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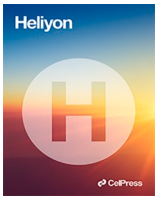

Case report

Case report and literature review: A thyroid storm patient with severe acute hepatic failure treated by therapeutic plasma exchange and a double plasma molecular absorption system☆

Fuquan Tu [a,b,1], Yiqin Lin [b,1], Junnian Chen [b], Lili Zhou [b], Liyong Lin [a], Qin Liu [a], Wenwei Wu [a,b,*]

[a] Department of Emergency Medicine, Fujian Medical University Union Hospital, Fujian, China
[b] Intensive Care Unit, Fujian Medical University Union Hospital Qishan Campus, Fujian, China

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ABSTRACT

Thyroid storm (TS) leading to acute liver failure is rare but fatal in clinical practice and hepatic failure can remarkably limit medication options for TS. We successfully cured a patient with TS complicated with acute hepatic failure using therapeutic plasma exchange (TPE) and a double plasma molecular absorption system (DPMAS) and summarized the case characteristics of 10 similar critical patients reported worldwide. We recommend that patients with TS complicated with liver failure disuse propylthiouracil or methimazole. TPE should be utilized to rapidly decrease thyroid hormone levels, and DPMAS should be considered for supportive treatment in the presence of hepatic encephalopathy or dramatic bilirubin elevations.

1. Introduction

Thyroid storm (TS) is a rare but life-threatening endocrine emergency [1]. Clinically, TS is characterized by sudden onset of high fever, severe tachycardia, congestive heart failure, gastrointestinal symptoms, and central nervous system disturbance [2]. However, cases of severe acute hepatic failure caused by TS are infrequent and not a few case have been reported worldwide. We now report a case of a 37-year-old Asian man who recently presented to our hospital with a dramatic increase in bilirubin, which successfully resolved with the support of therapeutic plasma exchange (TPE) and a double plasma molecular absorption system (DPMAS). Meanwhile, we review the feasible causes, case characteristics, and treatment of acute hepatic failure caused by TS.

2. Case presentation

In May 2023, a 37-year-old Asian male presented to our emergency department with “abdominal pain” as the first symptom. The patient had a history of hyperthyroidism for 3 years and was irregularly taking “methimazole” for treatment. Despite having roughly normal laboratory examinations and having been given symptomatic treatment for “abdominal pain”, the patient had no obvious

☆ All authors are also from Union Clinical Medical Colleges, Fujian Medical University, Fuzhou, China.

* Corresponding author. Department of Emergency Medicine, Fujian Medical University Union Hospital, 29 Xinquan Road, Fuzhou 350001, China.
E-mail address: wuwenwei1974@fjmu.edu.cn (W. Wu).

[1] These authors contributed equally to this work and should be considered as co-first authors.

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improvement. One day later, the patient developed dyspnoea, fever, and "congestive heart failure". The patient immediately underwent mechanical ventilation with endotracheal intubation and was transferred to the intensive care unit. The body temperature was 39.5 °C, the heart rate was 176 bpm with atrial fibrillation, and the blood pressure was 148/92 mmHg. He was receiving mechanical ventilation and the SpO2 was 97% (P-SIMV, FiO_2 60%, P support 16 cmH_2O, F 18 breaths per minute, PEEP 8 cmH_2O). The thyroid gland was diffusely enlarged, moist rales could be heard throughout the lung fields, and jaundice was observed. The thyroid hormone levels were significantly higher than normal (see Supplementary Table). The Burch-Wartofsky Point Scale (BWPS) [3] was calculated to be as high as 120 points (≥45 indicating TS) and this patient could be diagnosed with TS1 according to "the 2016 Guidelines" [4,5], so the patient was suffered with TS. In the ICU, we administered standard medical therapy, including mechanical ventilation, propranolol, dexamethasone, physical cooling, and enteral nutritional support (2000 kcal/d). Remarkably, the patient presented with both transaminase and bilirubin abnormalities, and the increase was substantial. Viral (hepatitis virus, Epstein–Barr virus, HIV, etc.), obstructive, autoimmune, alcohol abuse, and drug-induced liver injury were ruled out. Because of hepatic failure, the patient did not receive methimazole or propylthiouracil (PTU). On the third day of admission, the patient's total bilirubin reached 744.5 μmol/L, and we immediately carried out TPE + DPMAS treatment, which could reduce circulating thyroid hormone levels and remove bilirubin and macromolecular hepatic failure toxins (pseudo neurotransmitters, free fatty acids, aromatic amino acids, benzene, thiol, etc.). We performed DPMAS as previously described [6,7]. Briefly, the plasma was separated using the EC-50W facility (AsahiKASEI, Japan). The blood pump was set at a velocity of 150 mL/min. Then, a bilirubin absorber (BS330, Jafron, China) was placed into the plasma circuit, together with the application of a hemoperfusion device (HA330-II, Jafron, China), and finally returned to the patient with a duration of approximately 3 h once. Following six cycles of TPE + DPMAS, the patient's bilirubin fell below 350 μmol/L and slowly spontaneously normalized and he did not have any adverse reaction including bleeding or infection. After 25 days of hospitalization, the patient was discharged from the hospital safely (see Fig. 1). After discharge, FT3 and FT4 were normal, TSH was low, and radioactive iodine therapy was performed 3 months later.

