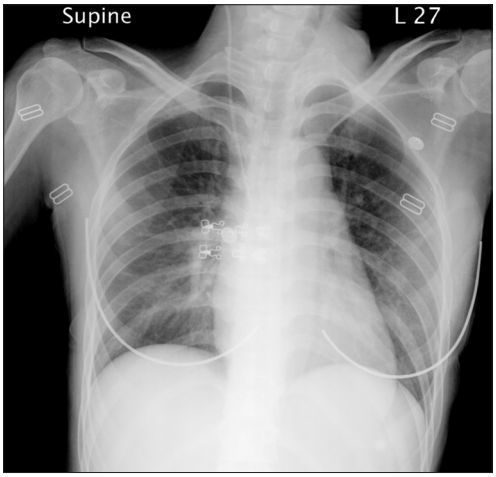

Figure 1: Chest X-ray revealed right lower lung pneumonia

Upon arrival in ICU, she experienced progressive dyspnea and sudden drowsiness. Her respiratory rate found to be 33 breaths/min, and respiratory muscle contractions were found. The arterial blood gas analysis revealed pH of 7.11, $PaCO_2$ 72 mmHg, PaO_2 206 mmHg, and HCO_3^- 22.9 mmol/L. The initial assessment conducted to determine the cause of hypercapnic respiratory failure was found to be TPP with severe hypokalemia and respiratory muscle weakness. Instead of immediate intubation with an invasive mechanical ventilator use, NIV was carried out to maintain adequate ventilation and rapidly correct hypokalemia. We consulted an endocrinologist and initiated the administration of propylthiouracil at 150 mg qid, propranolol 20 mg q6h, and Lugol's solution (5% iodine and 10% potassium iodide). We administered parenteral antibiotics (moxifloxacin 400 mg qd) for pneumonia treatment.

We aggressively corrected the patient's hypokalemia with intravenous and oral potassium chloride (KCl) administration under cautious monitoring of potassium level and arterial blood gas at 6-h intervals [Figure 3]. On the 1st day, we

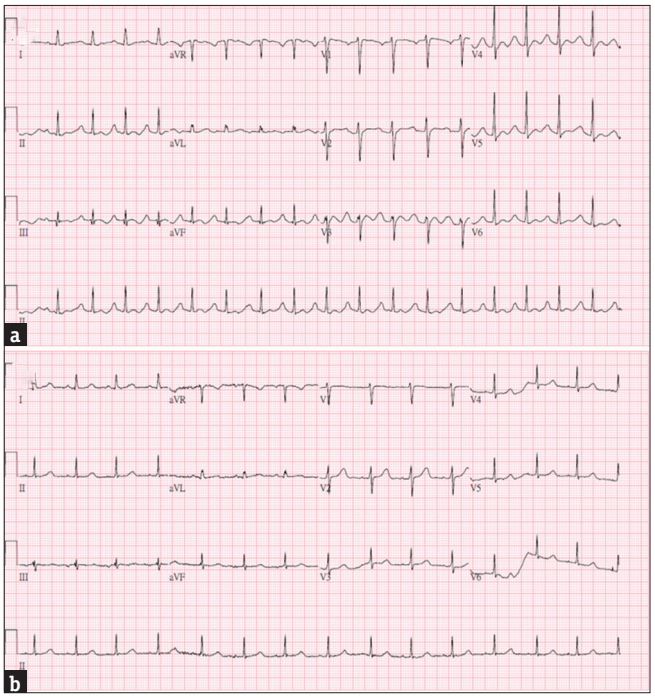

Figure 2: (a) An electrocardiogram showing sinus tachycardia with flattening and inversion of T-wave, ST depression, prominent U-waves, T and U fusion, and long QU associated with severe hypokalemia. (b) An electrocardiogram showing a normal sinus rhythm after the correction of hypokalemia

