



CASE REPORT

Medicine Science 2019;8(1):233-6

Amiodarone induced thyrotoxicosis may not respond to therapeutic plasma exchange like patients with graves' disease: A report of two cases and literature review

Ismail Yildiz, Gulsah Elbuken, Tugay Atasever, Sibel Ozkan Gurdal, Sayid Zuhur

Namik Kemal University, Faculty of Medicine, Department of Endocrinology and Metabolism, Tekirdag, Turkey

Received 08 August 2018; Accepted 26 November 2018
Available online 11.01.2019 with doi:10.5455/medscience.2018.07.8954

Copyright © 2019 by authors and Medicine Science Publishing Inc.

Abstract

The achievement of euthyroid state has been suggested in patients with thyrotoxicosis undergoing surgery to reduce the risk of thyroid storm. However, euthyroid state could not always be achieved by antithyroid drugs. Therefore, therapeutic plasma exchange (TPE) is an option in this condition. A 58-year-old male patient with a history of type-2 diabetes using 200 mg amiodarone per day, admitted for diabetic ketoacidosis (DKA), induced by thyrotoxicosis. with palpitation, sweating, polyuria, and polydipsia. Euthyroid state could not be achieved, despite all appropriate treatments for thyrotoxicosis. Therefore, preparation with TPE followed by total thyroidectomy was planned. A 35% decrease in fT3 (free T3) and fT4 (free T4) levels were achieved, after two sessions of TPE. A 74-year-old male patient, admitted for acute anterior myocardial infarction (AMI) induced by thyrotoxicosis due to Graves' disease. Multiple vessel disease was detected on primer percutaneous coronary angiography, and an emergency coronary artery bypass grafting (CABG) was planned. Therefore, preparation with TPE was planned before surgery. A substantial decrease in fT4 and fT3 levels (45% and 72%, respectively) levels were achieved, after one session of TPE. Most of the studies evaluating the efficacy of TPE in patients with thyrotoxicosis are including patients with Graves' disease and toxic multinodular goiter, and TPE was indicated as an effective option for preparation of these patients for surgery. However, as presented in case 1, TPE may not be effective in amiodarone induced thyrotoxicosis (AIT) as in cases with thyrotoxicosis due to Graves' disease.

Keywords: Thyrotoxicosis, amiodarone induced thyrotoxicosis, therapeutic plasma exchange

Introduction

The term thyrotoxicosis refers to the hypermetabolic clinical condition resulting from the elevation of the serum thyroid hormone levels [1]. The most common etiologies are Graves' disease, toxic multinodular goiter and toxic adenoma. Antithyroid drugs, radioactive iodine and thyroidectomy are three conventional treatment options generally selected according to the specific cause of hyperthyroidism [2].

Amiodarone is an antiarrhythmic agent used to maintain sinus rhythm after cardioversion of severe ventricular arrhythmias [3]. Each tablet contains 75 mg iodine and 10% of the iodine content is released as free iodine every day [4].

Amiodarone has some side effects on thyroid gland, which are due to amiodarone's high iodine content or its direct toxic

effect on thyrocytes. The type-1 AIT is resulting from excess thyroid hormone synthesis and release, whereas the type-2 AIT is resulting from the destructive thyroiditis that leads to the release of preformed thyroid hormones [5].

In a patient with severe thyrotoxicosis, or who is going to be operated for different causes, including thyroidectomy, the treatment options to achieve euthyroid state or to decrease fT4 and fT3 levels are lugol solution, glucocorticoids, lithium carbonate, beta blockers, cholestyramine, radiocontrast agents, and finally TPE [6].

TPE is a blood purification technique that patient's blood can be separated into its components, with selective removal of the full plasma [7].

*Corresponding Author: Sayid Zuhur, Namik Kemal University, Faculty of Medicine, Department of Endocrinology and Metabolism, Tekirdag, Turkey
E-mail: zuhur744@gmail.com

A huge body of evidence supports the use of TPE as a possible treatment option for patients with thyrotoxicosis undergoing surgery for any reason, who are resistant to antithyroid drugs, or those requiring urgent treatment for thyrotoxicosis. However, the effect of TPE on different causes of thyrotoxicosis is not well known so far. Therefore, herein, we present two cases of severe thyrotoxicosis due to AIT and Graves' disease who responded to TPE, differently.

