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OPIS PRZYPADKU CASE REPORT



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# A case of an (a)typical course of thyrotoxic storm

## Przypadek (a)typowego przełomu tarczycowego

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thyroid storm, thyroid crisis, hyperthyroidism

**Słowa kluczowe**
przełom tarczycowy, kryza tarczycowa, nadczynność tarczycy

Summary

Thyroid storm is a life-threating exacerbation of the hyperthyroid state, first described in 1926, that is combined with disturbances in function of one or more organs. Thyroid surgery, infection, radioiodine therapy, iodinated contrast dyes, withdrawal of anti-thyroid drug therapy, diabetic ketoacidosis, hypoglycemia and trauma could be the precipitating factors. The accurate incidence of thyroid storm is difficult to determine due to the variability in diagnostic criteria. The available scoring system is based on the clinical criteria. Typically, the patient suspected of thyroid storm has fever, usually accompanied by gastrointestinal, cardiovascular or neurologic symptoms. There are no laboratory criteria to diagnose thyroid storm, although patients have some findings consistent with thyrotoxicosis. The levels of thyroid hormones are highly elevated or similar to those in uncomplicated hyperthyroidism. Three components of the thyroid storm therapy are very important to decrease mortality which is high in this condition: correcting the hyperthyroidism, normalizing the decompensation of homeostatic mechanisms and treating the coexisting illnesses.

Streszczenie

Przełom tarczycowy to zagrażający życiu stan, po raz pierwszy opisany w 1926 roku, związany z dekompensacją czynności tarczycy, podczas którego dochodzi do niewydolności jednego lub kilku narządów. Chirurgia tarczycy, zakażenia, leczenie jodem radioaktywnym, jodowe środki kontrastowe, nagłe przerwanie leczenia tyreostatykami, kwasica cukrzycowa, hipoglikemia oraz uraz mogą być czynnikami wyzwalającymi. Dokładna ocena częstości występowania przełomu tarczycowego jest trudna do określenia z powodu zmienności kryteriów diagnostycznych. Jego rozpoznanie opiera się na kryteriach klinicznych. Zazwyczaj pacjent z podejrzeniem przełomu tarczycowego gorączkuje, zwykle występują objawy ze strony przewodu pokarmowego, sercowo-naczyniowe lub neurologiczne. Nie istnieją laboratoryjne kryteria pozwalające rozpoznać przełom tarczycowy, chociaż pacjenci mają odchylenia typowe dla nadczynności tarczycy. Stężenia hormonów tarczycy są znacznie podwyższone lub zbliżone do wartości stwierdzanych w niepowikłanej nadczynności tarczycy. Trzy elementy terapii przełomu tarczycowego są bardzo istotne, aby obniżyć śmiertelność, która jest wysoka w tej jednostce chorobowej: terapia nadczynności tarczycy, osiągnięcie homeostazy ustrojowej i leczenie chorób współistniejących.

**Conflict of interest**
**Konflikt interesów**
None
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## INTRODUCTION

Thyroid storm (thyrotoxic storm, thyrotoxic crisis) is a rare life-threatening emergency that, despite of medical progress, remains a diagnostic and therapeutic challenge. It is generally observed among patients with Graves' disease, but also with nodular goiter. Early detection of hyperthyroidism, due to increased availability of thyroid function tests and improved preoperative thyroid surgery management has led to marked reduction in the number of thyroid storm cases. The accurate incidence of thyroid storm is difficult to determine due to the variability in diagnostic criteria. Only 1-2% of hyperthyroid cases manifest as thyroid storm but the mortality ranges from 20 to 30%, despite treatment used. Thyroid storm occurs rapidly in hours or progressively in few days. Its most common precipitating cause is non-compliance with prescribed anti-thyroid treatment. Other precipitating factors include infection, radioiodine therapy (that happened to our patient), withdrawal of anti-thyroid drugs, trauma, cerebrovascular events, diabetic ketoacidosis, toxemia of pregnancy and severe emotional stress (1-7).

