

# Severe acute myxedematous psychosis; rare complication of hypothyroidism

Hasnae Guerrouj<sup>1\*</sup>, GhizlaneEnnibi<sup>2</sup>

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## ABSTRACT

**Background:** Severe acute myxedematous psychosis, or myxedema madness, is a rare and serious psychiatric complication of hypothyroidism. It is most often misdiagnosed, but it remains reversible after treatment with thyroid hormones.

**Case Presentation:** We report a case of a patient without a known past medical history who underwent total thyroidectomy for papillary thyroid carcinoma. During her withdrawal from thyroid hormone therapy to perform a diagnostic radioiodine whole-body scintigraphy, she presented with anxiety, delirium, and hallucinations, culminating in a suicide attempt. Laboratory testing revealed a high sensible-thyroid stimulating hormone (TSH) value of 35  $\mu$ IU/ml. The patient was hospitalized in a psychiatric unit, where she received antipsychotic medication and was started on thyroid hormones. After a week, there was a dramatic improvement. Psychiatric symptoms were completely gone a month later justifying the discontinuation of antipsychotics. Recombinant human TSH (rh-TSH) was necessary injected before radioiodine therapy to avoid thyroid hormone therapy suppression and to prevent a second episode of acute psychosis.

**Conclusion:** rh-TSH interest is both in the pre Ira therapy stimulation and for the post-treatment monitoring of patients with thyroid cancer, and helps avoiding hormonal treatment suppression.

**Keywords:** Myxedema, psychosis, hypothyroidism, carcinoma, rhTSH.

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Correspondence to: Hasnae Guerrouj

\*Nuclear Medicine Department, Faculty of Medicine and Pharmacy, University Mohammed V, Rabat, Morocco.

Email: [guerroujh@yahoo.fr](mailto:guerroujh@yahoo.fr)

Full list of author information is available at the end of the article.

## Background

Hypothyroidism is a common disorder [1], primarily caused by Hashimoto's thyroiditis in women and iatrogenic factors: interfering drugs with thyroid function, post-surgical, Post-external-beam radiation therapy, or after radioiodine therapy. Other less frequent etiologies are represented by a lack of thyroid stimulation by thyroid-stimulating hormone (TSH) (secondary or central hypothyroidism) [2].

Hypothyroidism can have different, but serious, consequences if not treated. The most common symptoms are mainly represented by cold intolerance, fatigue, menstrual disorders, edema, constipation, weight gain, change in voice, etc.

The predominant affective disorder experienced is depression [3] and sometimes more severe mental disorders such as delirium, hallucinations, persecuting, or even suicidal ideas are experienced. This serious form of acute psychosis when associated with myxedema is known as "myxedema madness" [4,5]. However, there is no correlation between the degree of hypothyroidism and the appearance of its psychiatric signs [6].

We report a case of myxedematous psychosis in a patient who has developed mental disorders as a result of hypothyroidism induced by thyroid hormone withdrawal for 3 weeks to perform diagnostic whole-body scintigraphy with iodine 131. We will discuss treatment possibilities in this case and strategies to avoid these serious complications of hypothyroidism.

## Case Presentation

We have been following a 51-year-old woman since 2016 for papillary thyroid cancer. She underwent a total thyroidectomy without lymph node dissection for multinodular goiter.

Initial whole-body scintigraphy with iodine 131 for the first time was requested after thyroid hormone therapy suppression. On the 15th day of withdrawal, the patient suffered from sleep disorders as well as persecuting ideas towards her children, anguish, and strong anxiety. the scan appointment has been maintained. On the day of the scan, after 3 weeks of withdrawal, high sensible-TSH was 35  $\mu$ IU/ml (normal values: 0.2-4  $\mu$ IU/

ml). The patient refused the exam and tried to run away from the hospital. She was very aggressive, and the scan was therefore not performed. Her son reported that she tried to throw herself out of the car on their way home from the hospital. The patient had an emergency psychiatric consultation and was hospitalized due to the severity of the symptoms.

Psychiatric assessment found intense aggressiveness and delirium with hallucinations. Physical examination revealed facial and body edema, hoarse voice, and bradycardia. She was put in isolation, and an antipsychotic treatment was implemented urgently. At the same time, it was decided to put her back on levothyroxine at a dose of 100 µg per day for 5 days, then 150 µg, and then 200 µg per day continuously. There was a considerable improvement after 1 week of treatment and a full resolution of symptoms after 1 month. Afterward, the psychiatrist decided to stop antipsychotic drugs.

The diagnosis of “myxedematous madness” was made based on the absence of psychiatric history, the clinical and biological hypothyroidism, the acute and severe onset of psychiatric signs, and finally the reversibility of symptoms after the reintroduction of thyroid hormones.

The patient received subsequently radioiodine therapy after injection of recombinant human TSH (rhTSH) to avoid thyroid hormone withdrawal and to prevent a similar second episode.

After 4 years of follow-up, the patient is in complete remission of her thyroid carcinoma. Thyroglobulin is undetectable with negative anti-thyroglobulin antibodies and normal cervical ultrasound. Her mental state is normal.