Case presentation

Case 1

A 58-year-old male patient with a history of type-2 diabetes, using 200 mg amiodarone per day due to ventricular arrhythmia for several years, admitted to emergency room with palpitation, sweating, polyuria, and polydipsia. The physical examination was unremarkable except for a sinus tachycardia with a heart rate of 130 beats/min. Laboratory analysis indicated the presence of DKA and thyrotoxicosis. His plasma glucose was 613 mg/dL, arterial pH was 7.19 log [H⁺], serum TSH was <0.005 mIU/mL (0.4-4), fT3 was 5.47 pg/ml (1.57-5.3), fT4 was 5.3 ng/dl (0.8-1.9) and TSH receptor antibody (TRAb) level was 5.3 IU/L (0-14).

Neither nodule nor excess blood flow were present on gray-scale and color Doppler ultrasonography of the thyroid gland. After appropriate physical examination and laboratory analysis, the underlying cause of DKA was shown to be associated with AIT. After appropriate treatment for DKA, propranolol 80 mg/day, methimazole 40 mg/day, and methylprednisolone 60 mg/day were started for thyrotoxicosis. Despite all above treatments, the patient's general condition deteriorated and his fT4 levels increased to >7.7 ng/dL, 3 weeks after admission (Figure 1). Therefore, total thyroidectomy and preparation with TPE before surgery was planned. TPE was performed with plasma exchange method by Spectra Optia Apheresis System and %5 albumin and isotonic saline were used for replacement of plasma. The exchange volume was 2 L for each session and every session was lasted for two and half hours. After two sessions, fT4 and fT3 levels decreased only modestly to 5.15 ng/dL and 2.22 pg/mL, respectively, which was consistent with a 35% decrease in thyroid hormone levels (Figure 1 and Figure 2). The patient underwent total thyroidectomy under medical treatment. No complication developed during or after surgery.