## CASE REPORT

57-year old woman was admitted to our clinic in August 2014, due to 6-day continuous fever up to 41°C, without any response to treatment with antipyretics (ibuprophen and metamizole) and antibiotic (cefuroxime) given for 4 days prior to the admission. The fever was accompanied by general weakness, dizziness and tremors occurring periodically. Patient denied any signs of infection, diarrhea, abdominal pain, profuse sweating, heat intolerance, irritability and loss of weight. At admission patient was in average general condition, conscious, with preserved verbal contact, periodically confused, febrile (41°C), with blood pressure of 160/90 mmHg, regular heart rate 110/min, skin of fine texture, dry, velvet and gleaming. Periodical muscle tremor was observed. Lung auscultation was correct, abdomen physical examination presented no deviation, and there were no signs of peripheral edema. The laboratory tests revealed leukocytosis with neutrophilia, without anemia or thrombocytopenia, normal inflammatory parameters (CRP – 1.9 mg/L, ESR – 11 mm/hr, procalcytonin concentration within normal range). Deviations in lab tests found at the admission were: slightly elevated liver enzymes (GOT > GPT) without features of cholestasis, elevated creatine kinase (CK – 2610 U/L), lactate dehydrogenase (LDH – 476 U/L), hyponatremia (125 mmol/L), hypokalemia (2.6 mmol/L) and hyperglycemia. Serum TSH concentration was slightly decreased (0.13 $\mu$IU/mL, n: 0.55-4.78). Chest X-ray revealed no pathology and abdominal USG showed the deposit in the gall bladder without other irregularities.

The infectious causes of the fever, such as urinary, pulmonary and gastrointestinal tract infections, hepatitis caused by EBV, CMV, HBV, HCV, HIV infections and endocarditis were firstly excluded. Blood and sputum cultures were negative. The other suspected causes of high fever as cancer, autoimmune diseases, and neuroinfection were also excluded. Contrast-enhanced CT scans of the chest, abdomen and pelvis revealed neither abscessus nor neoplasm. A check for wide panel of antibodies allowed to exclude autoimmune disorders of connective tissue. Because of permanent, idiopathic high fever, without any significant reaction to antipyretics, and periodic impaired conciousness it was decided to use glucocorticosteroid therapy. Methylprednisolone was given intravenously at a dose of 1,000 mg daily for 3 days, followed by therapy with oral prednisolone.

The interview with patients family, who arrived a few days after admission, revealed the history of thyroid disease. In October 2011 during the hospitalization in the Department of Nephrology due to the tubulo-interstitial nephritis, hyperthyroidism has been recognized. Patient was referred to an endocrinologist and the thyreostatic therapy with metamizole and propranolol was started. The drugs were taken for one month only, and then – after measurements of serum TSH and thyroid hormones concentrations, USG of thyroid gland with fine-needle aspiration biopsy which revealed benign cytological changes in both thyroid lobes – the drugs were discontinued. In the years 2012 and 2013 serum TSH and thyroid hormones concentrations were controlled twice a year and remained within a normal range. The last control prior to hospitalization in March 2014 also showed euthyreosis.

After excluding infections, cancers, haematological and autoimmune diseases, based on the clinical observations together with a support of scoring by Wartofsky scale (> 45 points), a thyrotoxic storm was identified as a cause of high fever and of deteriorating patient's condition. It was decided to extend diagnostic procedures towards thyroid diseases, taking into consideration that iodine contrast has been given prior to CT scans. Thyroid receptor antibodies (TRAb) were found negative. Thyroid ultrasound showed nodular goiter with asymmetrically enlarged thyroid right lobe with two nodules (25 and 10 mm in the diameter). Guided fine-needle aspiration biopsy of both nodules revealed benign lesions. Succeeding thyroid function lab tests showed low serum TSH (0.05-0.10 $\mu$IU/mL) and elevated serum thyroid hormones (fT3 – 3.3-3.0 pg/mL, fT4 – 2.5-2.1 ng/mL) concentrations.

Following the treatment with glucocorticoids the patient's body temperature dropped to 38°C and a logic contact with the patient has improved. Therapy with thiamazole 80-100 mg per day, propranolol 160 mg daily and prednisone at a dose of 40 mg/day resulted in the normalization of patient's body temperature. Thyroid function tests revealed normal thyroid function. Prior to discharge from the hospital, patient's general condition was good and abnormalities observed in laboratory tests were subjects to normalization. The patient was referred to an endocrinologist.

