Therapeutic plasma exchange in Graves' disease – A Case Report

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ABSTRACT

Therapeutic plasma exchange (TPE) is one possible treatment for patients resistant to conventional antithyroid drugs or requiring urgent attention for thyrotoxicosis. We report a 26-yr-old man with thyrotoxicosis, ultimately attributed to Graves' disease in whom antithyroid drug used initially was soon discontinued, due to agranulocytosis. Due to the agranulocytosis, antithyroid drugs were not an option, so radioactive iodine (RAI) treatment was the next resort. Unfortunately, the free thyroid hormone level was still elevated and euthyroid state was required prior to RAI treatment, so another strategy was needed to correct the thyroid function. So, we performed TPE to control the thyrotoxicosis.

Keywords: *Therapeutic plasma exchange, Graves' disease, Radioactive iodine*

INTRODUCTION

Hyperthyroidism is characterized by the excessive production and persistent release of thyroid hormones, whereas thyrotoxicosis denotes medical conditions resulting from the increased impact of thyroid hormones on tissues[1].The standard management of Hyperthyroidism incorporates three primary options: antithyroid drugs, radioactive iodine (RAI) therapy, and thyroidectomy[2].Any one of these modalities can be implemented, depending on the patient's preference and/or the physician's experience, according to the American Thyroid Association and American Association of Clinical Endocrinologists' guidelines. However, a recent systematic review suggests that surgery might be the most effective option based on particular outcomes[2,3].

In Asia and Europe, antithyroid medications are given preference as the initial treatment for Graves' disease (GD). However, extensive associated adverse effects (i.e., agranulocytosis or hepatotoxicity) may occur, necessitating the cessation of these medications and the consideration of RAI therapy or surgical intervention[2,3]. To prevent potential transitory exacerbation of thyrotoxicosis during or following RAI or surgery, it is essential for thyroid function to be at or near normal, necessitating supplementary therapy of thyrotoxicosis. Iodine solution is the most used adjuvant in this situation and is typically efficient in stabilizing thyroid function[2]. However, its effects are frequently ephemeral, and a phenomenon of escape may arise with prolonged usage. In individuals resistant to iodine solution, particularly those necessitating immediate surgery or at danger of organ failure due to thyrotoxicosis, an alternative method is required for effective management of thyroid function. The elimination of circulating thyroid hormone through therapeutic plasma exchange (TPE) has been documented as a beneficial adjuvant in these cases.

We presented a case of a patient with Graves' disease who received successful sequential TPE and RAI. The effectiveness of TPE as a supplementary treatment in the management of GD is also examined.

CASE DESCRIPTION

A 26-year-old male patient had been diagnosed with Graves 'disease about 1 years ago and treated with maximum dose of carbimazole. Upon further enqui-

ry, the patient admitted in Dhaka Medical College Hospital with a history of weight loss, palpitations, tremors, and lack of sleep. Vital signs showed a heart rate of 130/minute, blood pressure of 140/70mmHg, respiratory rate of 18/minute, and temperature of 98.8. Examination revealed an anxious patient with bilateral lid lag, large smooth goiter with a thyroid bruit, and tremors of upper extremities. Laboratory assessment revealed a suppressed TSH, high free T4(>3.43ng/dl), free T3(>22.8pg/ml), positive anti-thyrotropin receptor antibodies (TRab), and thyroid stimulating immunoglobulin (TSI). Thyroid study shows thyromegaly with uniform increased traced uptake. But unfortunately, patient was developed agranulocytosis and diagnosed as a carbimazole induced agranulocytosis. Due to the agranulocytosis, antithyroid drugs were not an option, so RAI treatment was the next resort. Unfortunately, the free thyroid hormone level was still elevated and euthyroid state was required prior to RAI treatment, so another strategy was needed to correct the thyroid function.

Then patient was referred to transfusion medicine for therapeutic plasma exchange to control hyperthyroidism. Consequently, 3 courses of TPE were performed via right femoral vein catheterization. We used the MCS+ apheresis machine for exchange, and 1 volume of plasma exchange was done every alternate day, and 5% albumin was used as a replacement fluid. The patient responded well to TPE (Table 1) with no complications observed following TPE and successfully received RAI.

