

Hypothyroidism-Induced Psychotic Disorder with Prolonged Antipsychotic Treatment: A Case Report

Длительное лечение антипсихотиками индуцированного гипотиреозом психотического расстройства: клинический случай

doi: 10.17816/CP15671

Case report

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ABSTRACT

BACKGROUND: Hypothyroidism, a common thyroid disorder, is typically associated with affective and cognitive symptoms. However, up to 15% of patients may also present psychotic symptoms, which represents a relatively rare and poorly understood manifestation. Existing literature on this condition consists primarily of isolated case reports, which describe short courses of antipsychotic treatment. In contrast, the present case illustrates a prolonged and more complex trajectory, contributing to a better understanding of the psychiatric presentations of hypothyroidism and their management.

CASE PRESENTATION: We report the case of a 42-year-old man hospitalized for violent behavior toward others and overt psychotic symptoms in untreated hypothyroidism. Tests revealed elevated thyroid-stimulating hormone levels of 34.925 mIU/L. Clinical evaluation confirmed significant psychiatric disturbance necessitating inpatient care. A diagnosis of secondary psychotic disorder due to hypothyroidism was established. The patient required prolonged antipsychotic treatment, and an initial attempt to discontinue treatment was unsuccessful. A second withdrawal attempt made several months later was successful, with full recovery and complete remission of symptoms. This remission was maintained despite recurrent thyroid-stimulating hormone level elevation, while thyroxine hormone levels remained within the normal range.

CONCLUSION: This case illustrates the importance of ruling out non-psychiatric medical causes in the differential diagnosis of psychiatric symptoms. It also highlights the need for individualized treatment plans and sustained follow-up, particularly in rare and poorly understood conditions for which no formal guidelines or standardized management protocols exist.

АННОТАЦИЯ

ВВЕДЕНИЕ: Гипотиреоз — распространенное заболевание щитовидной железы, часто сопровождающееся аффективными и когнитивными нарушениями. Однако примерно у 15% пациентов заболевание может также проявляться психотическими симптомами. Это относительно редкое и малоизученное проявление гипотиреоза. На данный момент публикации, посвященные данному феномену, ограничиваются описанием отдельных клинических случаев, в которых преимущественно рассматривается краткосрочное применение антипсихотических препаратов. В отличие от ранее опубликованных, представленный случай демонстрирует более продолжительный и сложный клинический сценарий, что позволяет глубже изучить психические проявления гипотиреоза и оптимизировать подходы к терапии.

ОПИСАНИЕ КЛИНИЧЕСКОГО СЛУЧАЯ: Авторы описывают случай 42-летнего пациента, госпитализированного с гетероагрессией и выраженными психотическими симптомами, которые развились на фоне нелеченого гипотиреоза с повышенным уровнем тиреотропного гормона (ТТГ) (34,925 мМЕ/л). Клиническое обследование подтвердило наличие серьезного психического расстройства, потребовавшего госпитализации. Пациенту был диагностирован вторичный психотический синдром на фоне гипотиреоза. Потребовалась длительная терапия антипсихотиками, при этом первая попытка отмены препаратов сопровождалась ребаунд-эффектом. Однако повторная попытка отмены, предпринятая спустя несколько месяцев, привела к полному восстановлению и стойкой ремиссии симптомов, даже несмотря на рецидивирующее повышение уровня ТТГ при стабильно нормальном уровне тироксина.

ЗАКЛЮЧЕНИЕ: Настоящий клинический случай указывает на важность исключения соматических причин при дифференциальной диагностике психических расстройств. Он подчеркивает необходимость длительного клинического наблюдения и индивидуализированного подхода к терапии, особенно при редких и малоизученных патологиях, в отношении которых отсутствуют официальные клинические рекомендации или стандартизированные протоколы лечения.

Keywords: *hypothyroidism; hallucinations; delusions; depression; case report*

Ключевые слова: *гипотиреоз; галлюцинации; бред; депрессия; клинический случай*

INTRODUCTION

Hypothyroidism is a common disorder, with a prevalence ranging from 0.2 to 1.3% in iodine-sufficient regions [1]. Among the psychiatric manifestations associated with hypothyroidism, cognitive and affective symptoms are the most frequently described, with estimated prevalences of approximately 27% and 60%, respectively [2, 3]. Less commonly, 5 to 15% of patients exhibit psychotic symptoms [4]. Historically, this condition was referred to as “myxedema psychosis” or “myxedema madness” [5]. The term “myxedema madness” was coined by Asher in a 1949 article describing 14 patients with myxedema and psychotic symptoms [5, 6].

