中文題目：血漿置換術作為甲狀腺風暴併發多重器官衰竭之有效治療手段-案例報告

英文題目：Therapeutic Plasma Exchange as an Effective Therapeutic Modality for Thyroid Storm Complicated by Multi-organ Failure: A Case Report

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## Introduction

Thyroid storm (TS) is a life-threatening endocrinology emergency with significant mortality ranging from 20-30%, characterized by multi-organ dysfunction of the cardiovascular, thermoregulatory, gastrointestinal-hepatic, and central nervous system. Several precipitating factors have been well recognized, including, but not limited to surgery, trauma, infection, iodine load, parturition, or poor anti-thyroid drugs (ATDs) adherence in patients with hyperthyroidism. Although ATDs are first line treatment, some clinical condition and adverse effects lead them to contraindicated, i.e. agranulocytosis, severe hepatitis, and vasculitis. We report a case of TS-induced multi-organ failure, caused by undiagnosed Grave's disease. Because of transaminitis, traditional pharmacotherapy was contraindicated, and patient was treated with therapeutic plasma exchange (TPE), combined with adjunct beta-adrenergic receptor (β-AR) antagonists and systemic steroids, resulting in improvement of thyroid function and symptoms.

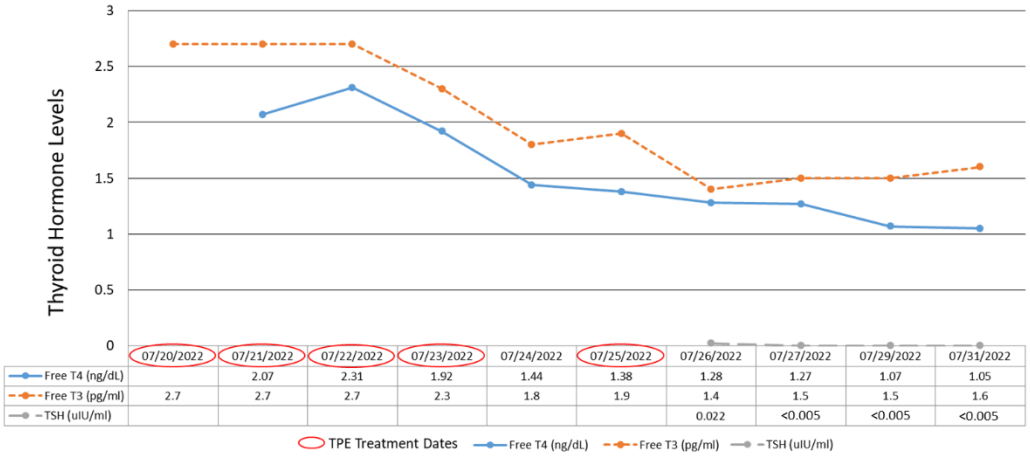
## Case presentation

We describe a 50-year-old woman, without known past history, developed chest tightness as well as tachycardia for 3 weeks, and unintentional weight loss 10Kg in a year, which led to her presence at secondary hospital emergency department. On presentation, she was unfebrile, tachycardic to 165 bpm, and agitated with dyspnea. On physical examination, irregular heart beats, bilateral crackles, internal jugular vein engorgement, and pitting edema were noted. Initial laboratory tests showed elevated inflammatory markers, metabolic acidosis, decreased partial pressure of oxygen, raised troponin I, but with normal electrolyte levels and hepatic enzymes. Electrocardiogram confirmed atrial fibrillation (Afib) with rapid ventricular response, with prominent pulmonary vasculature on chest radiograph. Point-of-care echocardiogram disclosed impaired left ventricular ejection fraction, 20-30%. Thyroid function tests, sent as part of investigation for Afib, revealed thyrotoxicosis with an elevated serum free T4 level of 3.03 ng/dL (normal 0.93-1.70) and a suppressed thyroid stimulating hormone (TSH) <0.005 uIU/ml (normal 0.270-4.200). Owing to respiratory distress, endotracheal intubation was performed, and patient was transferred to ICU for critical care.

On Burch-Wartofsky Point Scale (BWPS), our patient scored 50, highly suggestive of

TS. Endocrinologist suggested initiating treatment with methimazole, corticosteroids, β-AR antagonists, and inorganic iodide, whereas, severe transaminitis, coagulopathy, and hyperbilirubinemia were noted on Admission Day 5. Patient's BWPS was recalculated as 70, and was further referred to our hospital.

To investigate etiology of patient's hyperthyroidism, TSI, aTPO, and aTG test were arranged, with TSI 2.39 IU/L (normal <0.55) and aTG 204 IU/ml (normal <115), leading to the diagnosis of Grave's disease. Owing to severe transaminitis, thioamide was contraindicated. Five sessions of TPE were initiated daily from Admission Day 1, with adjunctive corticosteroids as well as β-AR antagonists, resulting in gradually improving levels of thyroid hormones (Figure 1) and biochemical data (Figure 2), as well as in weaning success of endotracheal intubation. Propylthiouracil (PTU) was administered after liver failure alleviated, in combination with angiotensin receptor blocker, mineralocorticoid receptor blocker, and direct oral anticoagulant for Afib and heart failure with reduced ejection fraction (HFrEF). Patient was discharged with PTU therapy on Admission Day 13.

