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THYROID STORM AND THERAPEUTIC PLASMA EXCHANGE. CASE REPORT

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Palabras clave: Tirotoxicosis; Plasmaféresis; Crisis tiroidea.

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RESUMEN

Introducción. La tormenta tiroidea es una afectación orgánica severa que se produce por la liberación de triyodotironina (T3) y tiroxina (T4). Su incidencia es de 0.20 casos por cada 100 000 habitantes y puede conllevar a una mortalidad de hasta el 30%. Esta es una entidad refractaria para la cual existen pocas opciones terapéuticas, siendo la terapia de intercambio plasmático una estrategia potencialmente útil para su manejo.

Presentación del caso. Paciente femenina de 17 años quien ingresó al servicio de urgencias de una institución de tercer nivel de atención por un cuadro clínico de aproximadamente 25 días de evolución consistente en palpitaciones, disnea en reposo, ortopnea, dolor torácico y abdominal, astenia, adinamia, mareo, cefalea y deposiciones líquidas; como antecedentes presentaba hipertiroidismo en manejo ambulatorio. Dada la sintomatología y gracias a que se obtuvo un puntaje de 65 en la escala de Burch-Wartofsky, se diagnosticó tormenta tiroidea, se dio orden de hospitalización y se inició manejo farmacológico, con el cual no se logró una mejoría. Al tercer día de hospitalización la joven presentó deterioro clínico continuo y un episodio convulsivo, por lo que se consideró tormenta tiroidea refractaria que fue tratada satisfactoriamente con terapia de intercambio plasmático como terapia puente previo a tiroidectomía total de urgencia.

Conclusión. La terapia de intercambio plasmático permite una rápida remoción de las hormonas tiroideas y, aunque su implementación no es ampliamente difundida por las guías de práctica clínica, existe evidencia que demuestra una disminución en el riesgo de complicaciones perioperatorias y una evolución exitosa tras su uso como terapia puente previo a tiroidectomía en pacientes con tormenta tiroidea refractaria.

ABSTRACT

Introduction: Thyroid storm is a life-threatening condition caused by an elevated release of T3 and T4. Its incidence is 0.20/100 000 inhabitants, with reported mortality rates of up to 30%. Due to its refractory nature, few therapeutic options are available, but plasma exchange is considered a potentially useful strategy for its treatment.

Case presentation: A 17-year-old female patient was admitted to the emergency department of a tertiary care institution due to the onset of symptoms approximately 25 days before consultation, consisting of palpitations, dyspnea at rest, orthopnea, chest and abdominal pain, asthenia, adynamia, dizziness, headache, and liquid stools. In addition, the patient had a history of hyperthyroidism treated on an outpatient basis. Thyroid storm was diagnosed considering the symptoms and a score of 65 on the Burch-Wartofsky scale. As a result, the patient was admitted to the hospital, and pharmacological management was initiated, although no improvement was achieved. On the third day of hospitalization, her condition deteriorated and she had a seizure, which led to consider a refractory thyroid storm. This condition was satisfactorily treated with plasma exchange as a bridge therapy prior to emergency thyroidectomy.

Conclusion: Plasma exchange therapy allows a rapid removal of thyroid hormones. Although its implementation is not widely disseminated in clinical practice guidelines, there is evidence of a decrease in the risk of perioperative complications and a successful evolution after its use as a bridge therapy before performing thyroidectomy in patients with refractory thyroid storm.

INTRODUCTION

Thyroid storm is a rare clinical condition characterized by the excessive release of the thyroid hormones triiodothyronine (T3) and thyroxine (T4), which affects the functioning of different body systems, generating severe clinical manifestations such as seizures, cardiac arrhythmias, etc. (1,2) Its incidence is 0.2 cases per 100 000 inhabitants and is considered the most severe manifestation of hyperthyroidism based on its associated mortality rates, which can reach up to 30% if it is not recognized and treated immediately (3).

Therapeutic plasma exchange (TPE), also known as plasmapheresis, was first implemented nearly five decades ago to treat hyperthyroidism. At present, however, not all clinical practice guidelines for this disease include it as an alternative for patients in whom thyrotoxicosis has not been treated with other therapeutic measures because there are no high-quality studies evaluating its effectiveness (1,2). Still, there are reports (1-4) that show that using TPE as a rescue measure can produce good results and that it can be considered as a strategy in patients with severe clinical conditions refractory to conventional management.

The following is the case of a patient successfully treated with TPE as a bridge therapy prior to definitive surgical management with emergency thyroidectomy in the context of a thyroid storm refractory to conventional pharmacological treatment.