This manifestation is sparsely described in the medical literature [5, 7], and no treatment guidelines are available. Clinical evidence is primarily limited to case reports, which indicate an average recovery time of about 2 weeks. Most patients require antipsychotic treatment for short periods, in addition to thyroid hormone replacement therapy. Although there is considerable heterogeneity in antipsychotic use, some patients were not treated with them at all.

Of the 75 cases included in a systematic review [7], only five required treatment longer than five months, two required 9 months, and none reached one year. In contrast, the present case involves a patient who required 12 months of antipsychotic treatment. An initial attempt to discontinue antipsychotic treatment was unsuccessful, but full symptom remission was achieved after prolonged therapy.

This case is presented under the CARE guidelines [8].

CASE PRESENTATION

Patient information

De-identified patient information and primary symptoms

We present the case of a 42-year-old Mexican man, divorced and unemployed at the time of evaluation. The patient exhibited delusional ideas of harm, persecution and guilt, accompanied by self-directed speech and passive suicidal ideation. Over time, these symptoms were compounded by apathy, loss of will (abulia) and social withdrawal, and neglect of personal hygiene. These features became prominent by July 2023. He also displayed aggressive behavior, including threatening a family member with a sharp object, which led to his psychiatric admission due to the severity of his hetero-directed aggression in August 2023.

Medical, family, and psycho-social history

The patient was diagnosed with hypothyroidism in November 2022, after nearly a year of physical symptoms, such as fatigue, weight gain, hair loss, and cold intolerance. He was prescribed levothyroxine 100 µg daily with inconsistent adherence. He had no history of surgeries, blood transfusions, allergies, or significant trauma. Family history included rheumatoid arthritis in his mother and hypothyroidism in his sister. There was no family history of mental disorders or suicide.

The patient had worked in the same administrative position for 25 years, resigning in November 2022 because

of diminished motivation and loss of interest. His history also included aggressive behavior during childhood and adolescence, directed toward both family members and partners. Depressive symptoms emerged in January 2021 in the context of financial problems and relationship issues. Occasional use of tobacco and alcohol was reported.

Relevant past interventions with outcomes

Between March and May 2023, the patient was admitted to a private clinic and treated with alprazolam and risperidone. While partial symptom relief was achieved during the stay, psychotic symptoms reappeared shortly after discharge.

Clinical findings

The patient appeared his stated age and had a mesomorphic build. He was uncooperative during the initial interview, without spontaneous speech. The patient was alert but drowsy, disoriented to time and situation, yet oriented to person and place. He answered questions in a sad tone, with decreased volume, limited verbal output, and speed.

His thought process was linear. The patient described delusions of harm and persecution. He did not report perceptual disturbances. He did not exhibit hallucinatory behavior at the time of the interview. However, he acknowledged having experienced auditory hallucinations with derogatory content in the preceding months. He described his mood as "tired". His affect was congruent and appropriate, though hypothymic and blunted. Overall mental functions appeared diminished. He was unaware of his illness.

Timeline

In Figure 1, a timeline of the patient's clinical case is presented graphically.

Diagnostic assessment

Upon admission, the initial diagnosis was schizophrenia. However, given the sudden onset of psychotic symptoms, the patient's age, and the absence of personal and family history of psychotic disorders, an underlying medical etiology was considered. Initial laboratory tests showed thyroid-stimulating hormone (TSH) levels at 34.925 mIU/L, free T₄ (FT₄) of 0.51 ng/dL and total T₄ (TT₄) of 3.05 µg/dL. During the first days of hospitalization, the patient had a score of 29 points on the Hamilton Rating Scale for Depression (HDRS), indicating severe depressive symptoms.

