Case Report

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Successful treatment of thyroid storm with therapeutic plasmapheresis in a geriatric patient

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ABSTRACT

Thyroid storm is a rare and fatal condition characterized by severe clinical manifestations of thyrotoxicosis. In geriatric patients, care should be taken in the follow-up of thyrotoxicosis due to comorbid diseases. Therapeutic plasmapheresis is an apheresis method that separates plasma from the components and removes the harmfull substances from the blood. This method may clear thyroid hormones from the blood and is recommended as an alternative option in the treatment of thyroid storm. In this case, we aimed to present an old patient with known alzheimer's disease and multinodular goiter induced thyrotoxicosis. The patient who could not get the first line treatments completely due to complications and were finally diagnosed with thyroid storm, recovered with therapeutic plasmapheresis treatment without any problem and was discharged.

Keywords: Lithium, Thyroid storm, Plasmapheresis

A thyroid storm is a rare and life-threatening condition characterized by severe clinical manifestations of thyrotoxicosis. It can be seen in 2-16% of patients with thyrotoxicosis and mortality may be up to 30%.[1] Thyroid storm is diagnosed clinically, as there are no specific diagnostic laboratory findings. Although not widely used in clinical practice, the scoring system developed by Burch and Wartofsky in 1993 can be used for an objective diagnosis. In this system, scoring is made based on body temperature, neurological findings, gastrointestinal-hepatic findings, tachycardia-atrial fibrillation, heart failure, and the presence of a precipitating factor, and the possibility of thyroid crisis diagnosis is tried to be determined (Table 1).[2] After the hemodynamic stabilization, improvement of the underlying causes that may trigger the storm, and antithyroid drugs are the management methods of the thyroid storm.

Therapeutic plasmapheresis (TP) is an effective treatment option that removes cytokines, antibodies, and thyroid hormones from plasma when the first-line treatments are not successful or cannot be used.[3] TP was first used in the treatment of hyperthyroidism by Ashkar *et al*.[4] in 1970 and continues to be an effective and safe alternative treatment option with technological advances. In this case report, we wanted to present a geriatric patient with Alzheimer's disease who was diagnosed with thyroid storm during the course of hyperthyroidism treatment and her clinic recovered successfully with TP treatment.

CASE REPORT

An 88-year-old female patient with known Alzheimer's disease who could not use any medication was diagnosed with multinodular goiter-related hyperthyroidism 1 month ago. Her thyroid ultrasonography (USG) showed bilateral multiple nodules with the largest of which was 16 mm.

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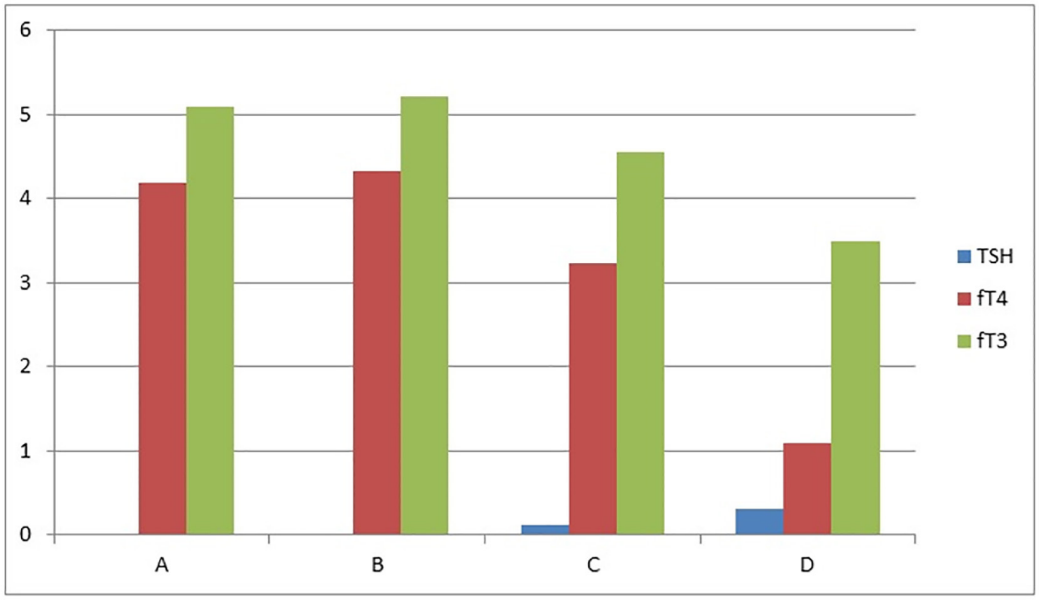

