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Successful Combination of Fresh Frozen Plasma and Albumin 5% in Plasma Exchange for a Patient with Concurrent Thyroid Storm and Guillain-Barré Syndrome: A Rare Case Report

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Thyroid storm is an endocrine emergency, and treatment must ensure primary goals, including reducing the production and release of thyroid hormones, mitigating the effects of thyroid hormones, increasing the elimination of thyroid hormones, treating systemic disturbances, and managing triggering factors. However, in a few cases where thyroid storm does not respond to initial treatment, therapeutic plasma exchange (TPE) should be considered. A 50-year-old male patient was admitted to the University Medical Center Ho Chi Minh City due to hypotonia and sensory disturbances gradually spreading from the lower extremities to the entire body. The patient was diagnosed with Guillain-Barré syndrome (GBS) and newly discovered hyperthyroidism. During the treatment course, the patient developed hospital-acquired pneumonia, acting as a trigger factor for a thyroid storm. Despite aggressive treatment for thyroid storm, the patient's condition worsened, leading to the decision to perform TPE. The replacement fluid was a combination of fresh frozen plasma (FFP) and albumin 5%. Subsequently, the patient returned to a euthyroid state and was discharged. Combining FFP and albumin 5% in TPE advantages FFP's high thyroid hormones-binding capacity and albumin's cost-effectiveness, safety, and efficiency. This reduces the drawbacks associated with high volumes of FFP and offers a balanced and effective approach to managing thyroid storms. Moreover, the concurrent presence of GBS and thyroid storm is extremely rare. Through this case, we aim to discuss the role of TPE in the treatment of thyroid storms and the effectiveness of the combination of FFP and albumin 5% as the replacement fluid.

Keywords: albumin 5%; fresh frozen plasma; Guillain-Barré syndrome; plasma exchange; thyroid storm
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Introduction

A thyroid storm is a disorder related to poorly controlled hyperthyroidism, a rare but potentially life-threatening condition with a mortality rate ranging from 10% to 30% (Satoh et al. 2016). The mortality rate for intensive care unit (ICU)-admitted patients with thyroid storm in France was 17% (Bourcier et al. 2020). Timely diagnosis and treatment play a crucial role in reducing the mortality rates associated with thyroid storms. Thyroid storm is an endocrine emergency, and treatment must ensure primary goals, including reducing the production and release of thyroid hormones, mitigating the effects of thyroid hormones on organs, increasing the elimination of thyroid hormones, treating systemic disturbances such as fever and hypovolemia, and managing triggering factors such as infections (Satoh et al. 2016). Typically, with initial treatments involving synthetic antithyroid drugs, iodine, corticoste-

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roids, beta-blockers, and removal of precipitating factors, clinical symptoms tend to improve within 12-24 hours (Satoh et al. 2016). However, in a few cases where thyroid storm does not respond to initial treatment, therapeutic plasma exchange (TPE) should be considered. Although there are no prospective or randomized studies evaluating the effectiveness of TPE in treating thyroid storms, case reports and retrospective studies (Akamizu et al. 2012; Bourcier et al. 2020) have demonstrated its efficacy in patients with this condition. Therefore, the Japan Thyroid Association (JTA) recommends considering TPE in patients with thyroid storms if symptoms related to the storm, such as high fever, tachycardia, and a reduction in consciousness, do not improve within 24-48 hours despite initial treatments (Satoh et al. 2016). Here, we report the successful management of thyroid storm in a patient with septic shock and Guillain-Barré syndrome (GBS) using TPE, which had failed with initial treatment, thereby discussing the role of TPE in thyroid storm treatment.

Case Presentation

A 50-year-old male patient was admitted to University Medical Center Ho Chi Minh City due to hypotonia and sensory disturbances gradually spreading from the lower extremities to the entire body. These symptoms began nine days before admission, initially presenting as weakness, numbness, and reduced sensation in lower limbs. At the time of admission, the patient exhibited dysarthria, severe generalized sensory disturbances, and urinary hesitancy. Physical examination revealed a regular pulse with a frequency of 113 beats per minute, blood pressure of 150/80 mmHg, respiratory rate of 18 breaths per minute, temperature of 37°C, and an oxygen saturation of 96% on room air. The neurological examination noted right-sided abducens nerve palsy, asymmetric peripheral facial nerve paralysis (more pronounced on the right), and limb muscle strength at the 2/5 level. No diarrhea or tremors were noted. Other organ examinations did not show any abnormalities.