3. Discussion

Hyperthyroidism is one of the most common endocrine diseases, and TS is the most serious clinical acute complication of the disease. Its course progresses rapidly and is complicated by organ failure. The common target organs are the heart, gastrointestinal tract, and central nervous system. Mild to moderate impairment of liver function due to hyperthyroidism or TS is not unusual, most patients present with mildly elevated bilirubin. However, it is rare that, as in this patient, progressive elevation of bilirubin to 805μmol/L in a short period of time and presentation with acute severe liver failure. The mechanism of hepatic failure in TS is not yet clear and may be associated with the following factors: hepatic congestion due to congestive heart failure [8], hypermetabolism-induced relative hepatocyte ischemia [9], direct damage of hepatocytes by thyroid hormone [10], and drug-induced hepatitis (PTU [11]). Additionally, the liver is an important organ for thyroid hormone degradation, so impaired hepatic metabolism may cause difficulty in clearing of circulating thyroid hormone [12].

In this paper, we summarize 11 patients with acute hepatic failure due to TS, including 10 published case reports worldwide and Chinese male patients (see Table 1). Unlike hyperthyroidism, which occurs in young women [13], there was no significant sex difference in TS with hepatic failure (male: female = 6:5). These 11 patients were between 22 and 57 years old, with a median age of 37 years, and those patients were more commonly young adults. We found that 36% (4/11) of TS patients did not have access to accurate predisposing factors, which is consistent with 24–43% of TS patients in epidemiological data [2]. All reported patients had abnormal transaminases and bilirubin, but most of them had abnormal AST elevation, which may be related to TS with heart failure, while a considerable part of circulating AST was derived from cardiomyocytes or muscles. In all cases, the patient we reported had the highest level of bilirubin, with values as high as 805.2 μmol/L, which suggests that he had severe hepatocellular destruction. Hepatocellular injury might be exacerbated by the utilization of PTU or methimazole (according to the medicine instructions) if hepatic impairment

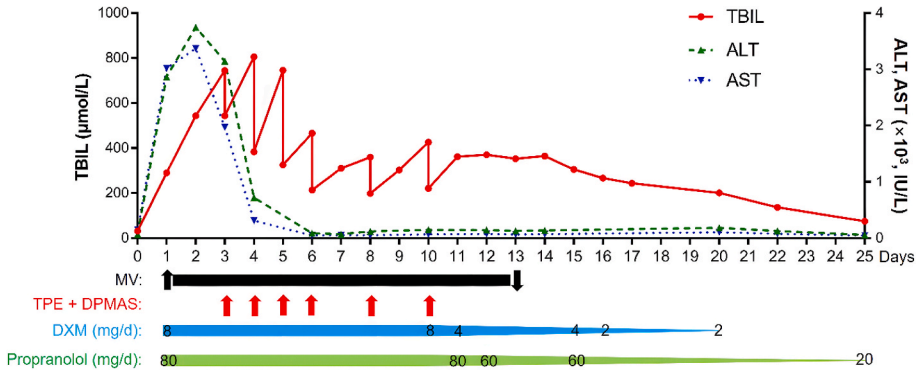

Fig. 1. Time course of hepatobiliary enzyme levels. On admission (Day 0), on the day of transfer to the intensive care unit (Day 1), on the day of transfer to the general ward (Day 20), and on the day of discharge from the hospital (Day 25). TBIL: total bilirubin, ALT: alanine aminotransferase, AST: aspartate aminotransferase, MV: mechanical ventilation, TPE: therapeutic plasma exchange, DPMAS: double plasma molecular absorption system, DXM: dexamethasone.