## DISCUSSION

Thyroid storm is a rare endocrine emergency associated with high morbidity and mortality if it is not promptly recognized and treated. All clinicians should be aware of its clinical features and treatment. It might be difficult to distinguish between the thyroid storm and infection in thyrotoxic patients as tachycardia and high fever may be present in both. Thyroid crisis may be mistaken for sepsis, heat stroke, acute gastrointestinal infection or an ischemic heart disease, especially in undiagnosed thyrotoxic patients. Definitive criteria of thyroid storm published by Burch and Wartofsky are helpful to establish the diagnosis (fig. 1) (1, 4). These criteria were used in case of our patient to confirm the diagnosis of thyroid storm. The treatment of thyroid storm should not be delayed even if a disease is only a suspicion. Hyperglycemia, leukocytosis with neutropenia, hypercalcemia, elevated liver enzymes may be considered the effects of hyperthyroidism. Alkaline phosphatase activity can be increased due to high bone turnover. Serum thyroid hormone levels typically show hyperthyroidism but it needs to be remembered that due to prompt rise of thyroid hormone concentrations, secondary to precipitating factors, patients cannot be able to adapt to the sudden metabolic stress.

| Diagnostic criteria for thyroid storm by Burch and Wartofsky | |
|---|---|
| 1) Thermoregulatory dysfunction: | Scoring points |
| 38.0-38.5°C | 5 pts |
| 38.6-39°C | 10 pts |
| 39.1-39.5°C | 15 pts |
| 39.6-40.0°C | 20 pts |
| 40.1-40.6°C | 25 pts |
| > 40.6°C | 30 pts |
| 2) Central nervous system dysfunction: | |
| absent | 0 pts |
| mild (agitation) | 10 pts |
| moderate (delirium, psychosis, extreme lethargy) | 20 pts |
| severe (convulsions, coma) | 30 pts |
| 3) Gastrointestinal and hepatic dysfunction: | |
| absent | 0 pts |
| mild (diarrhoea, nausea/vomiting, abdominal pain) | 10 pts |
| severe (jaundice) | 20 pts |
| 4) Cardiovascular dysfunction: | |
| a) tachycardia (beats per min.): | |
| < 90/min | 0 pts |
| 90-109/min | 5 pts |
| 110-119/min | 10 pts |
| 120-129/min | 15 pts |
| 130-139/min | 20 pts |
| ≥ 140/min | 25 pts |
| b) congestive hart failure: | |
| absent | 0 pts |
| mild (leg edema) | 5 pts |
| moderate (bibasal rales or crackles) | 10 pts |
| severe (pulmonary oedema) | 15 pts |
| c) atrial fibrillation: | |
| absent | 0 pts |
| present | 10 pts |
| 5) Predisposing factors: in patients without or improper treatment of hyperthyreosis: infection, trauma, burgery, parturition, ketoacidosis, myocardial infarct, stroke, TIA, radioiodine therapy or iodine contrast: | |
| absent | 0 pts |
| present | 10 pts |

**Fig. 1.** Diagnostic criteria for thyroid storm (1, 4)

Treatment of thyroid storm includes correction of severe thyrotoxicosis, precipitating illness and associated active thyroid eye disease in Graves disease. All diagnosed cases should be managed with anti-thyroid drugs, beta-receptor blocking agents and iodine solution along with supportive care preferably at the intensive care unit. The patient with thyroid storm require intravenous fluid infusions because of dehydration, thioamides to block new thyroid hormone synthesis, iodine solution to stop the release of thyroid hormones and treatment with glucocorticoids because of their influence on the conversion of T4 to T3. Thioamides should be given intravenously, especially in severely ill patients. Beta-receptor blocking drugs (especially propranolol, but all β1-selective beta-adrenolytics are effective) should be used to control adrenergic symptoms. The drugs should be used cautiously in the presence of congestive heart failure. Among thioamides, methamizole (60-120 mg/day in 4-6 doses) is preferred due to hepatotoxic effect of propylthiouracil. Iodine radio contrast, iopanoic acid, can also be used although it is not easily available. The use of SSKI (5 drops every 6 hours) or Lugol's solution (8 drops every 6 hours) as a iodine source is also recommended (1, 2, 4, 8). Glucocorticoids should be given at a dose of 300 mg of hydrocortisone intravenously, followed by 100 mg every 8 hours or dexamethasone 2 mg every 6 h (2, 4, 8).

A key point in our case is whether or not the patient really had thyrotoxicosis at the time of admission. It was difficult to establish what happened first: thyrotoxicosis in patient with high fever which has developed to thyrotoxic storm or thyrotoxic storm generated by the iodine contrast given prior to CT scans.

## CONCLUSIONS

In conclusion we would like to emphasize how extremely important is to think about thyroid storm as a possible cause of idiopathic fever, especially in patient with promptly deteriorating condition and to employ Burch and Warthofsky thyroid storm criteria to make an appropriate diagnosis.

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