Laboratory test results at the time of admission showed a white blood cell (WBC) count of 8,000 cells/mm^3, ALT 84 IU/L, AST 42 IU/L, TSH < 0.005 mIU/L (0.27-4.2), and fT4 68.39 pmol/L (9.0-19.0). The cerebrospinal fluid analysis revealed total bilirubin of 0.6 mg/dL, glucose of 3.2 mmol/L (simultaneous blood glucose of 6 mmol/L), protein of 172.6 mg/dL, lactate of 2.5 mmol/L, and 9 WBC/mm^3 with a 100% lymphocytic predominance. Chest X-ray did not show any abnormalities. An electrocardiogram (ECG) showed a sinus rhythm with a frequency of 113 beats per minute. Ultrasound revealed a goiter with heterogeneous echogenicity and mild increased vascularity, and the thyroid isthmus was thickened at 9 millimeters. The electromyography (EMG) results indicated a sensory and motor axonal polyneuropathy, characterized by acute inflammatory demyelinating polyradiculoneuropathy (AIDP), which is consistent with the acute phase of GBS. The patient was diagnosed with the AIDP subtype of GBS, hyperthyroidism, and hypertension. Subsequently, intravenous immune globulin (IVIG) at a dose of 0.4 mg/kg/day for 5 days, thiamazole 20 mg/day, and antihypertensive drugs were administered.

From the 3rd to the 6th day post-hospitalization, the patient developed fever and progressive respiratory failure required endotracheal intubation, and was transferred to the ICU. The patient was conscious, anxious, and agitated in the ICU, with a pulse rate of 155 beats per minute and blood pressure of 180/95 mmHg. Laboratory tests revealed a WBC of 16,200/mm^3, procalcitonin level of 0.44 μg/L, ALT 101 UI/L, and AST 49 UI/L. Computed tomography pulmonary angiography did not reveal pulmonary embolism but noted mucus plugs completely obstructing the lower left bronchus and partially obstructing the upper left and lower right bronchus. Based on these findings, the patient was diagnosed with hospital-acquired pneumonia, atelectasis due to mucus plugging caused by muscle weakness due to GBS with the AIDP subtype. The ECG showed rapid atrial fibrillation with a frequency of 155 beats per minute. The patient was mechanically ventilated and given intravenous antibiotics, antipyretics, and thiamazole 20 mg/day.

However, from the 6th to the 10th day after hospitalization, the patient's condition deteriorated with a persistent high fever of 40-41°C, atrial fibrillation with a frequency of 180 to 200 beats per minute, and blood pressure of 71/40 mmHg which required the use of vasopressors, fluid resuscitation, intravenous antibiotics, increased dose of thiamazole to 60 mg/day, hydrocortisone 100 mg × 4 times/day, and lugol's solution 1% 20 drops orally every 8 hours. Laboratory tests showed TSH 0 mIU/L, FT4 48.7 pmol/L, ALT 66 UI/L, AST 219 UI/L, procalcitonin level of 49.7 μg/L, and creatinine level of 1.9 mg/dL. The patient was diagnosed with thyroid storm, septic shock, hospital-acquired pneumonia, acute kidney injury, atrial fibrillation, acute liver injury, and GBS AIDP subtype. The patient received additional intravenous digoxin, vitamin B1, continuous renal replacement therapy (CRRT) with Oxiris filter, and TPE. TPE was indicated due to the thyroid storm's poor response to initial treatment. The TPE volume was set at 1.0 times the patient's plasma volume, with a replacement fluid consisting of 75-85% albumin 5% (at the beginning of the session), and 15-25% of fresh frozen plasma (FFP) (at the end of the session). We performed TPE once daily for three consecutive days. The changes in TSH and thyroid hormones after each session are shown in Fig. 1, with FT4 decreasing approximately 30% after each session. Following three TPE sessions, the patient became afebrile, with a heart rate of 70-90 beats per minute, and vasopressors were discontinued.