CASE PRESENTATION

A 17-year-old female student of low socioeconomic status from Magdalena, Colombia, was admitted to the emergency department of a tertiary care institution due to symptoms consisting of palpitations, dyspnea at rest,

orthopnea, chest and abdominal pain, asthenia, adynamia, dizziness, headache, and liquid stools for 15 days. The patient did not have a significant family history but reported hyperthyroidism that was being treated on an outpatient basis with 80mg propranolol every 12 hours and 30mg methimazole, 5mg prednisolone and 1 mg folic acid daily.

On admission, physical examination revealed tachycardia (heart rate: 142 bpm), third heart sound (S3), exophthalmos (Figure 1), class III enlarged thyroid gland with a painful goiter and grade 3 edema in lower limbs; no fever was reported, and blood pressure was 110/60 mmHg. An electrocardiogram showed sinus tachycardia.

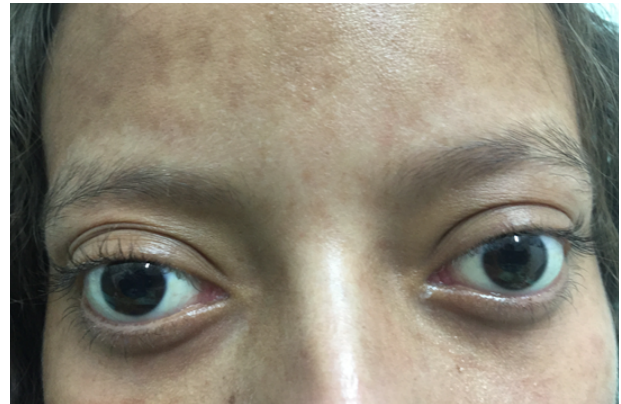


Figure 1. Exophthalmos, a common characteristic of Graves' disease.

Source: Document obtained during the study.

Based on the symptoms and a score of 65 obtained on the Burch-Wartofsky scale, her clinical condition was considered compatible with thyroid storm. Treatment was started with 7 drops of Lugol's iodine every 8 hours during the first 24 hours and then 7 drops daily plus 20mg methimazole every 8 hours, 80mg of propranolol every 8 hours, 100mg cholestyramine IV every 8 hours and 100mg hydrocortisone IV every 8 hours. No clinical improvement was observed for 48 hours. On

the third day of admission, the patient had decreased consciousness and severely elevated blood pressure. Propranolol was discontinued and 1 mg/min intravenous labetalol was administered for 24 hours. Also, on the third day of hospital stay, the patient's condition deteriorated and had a convulsive episode that was controlled with intravenous benzodiazepine; no additional electrolyte or metabolic alterations were reported at that time.

Considering that the patient had a thyroid storm refractory to medical treatment, on the fourth day of hospitalization it was decided to initiate TPE as a bridge therapy prior to total

emergency thyroidectomy. Following the first and only plasmapheresis session, a significant decrease in thyroid hormone levels was achieved and no associated complications were observed (Table 1). The results achieved allowed for the discontinuation of labetalol, the reduction of blood pressure, and the improvement of her neurological status. Consequently, the patient underwent total thyroidectomy the next day with no complications. The young woman progressed satisfactorily and was discharged on day 16 of hospitalization with an indication of outpatient treatment with 100mcg levothyroxine daily and 600mg calcium carbonate every 6 hours.

Table 1. Free thyroxine levels during hospitalization and therapeutic plasma exchange and thyroidectomy.

| Days of hospital stay | 1 | 2 | 3 * | 4 | 5 † | 6 | 7 | 8 | 9 | 10 | 11 |
|---|---|-----|-----|-----|-----|----|-------|------|-------|------|------|
| Free thyroxine (reference value: 0.9-2.3 ng/dL) | | 320 | 100 | 100 | 85 | 85 | 79.67 | 37.4 | 19.94 | 12.6 | 9.56 |

* First day of therapeutic plasma exchange.

† Day of emergency thyroidectomy.

Source: Own elaboration.

Pathology results showed multinodular goiter associated with thyroiditis without malignancy. The patient was monitored by telephone one month after discharge and she reported a reduction in symptoms and adequate adherence to the proposed pharmacological therapy.

DISCUSSION

Thyroid storm can be triggered by stressful conditions including surgical procedures, infections, trauma, Graves' disease, Hashimoto's thyroiditis, molar pregnancy, use of drugs such as amiodarone, or discontinuation of antithyroid treatment in patients with hyperthyroidism (4,5); none of these conditions was identified as a trigger in the case described.