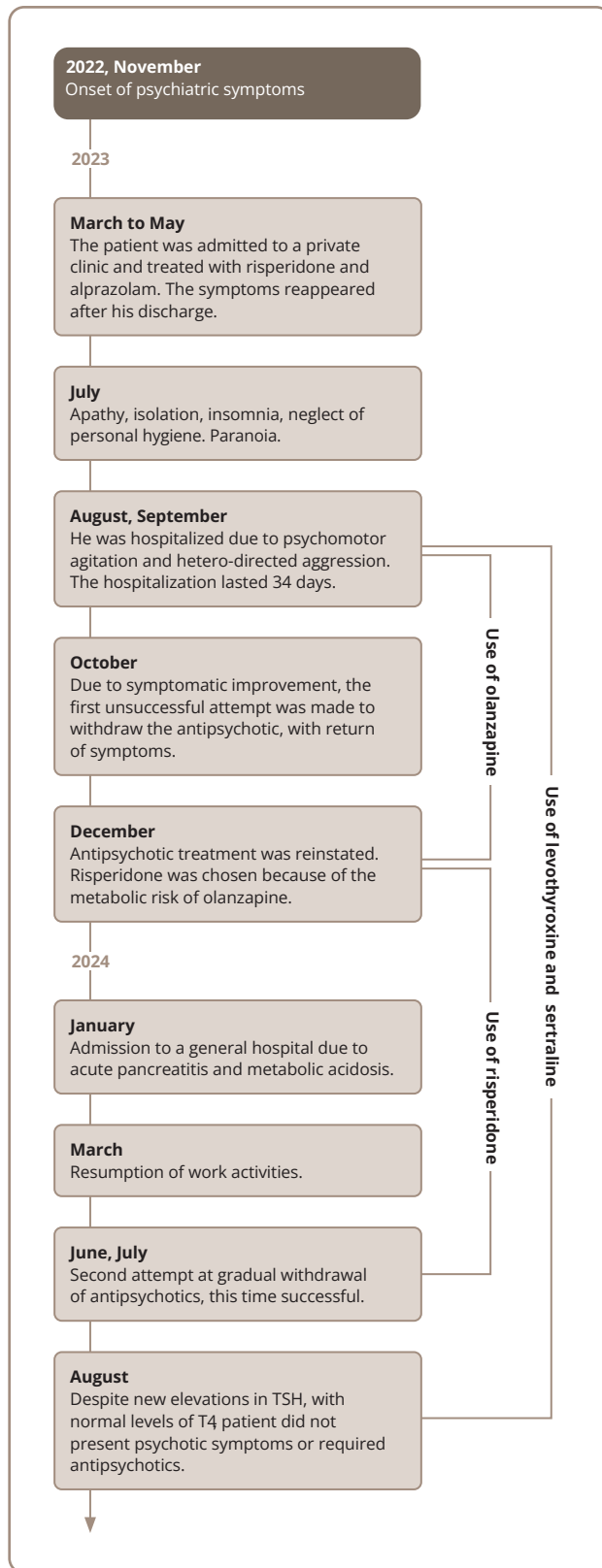


Figure 1. Clinical timeline of the patient's case.

Note: T₄ — thyroxine hormone; TSH — thyroid-stimulating hormone.

Source: López-Villa & Martín-Escoto, 2025.

Computed tomography (CT) and magnetic resonance imaging (MRI) were performed as outpatient procedures several weeks after hospitalization, as imaging services were unavailable at our center. CT revealed a thyroid nodule at the isthmus and hypotrophy of the right thyroid lobe. MRI (without contrast) showed findings consistent with the patient's age, according to the attending neurologist. An electroencephalogram (EEG) was also performed and reported within normal parameters.

Owing to diagnostic challenges, such as delayed radiologic studies and limited information, a provisional diagnosis of psychotic disorder under investigation was made, with the main hypothesis being psychotic disorder due to another medical condition (hypothyroidism).

Therapeutic interventions

The patient received pharmacologic treatment addressing both endocrine and psychiatric symptoms. In addition, he was also provided with multidisciplinary support, including assessment by internal medicine specialists, care from a nutritionist, social workers, nursing staff, and psychologists employing a cognitive-behavioral therapy approach.

Due to the significantly elevated TSH levels, levothyroxine was initiated at 150 µg daily (1.8 µg/kg/day). Likewise, olanzapine was prescribed at a dose of 10 mg per day for its sedative properties to manage psychotic symptoms and hetero-aggressive behaviour. For behavioral containment, benzodiazepine clonazepam was used at a dose 2 mg per day, and was gradually tapered prior to discharge.

For affective symptoms, the selective serotonin reuptake inhibitor (SSRI) sertraline was started at a dose of 50 mg daily. After 16 days, the dose was increased to 100 mg daily due to partial response. During the 34-day hospitalization, the patient experienced gradual improvement in psychotic and affective symptoms, with reduced social isolation, increased energy, and better interaction with family members.

Follow-up and outcomes

Clinician- and patient-assessed outcomes

During the follow-up, the patient showed a progressive reduction in affective symptoms and complete remission of psychotic symptoms. He could also reintegrate into his family life and resume caregiving responsibilities. By March 2024, the patient had returned to work and reported a good sleep pattern and functional recovery. In July 2024, he scored 4 points on the HDRS, indicating remission of affective symptoms.

Follow-up diagnostic

Serial laboratory monitoring showed a gradual decline in TSH levels (Table 1), particularly after increasing the dose of levothyroxine to 200 µg daily in March 2024. Despite a TSH level elevation in August 2024 (28.02 mIU/L), free and total T₄ levels (total 5.25 µg/dL and free 0.86 ng/dL) remained within the normal range, and no recurrence of psychotic symptoms was observed.