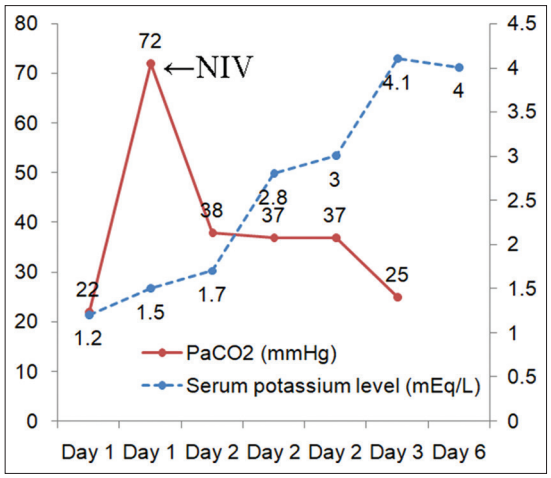

Figure 3: Serial changes in serum potassium level and arterial $PaCO_2$ level

prescribed 180 mEq/day of intravenous KCl and 8 mEq qid of oral KCl. Consequently, her potassium level increased from 1.2 to 1.7 mEq/L. On the 2nd day, we maintained the dose of oral KCl at 8 mEq qid but decreased intravenous KCl dosage to 120 mEq/day. Consequently, her potassium level increased from 1.7 to 3.0 mEq/L. Her $PaCO_2$ levels also decreased after NIV was performed. On the 3rd day, her potassium level was 4.1 mEq/L. We stopped oral or intravenous KCl supplementation and continued to monitor the patient's serum potassium level. Her respiratory pattern was found to be smooth and weakness in all her four limbs had considerably subsided. Her ECG revealed a normal sinus rhythm after the correction of hypokalemia [Figure 2b]. NIV was subsequently stopped, and the patient showed a stable respiratory pattern and oxygen hemoglobin saturation. Further monitoring of serum potassium levels showed no rebounding hyperkalemia. Further laboratory workup revealed the antithyroid peroxidase antibody level of 2615.5 U/mL (reference range: <60 U/mL) and confirmed the diagnosis of TPP caused by Grave's disease.

Discussion

This patient had an unusual presentation of TPP complicated with respiratory muscle weakness and acute hypercapnic respiratory failure. For the rapid correction of hypokalemia to resolve muscle weakness, immediate endotracheal tube intubation was not performed. Instead of endotracheal intubation, NIV and rapid correction of hypokalemia were performed. Her respiratory pattern improved after the correction of hypokalemia. For patients with TPP, hypokalemia-related life-threatening arrhythmia is typically considered to be a potential complication by physicians [7]. However, herein, we report another potentially fatal complication of TPP, acute hypercapnic respiratory failure. Consistent with the findings in the present case, we suggest that a combination of NIV and rapid correction of hypokalemia is a strategy to prevent endotracheal intubation.

TPP is often missed or delayed in the diagnosis [8]. The typical presentation of TPP is limb muscle weakness [2]. The differential diagnoses of muscle weakness and respiratory failure include familial periodic paralysis, spontaneous periodic paralysis, Guillain–Barre syndrome, transverse myelitis, myasthenia gravis, and botulism [1]. As TPP often causes serious complications, early recognition and treatment are of great importance. However, family history is not related to TPP. Severe hypokalemia with elevated free levels of T3 and T4 and very low values of TSH is the main feature of this condition. A history of hyperthyroidism is an important clue for TPP diagnosis. For patients without a history of hyperthyroidism, the measurement of thyroid functions should also be considered. Some patients report with TPP as an initial presentation of hyperthyroidism [9].

Hyperthyroidism occurs more frequently in women (female-to-male ratio of 9:1), but TPP has a higher prevalence among men (male-to-female ratio of 26:1) [1,2]. Higher muscle mass, serum androgen, and catecholamine levels in response to stress may explain male predominant of TPP [3]. Androgens lead to higher muscle mass and Na^+/K^+-ATPase abundance in males [3]. Catecholamines are the strong activators of Na^+/K^+-ATPase and have been found to be released more in response to stress in males [3].

It is important to identify the trigger factors in these patients. Medications or foods-containing thyroxine, caffeine, steroid, and β2-adrenergics are known to induce TPP-related hypokalemia [10,11]. High-carbohydrate intake can induce an intracellular shift of potassium and decrease serum potassium levels [10,11]. Vigorous exercise and physical or emotional stress are also known to trigger TPP-related hypokalemia [10,11]. For this reported case, she had emotional stress (work stress), physical stress (pneumonia), consumed high amounts of coffee, and poor intake, which triggered the occurrence of TPP-related hypokalemia. This condition finally progressed to respiratory muscle weakness and hypercapnic respiratory failure.