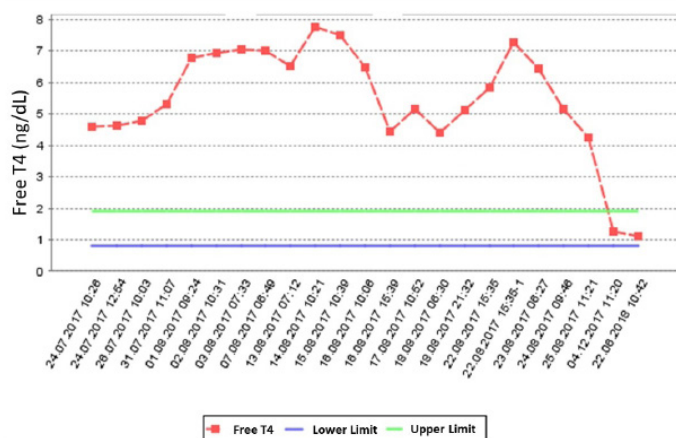


Figure 1. The fT4 levels of case 1 before and after TPE

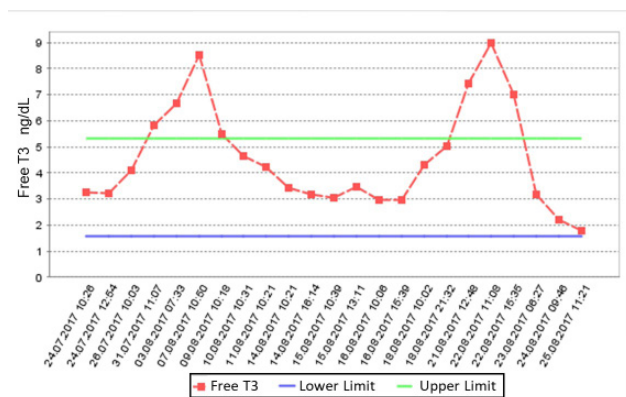


Figure 2. The fT3 levels of case 1 before and after TPE

Case 2

A 74-year-old male patient admitted to emergency department with chest pain, palpitation, and sweating. On biochemical analysis his serum TSH was <0.005 mIU/mL, fT3 was 10.6 pg/mL, fT4 was 4.5 ng/dL, and TRAb level was 24 IU/L (0-14). A diagnosis of AMI induced by thyrotoxicosis due to Graves' disease was made according to ECG and biochemical analysis. Treatment with propranolol 80 mg/day, methimazole 40 mg/day, and 10 drops/ 3 times/ day of lugol solution was started. Multiple vessel disease was detected on primer percutaneous coronary angiography and an emergency CABG was planned by cardiology department. Therefore a TPE was performed, after one session, fT4 and fT3 decreased to 2.48 ng/dL, and 2.96 pg/mL (Figure 3 and Figure 4), respectively, which were consistent with 45% and 72% decrease in fT4 and fT3 levels. The patient underwent CABG surgery without any complication. The patient became euthyroid after one month of treatment with antithyroid drugs. Both patients' fT3 and fT4 levels, before and after TPE, was presented in Figures 1, 2, 3, and 4. Informed consents were obtained from both patients.

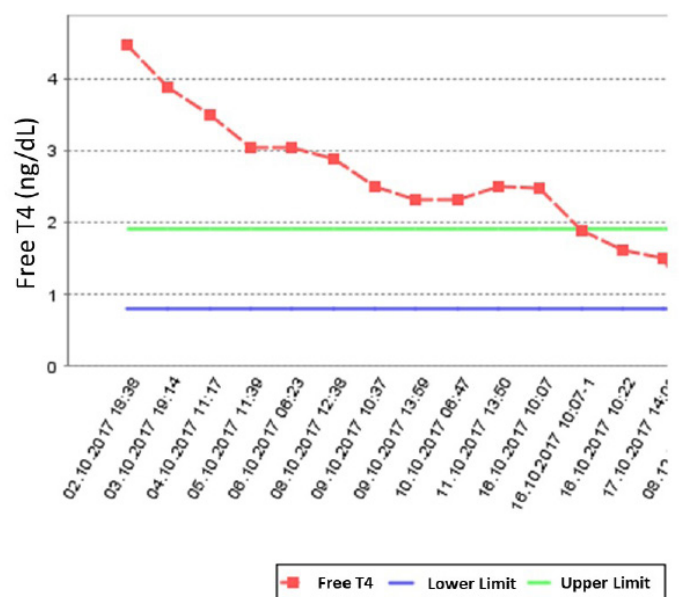


Figure 3. The fT4 levels of case 2 before and after TPE

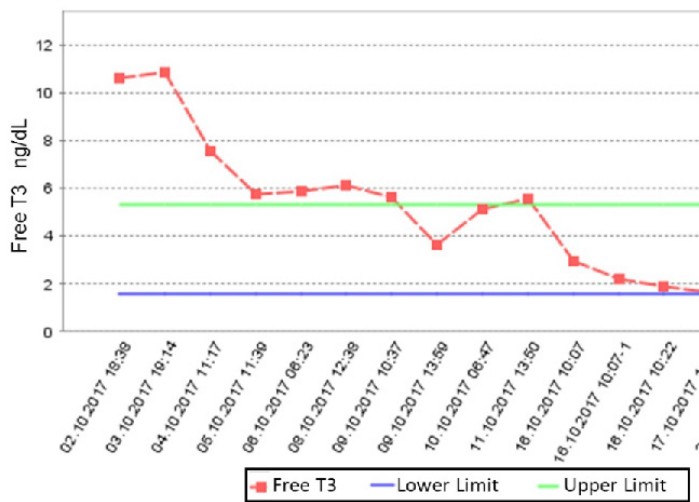


Figure 4. The fT3 levels of case 2 before and after TPE

Discussion

Antithyroid drugs, total thyroidectomy and radioactive iodine ablation are three conventional treatment modalities for the treatment of thyrotoxicosis [2]. In a patient with thyrotoxicosis, an euthyroid state should be achieved or the thyroid hormone levels should be decreased maximally, to minimize the risk of thyroid storm during surgery [8].