When blood concentrations of thyroid hormones increase, they are more bound to specific receptors (T3 and T4) and interact with segments of nucleic acid that stimulate genetic expression on various tissues and the appearance of multiple clinical manifestations, particularly fever, cardiovascular dysfunction due to tachycardia, atrial fibrillation, and supraventricular arrhythmia. This condition may also cause neurological manifestations such as insomnia, psychosis, confusion, delirium, or seizures; gastrointestinal disorders such as vomiting, diarrhea, or abdominal pain; and other systemic disorders such as liver failure, kidney failure, and disseminated intravascular coagulation (4,5). Although the patient described here presented with many of these manifestations, it is noteworthy that

her neurological symptoms were severe and persisted after implementing and exhausting the available therapeutic options.

As described by Baena *et al.* (6), in 1993 Burch and Wartofsky developed a scale to estimate the probability of developing a thyroid storm according to some clinical features. This tool was successfully implemented in the reported case. Once diagnosed, the management of thyroid storm refractory to pharmacological treatment consists of the administration of propylthiouracil, methimazole, propranolol, radioactive iodine, or emergency thyroidectomy (7). It is important to keep in mind that even though surgical management is an option, the patient should be in the best possible condition before undergoing thyroidectomy, which means considering non-pharmacological interventions to control persistent symptoms and reduce circulating levels of thyroid hormones to the lowest possible concentrations to also reduce the risk of perioperative complications.

In response, TPE was proposed as an adjuvant treatment for refractory thyroid storm in 1970. This strategy helps to control thyrotoxicosis and significantly reduces the risk of perioperative complications, favoring its use as a bridge therapy for emergency thyroidectomy (2). The mechanism of action of TPE acts by removing T3 and T4 hormones that are bound to albumin, plasma proteins and transthyretin, thus balancing the amounts of the hormone in the extravascular and intravascular space. This technique also reduces the number of antibodies that stimulate thyroid hormone release in cases of Graves' disease and the concentration of catecholamines and cytokine 3.

Several studies have shown that TPE can decrease plasma thyroid hormone concentrations by up to 85% in 24 hours, demonstrating that this is an excellent alternative for patients who have been refractory to other conventional therapies, including those with subacute

thyroiditis in whom antithyroid drugs are not useful and require corticosteroids (3,7-9).

Although refractory thyroid storm has not been described in the literature, TPE is a viable option to consider when all first-line treatment options fail and progressive clinical deterioration, characterized by heart failure, uncontrolled arrhythmia and/or neurological involvement, occurs, as was the case of the reported patient (8,9). According to authors such as Padmanabhan *et al.* (9), Yamamoto *et al.* (10) and Simsir *et al.* (11), since TPE was introduced as an adjuvant treatment for thyroid storm, more than 300 cases in which TPE was implemented have been reported worldwide. Moreover, in 41.3% of those patients, the use of this therapy was supported by the lack of response to pharmacological management, while in 87% of them, the therapy served as a bridge for total thyroidectomy (11-12).

This information has been the basis of the American Society for Apheresis (ASFA) for considering the use of TPE in the treatment of thyroid storm refractory to pharmacological management, establishing it as a grade 3 recommendation (7-9). Padmanabhan *et al.* (9) recommended 3 to 6 sessions based on the response observed. However, it is worth highlighting that in the case described here, a single session was required to stabilize the patient sufficiently to be taken to emergency thyroidectomy, obtaining a good postoperative course. This is relevant because additional sessions at a cost of approximately 204 USD each were avoided (2016). Potential associated risks such as hypocalcemia, air embolism or allergy to the implemented components were also avoided.

Consequently, the present case highlights the importance of considering TPE as part of the treatments available for patients with thyroid storm associated with severe symptoms that are refractory to pharmacological management

according to current clinical practice guidelines (12). It also describes a successful experience in which a single plasmapheresis session managed to clinically stabilize the patients, so that she could undergo emergency thyroidectomy and have an adequate postoperative course. Thus, it is evident that this is a field of research that requires further studies to consolidate with better evidence the benefits of TPE as a rescue measure in patients with thyroid storm.

CONCLUSION

This is the case of a patient with severe thyroid storm who was successfully treated with TPE as bridge therapy prior to total thyroidectomy. Given the results, it is concluded that this therapy could be considered in patients refractory to pharmacological management in order to rapidly decrease circulating levels of thyroid hormones prior to surgery.

ETHICAL CONSIDERATIONS

For the preparation of this case report, the patient signed an informed consent form, authorizing the publication of her pictures and clinical information.

CONFLICT OF INTEREST

None stated by the authors.

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