The patient underwent a tracheostomy on the 20th day after admission due to respiratory muscle weakness and was discharged after 47 days of hospitalization. Three years post-discharge, the patient has fully recovered muscle function and currently maintains euthyroidism with a thiamazole dose of 2.5 mg/day.

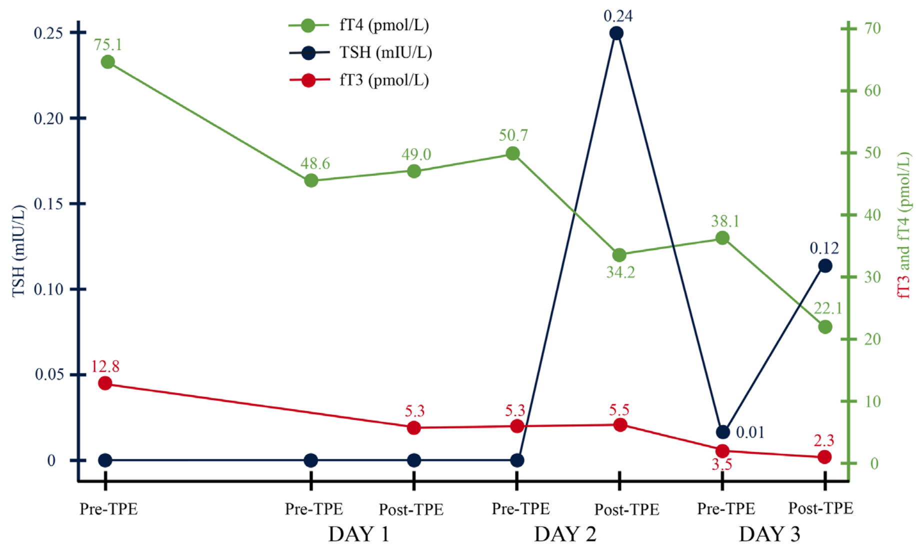

Fig. 1. Changes in thyroid hormone levels after each therapeutic plasma exchange session.
TPE, therapeutic plasma exchange; TSH, thyroid-stimulating hormone.

Discussion

We report a case of a patient initially admitted for GBS with newly discovered hyperthyroidism. Although the patient received prompt treatment upon admission, the hyperthyroidism progressed to a thyroid storm in the setting of septic shock, respiratory failure, and mechanical ventilation.

GBS is an acute, inflammatory demyelinating polyneuropathy that disrupts the peripheral nervous system (Rodriguez et al. 2018). The pathophysiological mechanism of GBS involves an autoimmune response targeting neurospecific molecules. Viral and bacterial infections are potential autoimmune triggers implicated in the onset of GBS (Rodriguez et al. 2018). However, our patient exhibited no symptoms or signs of viral or bacterial infection before hospitalization. While both Graves' disease (GD) and GBS are autoimmune disorders, their concurrent occurrence is rare. The mechanism underlying this association remains unclear, though autoimmunity may be the primary etiological factor for both conditions. Majumder proposed three pathophysiological mechanisms for the simultaneous presentation of GD and GBS (Majumder and Basu 2019). Firstly, gangliosides, which can produce autoantibodies leading to GBS, are abundant in the plasma membranes of both thyrocytes and neuronal cells. Secondly, elevated serum intercellular adhesion molecule (ICAM) levels have been observed in autoimmune conditions such as autoimmune thyroid disease and GBS. Lastly, viruses and bacterial infections are often partially responsible for the development of autoimmune diseases. Despite the differing infectious agents involved in the pathogenesis of GD and GBS, a common infectious etiology might explain their concurrence. These proposed mechanisms highlight the complex interplay between immune responses and the potential shared pathways in the development of these autoimmune conditions (Majumder and Basu 2019).

Thyroid storm is a rare condition. According to a national survey in Japan, the annual incidence of thyroid storms is 0.2 per 100,000 population, accounting for 0.22% of all cases of thyrotoxicosis and 5.4% of hospitalized thyrotoxicosis patients (Akamizu et al. 2012). The diagnosis of thyroid storm is primarily based on clinical features, as there are no specific symptoms or tests that can be the "gold standard" in diagnosis. There are two scoring methods available for diagnosing thyroid storm: the Burch-Wartofsky scoring system, which was released in 1993 (Burch and Wartofsky 1993; Wartofsky and Klubo-Gwiezdzinska 2019), and the JTA scoring system, which was established in 2016 (Satoh et al. 2016).