If the euthyroid state is not achieved, mortality associated with surgery can be up to 46%. Thyroid surgery should be considered for cases of thyrotoxicosis resistant to antithyroid drugs, and/or complicated with end organ failure that has not responded to the antithyroid drugs and appropriate treatments [9].

Lugol solution, glucocorticoids, lithium carbonate, beta blockers and radio contrast agents are therapeutic options for perioperative preparation of thyrotoxic patients. Sometimes all of these options can fail to achieve euthyroid state, immediately before surgery. TPE may be considered as a rescue treatment option before surgery in this condition, however, its effect is transient and it can not be used as definitive therapy.

Our two patients were considered eligible for TPE because other treatment options failed to achieve an euthyroid state and there was no evident contraindication for TPE, such as hemodynamic instability, active infection, bleeding tendency or allergic reaction to albumin [10].

When using TPE as a rescue therapy before thyroidectomy in thyrotoxic patients, the timing for plasma exchange, the type of replacement fluid used, and the number of sessions needed before surgery have to be considered [11]. The number of sessions and the result of every session differ from patient to patient.

AIT is an uncommon cause of serious thyrotoxicosis. Little is known about the role of TPE in the treatment of severe AIT, because of the rare occurrence of this condition. Ling Zhu et al. have described a case of type-2 AIT who achieved normal fT3 levels after 2 sessions of TPE [11]. However, in the present case, only 34 and 36% decrease were achieved after two sessions of TPE, in fT4 and fT3 levels.

We used albumin for the replacement of plasma for both patients, because we thought that albumin would increase the binding of free thyroid hormones. However, in most case reports, fresh frozen plasma has been used for this purpose, due to its ability to increase the concentration of thyroglobulin to bind free thyroid hormones [11]. Whether the use of albumin or fresh frozen plasma is more effective in reducing thyroid hormone levels after TPE is not well understood and should be evaluated further.

Recently, in a study including 46 patients (87% with Graves' disease and 13% with AIT and toxic nodular goiter), Simsir et al. found a significant decrease in fT4 levels after TPE. While 40 patients with Graves' disease were treated with TPE for an average of 4 sessions, 6 patients with thyrotoxicosis other than Graves' disease were treated with TPE for an average of 3 sessions. In their study, no significant difference was found between the two groups in terms of the number of TPE sessions [12]. However, the number of patients with AIT in their study was too low to make a comment on this issue.

The disease group in which TPE is most effective is autoimmune diseases. Therefore, as an autoimmune disease, Graves' disease is expected to benefit significantly from TPE. The results of case 2 in this paper supports this argument as a 45 and 72% decrease were achieved in fT4 and fT3 levels, respectively. Nevertheless, some cases of Graves' disease unresponsive to TPE have been reported. Guillermo E. et al. described a patient with Graves' disease who did not achieve a decrease in fT3 and fT4 levels after 2 sessions of TPE [13]. It is still unclear why some patients achieve the maximum benefit from TPE, regardless of the etiology, while some others did not respond. Up to date, it is not clear which factors are responsible for determining the patient's response to TPE. Now, it is believed that the levels of fT4, fT3 and anti thyroid antibodies is a good initial way to approach the problem. If no change is noted in the levels of fT4 and fT3 six hours after the first session of TPE, there is no justification for an additional TPE session [13].

TPE is indicated as a bridge therapy before surgery for patients unresponsive to medical therapy for thyrotoxicosis, and is an option for the prevention of thyroid storm. In our first case thyrotoxicosis was due to AIT and TPE achieved only 35% decrease in plasma thyroid hormone levels, but it was still a good result before surgery. If euthyroid state is not possible to achieve, decreasing plasma thyroid hormone levels, as low as possible, may prevent the development of thyroid storm during surgery.