Table 1
Summary of the characteristics of the published cases.

Sex, age (years)	Country	Thyroid storm	Triggers	Max ALT (U/L)	Max AST (U/L)	Max TBIL (μmol/L)	Therapy	Reference
Female, 57	UK	Yes	RAI	852	*NM*	46	PTU propanolol prednisolone	Tufton [20]
Female, 48	USA	Yes	*NM*	607	1367	50	methimazole propranolol glucocorticoids	Kim [21]
Female, 22	USA	Yes	*NM*	293	964	296	PTU & methimazole propranolol steroids	Hayat [22]
Male, 22	Japan	Yes	Infection	3550	9258	470	methimazole landiolol & bisoprolo prednisolone **TPE**	Zeng [14]
Female, 22	USA	Yes	discontinue therapy	1218	1803	478.8	propranolol hydrocortisone **thyroidectomy & OLT**	Catherine [23]
Female, 35	Singapore	Yes	cesarean section	739	1658	30	PTU propranolol hydrocortisone	Chong [24]
Male, 28	USA	Yes	discontinue therapy	1600	2101	*NM*	beta-blockade **thyroidectomy & OLT**	Kandil [11]
Male, 41	Turkey	Yes	*NM*	2045	3040	90.6	steroids propranolol	Mustafa [25]
Male, 38	UK	Yes	*NM*	1050	*NM*	90	PTU esmolol & propranolol dexamethasone	Ali [26]
Male, 55	Japan	Yes	Infection	2400	1100	359.1	methimazole landiolol hydrocortisone **TPE**	Nakao [15]
Male, 37	China	Yes	discontinue therapy	3748	3371	805.2	propranolol dexamethasone **TPE & DPMAS**	Our case

Standardized treatment includes elimination of triggers, cooling, glucocorticoids, β-blockers, inhibition of thyroid hormone synthesis and secretion, organ support, and nutritional support.
RAI: radioactive iodine, PTU: propylthiouracil, TPE: therapeutic plasma exchange, DPMAS: double plasma molecular absorption, OLT: orthotopic liver transplantation, *NM*: not mentioned, ALT: alanine aminotransferase, AST: aspartate aminotransferase, TBIL: total bilirubin.

was detected, while in 70% (7/10) of the cases, the patients remained on PTU or methimazole. In our case, we avoided PTU or methimazole throughout the course but chose TPE, as in the other two reported cases [14,15]. In the presence of definite hepatic failure, there is a risk of aggravating liver injury with PTU, which is not consistent with the medical environment under China ‘s national conditions. Other anti-thyroid drugs, such as beta-blockers and glucocorticoids, have been used in almost all cases. And for inorganic iodide, we identified with that it could effectively inhibit the release and synthesis of thyroid hormone in TS [16], but due to TPE was effective in removing thyroxine concentrations from the circulation, so iodide was not added for therapy. Additionally, inorganic iodide was added in only one of the other 10 patients listed in Table 1.

TPE is the process of replacing patient plasma with healthy donor plasma with the help of a plasma separator to achieve treatment. More than 99% of circulating thyroid hormones exist are their bound form to thyroglobulin and albumin [17], so removing these thyroid hormones is supposed to benefit the treatment of TS. TPE is recommended for patients with TS when their general condition does not improve after 24–48 hours of treatment for hyperthyroidism [4]. TPE is a safe, fast, and effective treatment option for patients who have side effects or in whom antithyroid drugs have been ineffective [17]. However, the patient in this case also presented with severe acute hepatic failure, manifested as steep bilirubin elevation, coagulation abnormalities, and hepatic encephalopathy. Artificial liver support systems (ALSSs) have been applied for decades to treat acute, and acute-on-chronic hepatic failure patients [18]. In addition to TPE, plasma adsorption is also an important mode of ALSSs, while DPMAS can not only adsorb bilirubin but also effectively eliminate macromolecular hepatic failure toxins. Our patient underwent TPE followed by DPMAS (see Fig. 2), which might have eliminated the bilirubin and toxic substances that accumulated due to hepatic failure. DPMAS is crucial to decrease the mortality of hepatic failure [19]. In addition, we also need to consider that TPE and DPMAS also have some flaws, including the risk of bleeding from vascular puncture and worsening congestive heart failure [15], allergic reactions, and high prices.