In our case, when assessing the diagnostic criteria for thyroid storm according to the Burch-Wartofsky scoring system, the patient exhibited the following: (1) temperature ≥ 40°C: 30 points (although it is challenging to differentiate fever due to septic shock, the scoring system favors giving the highest score for thyroid storm); (2) neurological involvement: the patient was on mechanical ventilation and received sedation, making examination difficult; (3) gastrointestinal-hepatic dysfunction: challenging to evaluate; (4) heart rate 180 beats/min (≥ 140 beats/min): 25 points; (5) congestive heart failure: absent; (6) atrial fibrillation: 10 points; (7) precipitating event: 10 points. Thus, this case scored a total of 75 points according to the Burch-Wartofsky scoring system, indicating a high likelihood of a thyroid storm. The patient exhibited thyrotoxicosis (elevated FT4 and FT3), high fever, and tachycardia when assessing the diagnostic criteria for thyroid storm, according to the JTA's criteria. Therefore, the patient is classified as having a definite thyroid storm, with the precipitating factor being a septic shock.

The treatment of thyroid storm involves multidisciplinarity due to its impact on various organs, particularly the cardiovascular system. Therefore, managing thyroid storm requires cautious and close monitoring. Thyroid storm is an endocrine emergency, and treatment must ensure primary goals, including reducing the production and release of thyroid hormones, mitigating the effects of thyroid hormones on organs, increasing the elimination of thyroid hormones, treating systemic disturbances such as fever and hypovolemia, and managing triggering factors such as infections. In our case, the patient has been experiencing standard thyroid storm treatment with thiamazole at a dose of 60 mg/day, lugol's solution 1% at 60 drops/day, and hydrocortisone at 400 mg/day. Other treatments include antibiotics, antipyretics, and fluid resuscitation. Beta-blockers are contraindicated due to hypotension. However, after 48 hours of treatment, the patient's condition did not improve, prompting the initiation of TPE. In a study involving 126 patients with thyroid storm treated with TPE, the indications included: (1) severe symptoms (cardiac, neurological, altered level of consciousness, severe muscle weakness); (2) rapid deterioration; (3) contraindications to other treatments (including neutropenia, heart failure, kidney failure, and asthma); and (4) failure with standard treatments (Muller et al. 2011; Satoh et al. 2016). The timing for initiating TPE has yet to be uniformly approved. However, symptoms of a thyroid storm are expected to improve within 12-24 hours with treatment according to recommended protocols. Therefore, TPE should be considered if symptoms of a thyroid storm, such as high fever, tachycardia, and level of consciousness, do not improve within 24-48 hours after treatment following JTA's guidelines (Satoh et al. 2016).

TPE is a therapeutic procedure using a specialized filter to remove plasma components containing disease-causing elements such as antibodies and toxins. The removed plasma is replaced with FFP, albumin, or other fluids (Muller et al. 2011). TPE is typically considered when there is a need to eliminate harmful substances that other methods cannot effectively manage. These substances circulate in the vascular system, have a molecular weight greater than 30,000 Dalton, possess a prolonged half-life, or are bound to proteins and cannot be effectively eliminated by other approaches (Kiss et al. 2016). Therefore, TPE is highly effective in treating thyroid storms as most thyroid hormones are bound to proteins (99.97% for T4 and 99.7% for T3). The protein-bound hormones (comprising 99% of thyroid hormones in the body) are removed along with the patient's plasma and replaced with FFP or albumin 5% (Miller and Silver 2019). TPE can also eliminate substances that exacerbate thyroid disorders, such as autoantibodies in Graves' disease, catecholamines, and cytokines. TPE is sometimes used to achieve a euthyroid state before thyroid surgery (Tizianel et al. 2023). However, it's crucial to recognize that TPE is a temporary treatment, and thyroid hormone levels may increase after discontinuing TPE if no further treatments are applied to reduce thyroid hormone levels. The American Society for Apheresis (ASFA) recommends TPE for thyroid storm at a level II recommendation (Connelly-Smith et al. 2023). Thyroid storm is a rare condition, making it challenging to perform controlled studies to evaluate the role of TPE. The current evidence is mainly derived from case reports or case series; hence, the level of evidence for TPE is weak (evidence grade 2C) (Connelly-Smith et al. 2023).