A: First thyroid function tests levels B: Before plasmaphresis
C: After the 2nd session of plasmapheresis D: After the 4th session of plasmapheresis
TSH: thyroid stimulating hormone (normal range; 0.34-5.8 µIU/mL)
fT4: free T4 (normal range; 0.61-1.12 ng/dl)
fT3: free T3 (normal range; 2.5-3.9 ng/L)

Figure 1. Change of patient's thyroid hormones levels during the clinical course

Thyroid-stimulating hormone (TSH) has been found < 0.01 µIU/mL (normal range = 0.34-5.86), free T4 has been found 4.18 ng/dL (normal range = 0.61-1.12) and free T3 has been found 5.1 ng/L (normal range = 2.5-3.9) at the laboratory tests (Figure 1, column A). The patient was prescribed methimazole at first, but it was changed to propylthiouracil (PTU) due to agranulocytosis. Because agranulocytosis did not improve, the patient was referred to our hospital's endocrinology department. The patient's antithyroid medications were stopped and radioactive iodine (RAI) treatment was planned. Lithium 2x300 mg was prescribed until the RAI treatment. On the 8th day of lithium treatment, the patient was admitted to the emergency service with complaints of unconsciousness, fever, and palpitation. Her peripheral pulses were filiformic and 120/minute, her fever was 38.9 °C and her blood pressure was 105/75 mmHg. In electrocardiography (ECG), the pulse was 110/minute and the rhythm was atrial fibrillation (AF). In laboratory tests, hemogram, electrolytes, and liver function tests were normal. But, serum BUN [89 mg/dL (normal range= 8-20)], creatinine [1.7 mg/dL (normal range = 0.66-1.09)], and C-reactive protein (CRP) [38 mg/L (normal range = 0-5)] were measured abnormal. No pathology was detected in computed tomography (CT) and magnetic resonance (MR) of the brain. The patient was consulted by neurology as the electroencephalography (EEG) in the emergency room was compatible with mildly diffuse cerebral dysfunction and valproic acid treatment was started with the preliminary diagnosis of epilepsy. Since the serum lithium level was 1.9 mmol/L (normal range = 1-1.2), she was admitted to the intensive care unit (ICU) with the diagnosis of lithium intoxication, and hemodialysis (HD) was performed. On the 2nd day of ICU hospitalization, the patient was transferred to the internal medicine clinic.

When she was admitted to the internal medicine clinic, the patient was conscious but had meaningless speech, and her orientation and cooperation were still incomplete. Her blood pressure was 115/74 mmHg, pulse was 105/minute, AF rhythm, and fever was 37.9 °C.

The TSH measured in our clinic was < 0.01 µIU/mL, free T4 was 4.32 ng/dl and free T3 was 5.22 ng/L (Graphic 1, column B). Since there was no additional infectious and neurological pathology to explain the current clinical status and Burch&Wartofsky score was 45 points (fever; 10 points, agitation; 10 points, pulse; 5 points, AF; 10 points, precipitating condition; 10 points), the patient was diagnosed as thyroid storm and TP treatment was initiated. TSH (0.12 µIU/mL), free T4 (3.23 ng/dl), and free T3 (4.56 ng/L) were

Table 1. Burch and Wartsofsky scoring system for the identification of thyroid storm.

Thermoregulatory dysfunction [Temperature (°C)]	
37.2 to 37.7	5
37.8 to 38.2	10
38.3 to 38.8	15
38.9 to 39.4	20
39.4 to 39.9	25
> 40.0	30
Central nervous system effects	
Mild (Agitation)	10
Moderate (Delirium, Psychosis, Extreme lethargy)	20
Severe (Seizure, Coma)	30
Gastrointestinal-hepatic dysfunction	
Moderate (Diarrhea, Nausea/vomiting, Abdominal pain)	10
Severe (Unexplained jaundice)	20
Cardiovascular dysfunction (Tachycardia)	
99 to 109	5
110 to 119	10
120 to 129	15
130 to 139	20
≥ 140	25
Atrial fibrillation	10
Heart failure	
Mild (Pedal edema)	5
Moderate (Bibasilar rales)	10
Severe (Pulmonary edema)	15
Precipitant history	
Negative	0
Positive	10

A score of ≥ 45; highly suggestive of thyroid storm, 25-44; supports the diagnosis, < 25 makes thyroid storm unlikely.

improved after 2 sessions of TP (Graphic 1, column C). She was orientated and cooperated, and vital signs were normal after TP. Valproic acid was gradually decreased and discontinued. The patient received a single dose of RAI therapy for hyperthyroidism and was discharged for polyclinic follow-up.