## Discussion

Severe acute myxedematous psychosis or “myxedematous madness” is a rare entity [7]. The first case of myxedema with psychiatric disorders was observed at the beginning of the 19th century. It was “Asher” who introduced the term “Myxedema Madness” in 1949, to describe severe mental disorders complicating hypothyroidism [8]. Every patient with no psychiatric history presenting with psychotic features and signs or symptoms suggestive of hypothyroidism should have a TSH testing [8]. When hypothyroidism is confirmed, urgent treatment with thyroid hormones should be initiated, as it results in complete resolution of the symptoms [9].

The underlying pathophysiology of the link between psychosis and hypothyroidism is still unclear. Bauer et al. [10] investigated cerebral glucose metabolism of hypothyroid patients using positron emission tomography coupled with computed tomography before and after levothyroxine replacement therapy. They found a decrease in metabolic activity in several brain regions compared to healthy controls. In addition, cerebral glucose metabolism returned to normal after levothyroxine treatment. Thvilum et al.

[11] indicated that hypothyroidism is associated with an increased prevalence of psychiatric morbidity. Although hypothyroidism is mainly associated with depression, other psychiatric manifestations include delusions, visual, and auditory hallucinations. Suicide attempts have been reported, as is the case with our patients. Many authors have reported that in cases of myxedematous psychosis, the clinical signs of hypothyroidism preceded psychosis by several months or years. Few cases have been observed in the course of acute hypothyroidism as is the case for our patient [12].

As soon as the diagnosis of myxedematous psychosis is established, thyroid hormone therapy must be initiated. Symptoms usually disappear about a week after starting a good thyroid hormone substitution. Stowell and Barnhill [13] recommended treatment with 100 µg of T4 intravenously combined with oral risperidone. They reported that, on the 6th day of treatment, their patient no longer presented symptoms of mania. Our patient initially received a dose of 100 µg of T4 per day orally, which was gradually increased to 200 µg per day. As in most reported cases, our patient was also treated with antipsychotic medication. However, this therapy was interrupted shortly afterward by her psychiatrist, given the improvement in her mental state.

Recombinant TSH remains an alternative for thyroid cancer patients with a history of severe acute myxedematous psychosis since it allows stimulation of TSH without having to discontinue thyroid hormone therapy. The routine use of this molecule is limited by its cost. However, this could be compensated by the improvement in the quality of life of the patients [14-16]. Indeed, it has been established that in the therapeutic setting, rhTSH is the only option in patients with hypopituitarism, ischemic heart disease, history of myxedematous psychosis, impairment due to advanced disease, and in the case of continued thyroxine production by thyroid remnant or metastatic tumor [14-16].

The present clinical case illustrates the problem associated with thyroid hormone withdrawal and the usefulness of recombinant TSH as an alternative before radioiodine therapy given the psychiatric episode. Thyroglobulin and anti-thyroglobulin antibodies were undetectable, which did not justify thyroid hormone withdrawal in further follow-up.

## Conclusion

Severe acute myxedematous psychosis complicating hypothyroidism, or “myxedematous madness” is a rare entity that can have serious consequences if not diagnosed and treated emergently. Patients presenting with hypothyroidism and psychiatric disorders should receive thyroid hormones as soon as possible. Whatever the degree of the signs, it is the only treatment that provides reversibility of symptoms. It is also recommended to use of recombinant TSH in thyroidectomized patients

with well-differentiated thyroid carcinoma before radioiodine therapy and in the follow-up, especially in cases with a history of acute psychosis associated with hypothyroidism.

**List of Abbreviations**

rh-TSH Recombinant human thyroid stimulating hormone

**Conflict of interest**

The authors declare they have no conflict of interest regarding the publication of this case report.

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**Consent for publication**

Written informed consent was obtained from the patient.

**Ethical approval**

Ethical approval is not required at our institution to publish an anonymous case report.

**Author details**

Hasnae Guerrouj<sup>1</sup>, GhizlaneEnnibi<sup>2</sup>

1. Nuclear Medicine Department, Faculty of Medicine and Pharmacy, University Mohammed V, Rabat, Morocco
2. Oncology Centre of Hospital Hassan II, Agadir, Morocco

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**Summary of the case**

1	<b>Patient (gender, age)</b>	Female; 51 years old.
2	<b>Final diagnosis</b>	Myxedematous psychosis
3	<b>Symptoms</b>	Psychiatric assessment found intense aggressiveness and delirium with hallucinations. Physical examination revealed facial and body edema, hoarse voice, and bradycardia.
4	<b>Medications</b>	An antipsychotic treatment urgently and the levothyroxine at a dose of 100 µg per day for 5 days, then 150 µg, and then 200 µg per day continuously.
5	<b>Clinical procedure</b>	Radioiodine therapy after injection of rh-TSH. After 4 years of follow-up, the patient is in complete remission of her thyroid carcinoma. Her mental state is normal.
6	<b>Specialty</b>	Nuclear medicine