FFP contains thyroxine-binding globulin (TBG), and free thyroid hormone in the blood will bind to TBG (when using FFP as replacement fluids), and this complex will be rapidly removed through TPE (Connelly-Smith et al. 2023). However, FFP has disadvantages such as high cost, the risk of transfusion reactions, transfusion-related lung injury, infections, and the presence of a certain amount of thyroid hormone. The use of albumin as replacement fluids is cheaper than FFP, has fewer side effects, a lower risk of infection, a lower concentration of thyroid hormones, and requires less workforce (such as no need for thawing FFP or cross-matching blood). However, albumin contains fewer TBG, resulting in a less effective reduction of thyroid hormone than FFP. However, albumin exhibits a weak affinity for free thyroid hormones, thereby retaining the potential to decrease thyroxin levels (Connelly-Smith et al. 2023). Although no randomized study has assessed the effectiveness of these two replacement fluids, numerous reports have favored the use of FFP. The JTA recommends FFP over albumin, assuming that the effectiveness of thyroid hormone reduction is higher with FFP (Satoh et al. 2016). However, ASFA recommends that both FFP and albumin can be used as replacement fluids (Connelly-Smith et al. 2023).

Using a combination of 5% albumin and FFP as replacement fluids has also been reported to have successful outcomes (Tizianel et al. 2023). This combination leverages the advantages and mitigates the disadvantages of each replacement fluid. Repeated use of albumin can lead to coagulation disorders due to the loss of coagulation factors through TPE, especially in patients with impaired liver function. FFP contains coagulation factors that reduce the risk of coagulation disorders caused by albumin replacement fluid. Additionally, FFP will supplement TBG compared to using albumin alone. Furthermore, reducing the volume of FFP also decreases the risk of transfusion reactions and anaphylactic shock. Depending on the treatment goals and the patient's condition, FFP, or albumin, can be used in the first half or the second half of the TPE session. For instance, if the aim is to prevent coagulation disorders, FFP can be used in the second half of the session. However, if the patient is experiencing severe coagulation disorders, FFP should be used in the first half of the session. In a report, two cases of thyroid storm were treated with TPE utilizing albumin 5% as a sole replacement fluid in the first two sessions and a combination of albumin 5% (70%) and FFP (30%) in the third session to prevent coagulation disorders. Subsequently, both cases achieved euthyroidism and underwent a successful thyroidectomy without experiencing coagulation disorders (Tizianel et al. 2023). Currently, there are no guidelines regarding the optimal ratio of albumin 5% to FFP or the preferred timing for using albumin 5% vs. FFP.

TPE, utilizing an exchange volume of 1.0-1.5 times the patient's plasma volume, can be performed daily or every 2-3 days until clinical improvement is observed (Burch and Wartofsky 1993; Kiss 2016). Monitoring both thyroid hormone levels and thyroid storm symptoms guides the TPE frequency. Typically, TPE is administered in 3-6 sessions, with a few cases requiring up to 10 sessions (Connelly-Smith et al. 2023). In our case, after three sessions of TPE, a significant improvement in symptoms was observed, and thyroid hormone levels returned to normal. This highlights the effectiveness of a combination replacement fluid of albumin 5% and FFP in managing thyroid storms.

Conclusion

Thyroid storm is a rare but potentially life-threatening disorder associated with a high mortality rate. Two scoring methods are available for diagnosing thyroid storm: the Burch-Wartofsky criteria and the Japan Thyroid Association criteria. Therapeutic plasma exchange is warranted if clinical conditions do not improve within 24-48 hours of optimal medical management. The use of replacement fluids, particularly a combination of fresh frozen plasma and albumin 5%, has shown effectiveness in managing thyroid storms.

Conflict of Interest

The authors declare no conflict of interest

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