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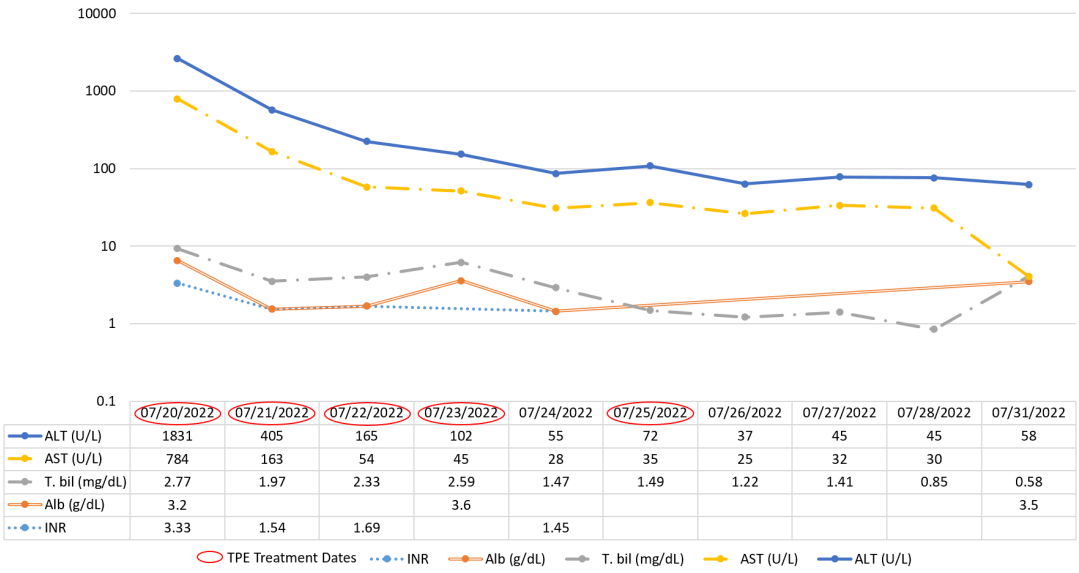
|---|---|---|---|---|---|---|---|---|---|---|
| Free T4 (ng/dL) | | 2.07 | 2.31 | 1.92 | 1.44 | 1.38 | 1.28 | 1.27 | 1.07 | 1.05 |
| Free T3 (pg/ml) | 2.7 | 2.7 | 2.7 | 2.3 | 1.8 | 1.9 | 1.4 | 1.5 | 1.5 | 1.6 |
| TSH (uIU/ml) | | | | | | | 0.022 | <0.005 | <0.005 | <0.005 |

**FIGURE 1** Changes in plasma TSH, fT4, and fT3 levels

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|---|---|---|---|---|---|---|---|---|---|---|
| ALT (U/L) | 1831 | 405 | 165 | 102 | 55 | 72 | 37 | 45 | 45 | 58 |
| AST (U/L) | 784 | 163 | 54 | 45 | 28 | 35 | 25 | 32 | 30 | |
| T. bil (mg/dL) | 2.77 | 1.97 | 2.33 | 2.59 | 1.47 | 1.49 | 1.22 | 1.41 | 0.85 | 0.58 |
| Alb (g/dL) | 3.2 | | | 3.6 | | | | | | 3.5 |
| INR | 3.33 | 1.54 | 1.69 | | 1.45 | | | | | |

**FIGURE 2** Biochemical data and coagulability during admission

## Discussion

For TS management, multiple-modality approach is highly suggested, with ATGs, inorganic iodide, corticosteroids, β-AR antagonists, bile acid sequestrants, and antipyretic agents to ameliorate thyrotoxicosis and its adverse effects on multiple organ symptoms.

TPE is an extra-corporeal therapeutic apheresis modality involves removal of pathogenic substances-containing patient's plasma, and replacement with allogenic or autologous plasma. In the 2019 American Society for Apheresis (ASFA) guidelines, TPE was assigned a category II indication, accepted as second-line therapy treating TS poorly responsive to first line therapeutic measures.

Several mechanisms have been postulated to explain how TPE treat thyrotoxicosis, including: 1) reducing circulating pool of thyroid-binding globulin (TBG), transthyretin, and albumin, 2) diminishing the levels of free and total T4 and T3, 3) reducing amiodarone plasma concentration in amiodarone-induced thyrotoxicosis, 4) lowering Th1 related autoantibodies and cytokines, comprising IL-2, INF-γ, and TNF-α, and 5) removing 5'-monodeiodinase which converts T4 to T3. Nevertheless, these effects usually only last for 24-48 hours, due to rapid re-equilibrium from extravascular thyroid hormones existing in the liver, lymph ducts, and interstitial tissue. These transient effects lead to potential risks of rebound thyrotoxicosis and require multiple procedures to achieve clinical stabilization. Both plasma as well as albumin is the choice of replacement fluid, with the former possessing theoretical advantage of containing TBG to bind free thyroid hormones, but lack of head-to-head trials.

TPE is generally safe and well-tolerated, with complication rates ranging from 5% to

36%, comprising nausea, vomiting, vasovagal attack, transfusion reaction, and hematoma. Risk of mortality is estimated incidence of 0.05%, and is almost attributed to the severe underlying disease.

## Conclusion

TPE exerts its beneficial effects on TS by removing autoantibodies, cytokines, catecholamines, and TBG from the blood and replacing with colloid or a combination of crystalloid/colloid solution. Giving the grade 2C recommendation in 2019 ASFA guidelines, TPE could be considered as a standalone or adjunct therapy in TS when conventional treatments are not responsive or are complicated by severe adverse effects.

## References


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