4. Conclusion

In summary, we successfully cured a patient with TS and severe acute liver failure. We recommend that TPE can be selected to rapidly and effectively decrease circulating thyroid hormone levels when TS is complicated with acute hepatic failure, and DPMAS can be used to effectively remove liver failure toxin and bilirubin for support therapy, to improve prognosis.

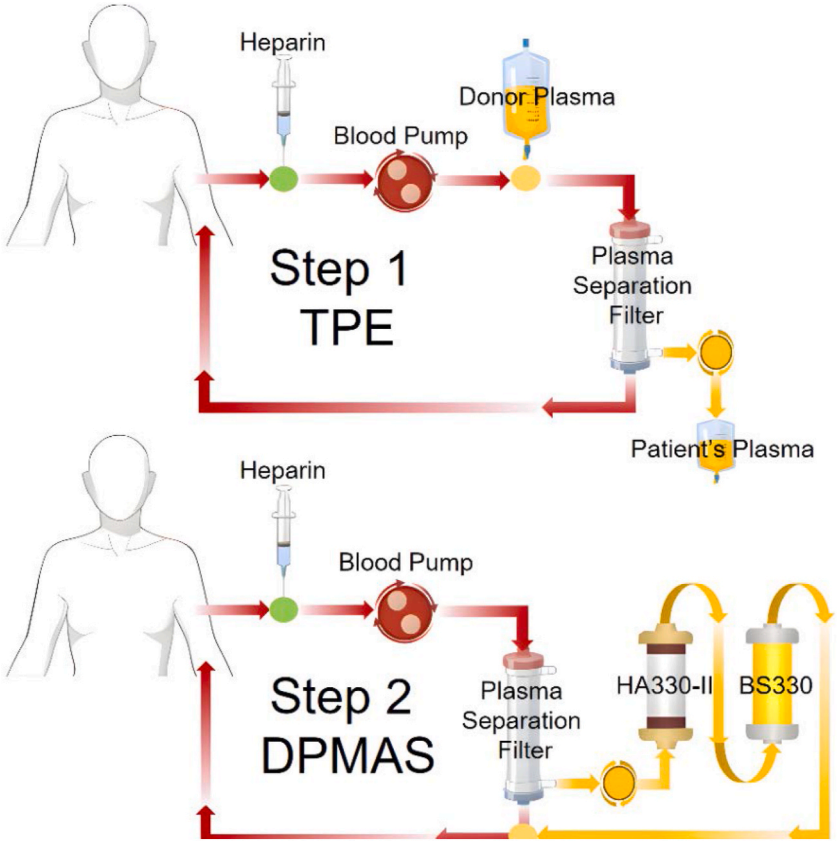

Fig. 2. Schematic of TPE and DEPMAS treatments. HA330-II (Jafron, China) is a perfusion device that removes inflammatory factors, pseudo neurotransmitters, free fatty acids, aromatic amino acids, etc. BS330 (Jafron, China) is a bilirubin absorber. TPE: therapeutic plasma exchange, DPMAS: double plasma molecular absorption system.

Ethics statement

The study involving a human participant was reviewed and approved by the Ethics committee of Fujian Medical University Union Hospital, Fuzhou, China. The patient provided his written informed consent to participate in this study. Written informed consent was obtained from the individual for the publication of any potentially identifiable images or data included in this article.

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Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further Chinese raw data can be directed to the corresponding author/s.

CRediT authorship contribution statement

Fuquan Tu: Writing – review & editing, Writing – original draft, Resources, Project administration, Funding acquisition, Conceptualization. **Yiqin Lin:** Writing – review & editing, Investigation. **Junnian Chen:** Writing – review & editing, Investigation. **Lili Zhou:** Writing – review & editing, Supervision. **Liyong Lin:** Writing – review & editing, Data curation. **Qin Liu:** Writing – review & editing, Supervision. **Wenwei Wu:** Writing – review & editing, Project administration.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to

influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e28867.

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