Conclusion

Plasmapheresis is a therapeutic procedure that is successfully used in the treatment of thyrotoxicosis in selected patients who need more rapid hormonal control, and who develop complications associated with anti-thyroid drugs.

Although the first case with AIT achieved a temporary decrease in thyroid hormone levels, it did not provide a significant decrease in thyroid hormone levels before surgery. But in the second case with Graves' disease, euthyroid state was achieved almost after one session of TPE.

Most of the studies evaluating the efficacy of TPE in patients with thyrotoxicosis are including patients with Graves' disease and toxic

multinodular goiter, and TPE was indicated as an effective option for preparation of these patients for surgery. However, as presented in case 1, TPE may not be effective in patients with AIT as much as in patients with Graves' disease. Further studies should be carried out to address the effect of TPE in patients with AIT.

Competing interests

The authors declare that they have no competing interest

Financial Disclosure

The financial support for this study was provided by the investigators themselves.

Ismail Yildiz ORCID: 0000-0002-4990-0216

Gulsah Elbuken ORCID: 0000-0002-0920-6895

Tugay Atasever ORCID: 0000-0002-3174-1050

Sibel Ozkan Gurdal ORCID: 0000-0001-5649-6699

Sayid Zuhur ORCID: 0000-0001-8084-848X

References

1. Braverman L, Utiger R. Introduction to thyrotoxicosis. In: Braverman L, Utiger R eds. *The Thyroid*. 9th ed. Philadelphia: Lippincott Williams & Wilkins; 2005;453-5.
2. Bahn Chair RS, Burch HB, Cooper DS, et al. Hyperthyroidism and other causes of thyrotoxicosis. Management guidelines of the American thyroid association and American association of clinical endocrinologists. *Thyroid*. 2011;21:593-646.
3. Goldschlager N, Epstein AE, Naccarelli G, et al. Practical guidelines for clinicians who treat patients with amiodarone. Practice Guidelines Subcommittee, North American Society of Pacing and Electrophysiology. *Arch Intern Med*. 2000;26;160:1741-8.
4. Kennedy RL, Griffiths H, Gray TA. Amiodarone and the thyroid. *Clin Chem*. 1989;35:1882-7.
5. Newman CM, Price A, Davies DW, et al. Amiodarone and the thyroid: A practical guide to the management of thyroid dysfunction induced by amiodarone therapy. *Heart*. 1998;79:121-7.
6. Fischli S, Lucchini B, Müller W, et al. Rapid preoperative blockage of thyroid hormone production / secretion in patients with Graves' disease. *Swiss Med Wkly*. 2016;14;146:14243.
7. Restrepo CA, Márquez E, Sanz MF. Plasmaféresis terapéutica, tipos, técnica e indicaciones en medicina interna. *Acta Med Colomb*. 2009;34:23-32.
8. Baeza A, Aguayo J, Barria M, Pineda G. Rapid preoperative preparation in hyperthyroidism. *Clin Endocrinol*. 1991;35:439-42.
9. Scholz GH, Hagemann E, Arkenau C, et al. Is there a place for thyroidectomy in older patients with thyrotoxic storm and cardiorespiratory failure? *Thyroid*. 2003;13:933-40.
10. Mokrzycki MH, Kaplan AA. Therapeutic plasma exchange complications and management. *Am J Kidney Dis*. 1994;23:817-27.
11. Zhu L, Zainudin SB, Kaushik M, et al. Plasma exchange in the treatment of thyroid storm secondary to type II amiodarone-induced thyrotoxicosis. *Endocrinol Diabetes Metab Case Rep*. 2016;160039.
12. Simsir IY, Ozdemir M, Duman S, et al. Therapeutic plasmapheresis in thyrotoxic patients. *Endocrine*. 2018;62:144-8.
13. Guzmán GE, Bautista DF, Arango LG, et al. Therapeutic plasmapheresis in patients with thyrotoxicosis. Report of Two Cases. *Rheumatology*. 2015;5:162.