Table 1: Investigation Reports

	Before TPE	After 1st Session	After2nd Session	After3rd Session
FT3	>22.8 pg/ml	>20pg/ml	>19pg/ml	>19pg/ml
FT4	>6.99 ng/dl	>3.43 ng/dl	>3.23 ng/dl	>3.03 ng/dl
hTSH	< 0.0100ql/ml	< 0.009ql/ml	< 0.008ql/ml	< 0.008ql/ml
TSH-R Antibody	positive			
Thyroid Study	Thyromegaly with uniformly increase tracer uptake			

DISCUSSION

Thyroxine (T4) exhibits the highest concentration of iodothyronines in plasma and is solely synthesized by the thyroid; triiodothyronine (T3) is predominantly generated (about 80%) from peripheral tissues through the deiodination of T4. T4 is approximately 68% bound to thyroxine binding globulin (TBG), 11% to transthyretin, and 20% to albumin. T3 is 80% linked to thyroxine-binding globulin (TBG), 9% to transthyretin, and 11% to albumin. The significant protein binding facilitates the elimination of thyroid hormones during TPE [4].

TPE is an extracorporeal blood purification method utilized for the removal of big molecular substances from plasma[5]. Unlike dialysis, which is incapable of removing protein-bound compounds, TPE can effectively eliminate them[6]. The procedure entails circulating the patient's blood through a medical apparatus to separate the plasma, which is subsequently replaced with a colloid (albumin or plasma) or a mixture of crystalloid and colloid. TPE eliminates protein-bound thyroid hormones; the colloid utilized to substitute the plasma offers new binding sites for thyroid hormones, which are subsequently removed in the following TPE session[7]. In addition to thyroid hormones, TPE may facilitate the elimination of cytokines, deiodinase enzymes, and Graves' antibodies, contributing to the remission of thyrotoxicosis, Graves' ophthalmopathy, and pretibial myxedema[8].

The application of TPE for the management of thyrotoxicosis was initially documented in the 1970's[9]. Three thyrotoxic patients, unresponsive to conventional antithyroid medications, exhibited favorable outcomes following therapeutic plasma exchange and subsequently received radioactive iodine therapy. Similarly, refractory thyrotoxicosis was a principal indication for therapeutic plasma exchange in previous studies[3,10,11]. Two to five sessions of TPE were given to individuals with GD or toxic nodular goiter when thyroidal hyperfunction was not regulated by antithyroid medications. TPE was used in certain cases when antithyroid medications were contraindicated due to

undesirable effects such as agranulocytosis or hepatotoxicity[11-13].

A retrospective multicenter study explored the effects of TPE in a large group of thyrotoxic patients 10. Administration of TPE to 22 patients with thyrotoxicosis, comprising 9 with Graves disease and 13 with toxic nodules, resulted in clinical improvement in the majority (20/22; 91%). A mean of four TPE courses (range, 2-9 courses) were conducted prior to the initiation of RAI therapy or surgery, resulting in a 41.7% decrease in free T4 levels. Our patient displayed a modest reduction in free T4 level after the three courses of TPE (43.34% reduction in free T4 from pre-TPE baseline).

Patients should often achieve a euthyroid state prior to RAI therapy or surgery to mitigate the adverse effects of hyperthyroidism[14-16]. TPE may serve as a secondary therapy when thyrotoxicosis is unmanageable through medical means or when immediate symptomatic relief is required. The patient was approved for TPE as there were no obvious contraindications, including hemodynamic instability, active infection, bleeding propensity, or allergic reactions to FFP or albumin[17]. Ultimately, RAI treatment was conducted as scheduled, despite the thyroid hormone levels remaining abnormal. He had no symptoms associated with thyrotoxicosis, and his thyroid hormone levels were not elevated (i.e., above three times the upper normal range); hence, RAI therapy was not contraindicated. Consequently, TPE facilitated the transition to RAI treatment without exacerbating thyrotoxicosis or inducing associated problems.

CONCLUSION

TPE serves as a valuable supplement in hyperthyroidism management, particularly in severe thyrotoxicosis cases with cardiac or neurological consequences, or when conventional antithyroid therapies are ineffective or inappropriate. TPE should be administered regularly until clinical improvement is observed.

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