DISCUSSION

A thyroid storm is an advanced and more severe form of thyrotoxicosis, and fever, nausea, vomiting, and unconsciousness can be observed. Acute events such as thyroid or non-thyroid surgery, trauma, infections, myocardial infarction, acute iodine load, or birth may trigger thyroid storm.[5] Since a fully formed thyroid storm is very rare, it should be considered in patients with severe hyperthyroidism findings, and treatment should be started immediately. Thionamides, beta-blockers, iodine solutions, glucocorticoids, and bile acid sequestrants are the first-line drugs used in the treatment of hyperthyroidism and thyroid storm.[6] Lithium is a drug used primarily in the treatment of mood disorders and may lead to hypothyroidism with effects such as blocking the intake of iodine into the thyroid gland, reducing the release of thyroid hormones into the periphery, and preventing the conversion of T4 to T3 in the blood.[7] Lithium can be used as an alternative treatment option in the treatment of hyperthyroidism when there is a lack of response or side effects to primary treatments. However, its use is

Table 2. Category definitions for therapeutic apheresis.

Category	Description
I	Disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment.
II	Disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment.
III	Optimum role of apheresis therapy is not established. Decision making should be individualized.
IV	Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. IRB approval is desirable if apheresis treatment is undertaken in these circumstances.

IRB = Institutional Review Board

limited due to its renal and neurological toxic effects and should be monitored very closely, especially in geriatric patients.

Apheresis is the general name of the procedure that has been used safely since 1944, where the blood is separated into one or more components by passing it through a medical device, and the remainder is returned to the patient with or without extracorporeal treatment.[4] TP, on the other hand, is an apheresis subtype in which plasma is separated from its components, and some unwanted substances are selectively purified with the help of different techniques and then returned to the patient by adding albumin or plasma.[4] Since the substances bound to the proteins cannot be purified from the blood by HD, they can be cleaned from the blood by TP. Antibodies, immunocomplexes, monoclonal proteins, cryoglobulins, complement components, lipoproteins, and protein-bound toxins are some of the substances that can be removed from the body by this method. TP has become one of the first-line treatments in the treatment of some neurological, hematological, autoimmune, and rheumatological diseases in recent years.[4] The American Apheresis Association periodically updates the indications and techniques for apheresis and published the last report (8th report) in 2019.[8] Diseases are divided into 4 categories (Table 2) according to the effectiveness of apheresis in this report and thyroid storm is classified as category II (disorders in which apheresis alone or combined with other options are considered a second-line treatment) with 2C level of evidence.[8]

In the thyroid storm, TP can be used if the patient's symptoms are severe and there is no adequate response within 24-48 hours with primary treatments or if side effects have developed.[8] In addition to reducing hormone concentrations, TP also reduces the severity of thyrotoxicosis by removing catecholamines and cytokines from the blood. However, the effectiveness of TP is temporary and hormone levels increase again the next day. Therefore, the TP procedure can be applied according to the patient's clinic, either daily or 2 or 3 days apart. The procedure is repeated until the patient's symptoms improve, and a clinical response can be obtained with an average of 3-6 sessions.[8] Colloidal solutions (plasma or albumin) or combinations of colloids and crystalloids can be used in the TP process as replacement fluids. Since plasma contains coagulation factors, it should be preferred in patients with coagulation disorder or before surgery.[9]

CONCLUSION

Authors' Contribution

Study Conception: MK, SU,; Study Design: IKS,; Supervision: EK,; Materials: EK,; Data Collection and/or Processing: FPE, MS,; Statistical Analysis and/or Data Interpretation: MK,; Literature Review: SU,; Manuscript Preparation: MK and Critical Review: IKS.

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