Understanding the mechanisms of TPP can help physicians in the diagnosis and treatment. The potential mechanism involves the increased activity of the Na^+/K^+-ATP pump in the skeletal muscle [11]. In TPP, hypokalemia is caused by a massive shift in potassium levels from serum into the intracellular fluid as a result of the activation of Na^+/K^+-ATP pump [11]. Thyrotoxic patients with periodic paralysis have been found to have higher Na^+/K^+-ATP pump activity than those without paralytic episodes. Active thyroid hormone freely enters into the mitochondria, which consequently activates the Na^+/K^+-ATP pump located in the cell membrane and causes the shift in potassium levels from serum into the intracellular fluid [11]. Therefore, high serum T4 and T3 and suppressed TSH levels are pathognomonic for TPP [2]. Grave's disease is the main cause of hyperthyroidism and also presents in the majority of TPP patients [2]. Normalization of potassium levels and treatment of hyperthyroidism can resolve the paralytic event. Besides of thyroid hormone, catecholamine can also increase Na^+/K^+-ATP pump activity in the skeletal muscle [11]. The enhanced beta-adrenergic response in thyrotoxicosis further increases Na^+/K^+-ATPase activity [11].

For patients with acute respiratory failure, endotracheal intubation combined with invasive mechanical ventilation is often performed immediately to maintain adequate oxygenation

and ventilation [12]. However, there are many complications associated with endotracheal intubation such as laryngeal injury, mucosal ulceration, sinusitis, vocal cord injury, ventilator-associated pneumonia, and tracheobronchitis [12]. A few case reports on TPP complicated with acute respiratory failure have been previously published [4-6]. However, all those patients having the above-mentioned conditions were treated by performing endotracheal intubation. We herein reported the first case report about the successful use of NIV in TPP-associated respiratory failure.

It is sometimes difficult to make the decision of endotracheal intubation in patients with acute respiratory failure. The indication of intubation is ventilation failure ($PaCO_2$ >55 mmHg with noncompensated acidosis, pH <7.25), insufficiency in oxygenation (PaO_2 <55 mmHg), respiratory failure with hemodynamically unstable, cardiac arrest, and apnea [13]. It is required to identify the causes of respiratory failure and determine whether the causes will be reversible in short-term care [13]. Before the decision of intubation is made, NIV should be considered. NIV assists ventilation by delivering positive pressure without the use of an endotracheal tube. NIV can improve gas exchanges, facilitate respiratory muscle rest, and decrease the work of breathing [14]. In general, good candidates for NIV are patients with respiratory failure but are hemodynamically stable. Appropriately chosen candidates with NIV can prevent endotracheal intubation.

Upon arrival in the ICU, this patient experienced progressive dyspnea, sudden drowsiness, and arterial blood gas analysis revealed pH of 7.11 and $PaCO_2$ 72 mmHg. Endotracheal intubation seemed to be an indication for her. However, for her stable hemodynamic status and rapidly correctable cause of respiratory failure, we performed NIV management for her. After rapidly correcting hypokalemia and using NIV, $PaCO_2$ dropped to 38 mmHg on the next day, and consciousness was restored. We, therefore, suggest that TPP patients with respiratory failure should undergo a trial of NIV with rapid correction of hypokalemia to avoid endotracheal intubation.

Rhabdomyolysis is another complication of TPP-related hypokalemia [15]. The mechanism of hypokalemia-related rhabdomyolysis is not fully understood [15]. Severe hypokalemia may contract muscle capillaries, reduce muscle perfusion, and lead to muscle cell necrosis [15]. Rhabdomyolysis is an extremely rare presentation in TPP-related hypokalemia. However, rapid diagnosis and appropriate treatment of rhabdomyolysis are important.

Comprehensive treatment of TPP includes the supplementation of potassium, treatment of the underlying hyperthyroidism, and administration of a nonselective beta-blocker. These treatments often result in complete resolution of the paralytic event [16]. The degree of hypokalemia is often proportional to the severity of paralysis [2]. To prevent serious complications, the initial therapy should be focused on aggressive potassium supplementation. However, as the mechanism of hypokalemia involves an intracellular shift, the total body potassium level is normal; hence, aggressive treatment may result in rebound hyperkalemia [1]. Intensive monitoring of serum potassium level is, therefore, recommended [16]. A high dose of propranolol (3 mg/kg) reportedly facilitates the normalization of serum potassium levels without the risk of rebound hyperkalemia [17] through decreased conversion of T4 to T3 and reversal of the adrenergic stimulation of the Na^+/K^+-ATP pump [17]. Thyrotoxicosis should also be treated to prevent the relapse of paralytic attacks [16]. Therefore, antithyroid drugs should be prescribed in a timely manner.

Conclusion

TPP is a rare but serious complication of hyperthyroidism, characterized by the sudden onset of hypokalemia and muscle paralysis. Acute respiratory failure is an unusual but lethal complication of TPP. Initial intervention with NIV and rapid correction of hypokalemia is one successful management strategy for TPP-related acute respiratory failure.

Declaration of patient consent

The authors certify that the patient has obtained appropriate patient consent form. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initial will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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