Intervention adherence and tolerability

The patient showed good adherence to pharmacological treatment. He tolerated levothyroxine, sertraline, and antipsychotics without significant side effects. Pregabalin (75 mg daily) was initially prescribed for sleep. A first attempt to withdraw olanzapine gradually between October and December 2023 led to recurrence of symptoms. Symptoms reappeared one week after discontinuation. The patient presented with social isolation, low energy, anhedonia, delusions of harm and insomnia. Due to this relapse, antipsychotic treatment was reinstated, with risperidone at 2 mg daily selected for its lower cardiovascular risk compared to olanzapine. Pregabalin was replaced with hydroxyzine at 25 mg daily for sleep. This adjustment led to renewed remission of psychotic symptoms.

In June 2024, a second attempt at gradual withdrawal of the antipsychotic was initiated. The dose was reduced to 1 mg, then to 0.5 mg one month later and, finally discontinued in August 2024, with a favorable clinical response. The antihistamine was also withdrawn at that time without adverse effects.

Table 1. Thyroid levels throughout patient follow-up

| Date | TSH (mIU/L) | Free T ₄ (ng/dL) | Total T ₄ (µg/dL) | Free T ₃ (pg/mL) | Total T ₃ (ng/mL) |
|------------|-------------|-----------------------------|------------------------------|-----------------------------|------------------------------|
| 27.08.2023 | 34.925 | 0.51 | 3.05 | 1.23 | 0.38 |
| 05.09.2023 | 24.429 | 0.63 | 3.92 | 1.27 | 0.41 |
| 12.10.2023 | 9.59 | 0.86 | 5.22 | 1.82 | 0.43 |
| 16.11.2023 | 8.09 | 0.59 | 3.55 | 3.09 | 0.71 |
| 15.03.2024 | 11.75 | 0.68 | 4.51 | — | 0.58 |
| 30.04.2024 | 4.59 | 0.75 | 7.61 | 2.90 | 1.06 |
| 28.08.2024 | 28.02 | 0.86 | 5.25 | 1.33 | 0.32 |
| 14.04.2025 | 9.38 | 0.73 | 5.70 | 3.11 | 1.03 |

Note: T₃ — thyroxine hormone; T₄ — thyroxine hormone; TSH — thyroid-stimulating hormone.

Adverse and anticipated events

In January 2024, the patient presented polyuria, polydipsia, polyphagia, asthenia and adynamia, prompting admission to a general hospital. He was diagnosed with acute pancreatitis and metabolic acidosis, with triglyceride levels of 8,051.8 mg/dL. He received treatment with insulin and intravenous fluids and was discharged with a new diagnosis of type 2 diabetes mellitus, dyslipidemia, and hypertension, for which he continues treatment under internal medicine supervision.

Final clinical status

By August 2024, the patient remained clinically stable with no recurrence of psychotic or affective symptoms. The patient did not require further antipsychotic treatment, maintained functional stability, and remained on sertraline at 100 mg daily. He also remained under internal medicine follow-up for hypothyroidism and associated metabolic conditions.

Informed consent

All patient-identifying data have been omitted. In August 2024, informed consent for publication was obtained from both the patient and the primary caregiver.

DISCUSSION

The present clinical case illustrates psychotic symptoms induced by hypothyroidism, a rare and poorly understood manifestation. Case characteristics — such as the sudden onset, age at presentation, and the specific nature of the delusions — are consistent with descriptions in the medical literature. Based on these features, the diagnosis of secondary psychotic syndrome (ICD-11 6E61) due to hypothyroidism (ICD-11 5A00) was established.

The clinical course of the condition is distinct from schizophrenia and psychotic depression [9], particularly considering the rapid symptomatic improvement following initiation of levothyroxine with adequate adherence. Other distinguishing features included the absence of prior psychiatric history (except for brief situational affective symptoms) and the rapid functional decline coinciding with the abrupt onset of psychotic symptoms and markedly elevated TSH levels.

This case is notable for the necessity of prolonged antipsychotic use. An initial withdrawal was unsuccessful, but the patient later achieved complete and sustained remission and functional recovery, despite subsequent TSH elevations and normal T₄ levels. It also demonstrates the difficulties

of treating rare conditions without formal guidelines, particularly regarding the duration of antipsychotic use.

The main limitation of this case is the inability to prove causality, despite the strong correlation observed between hypothyroidism and psychosis. Other limitations include the lack of objective measures of cognitive function and treatment adherence, with reliance instead on subjective reports from the patient and caregiver. This case's strengths are its long-term follow-up and structured treatment protocol.

The pathophysiology underlying psychotic symptoms in hypothyroidism remains unclear. Several hypotheses have been suggested, such as reduced cerebral metabolism [10], imbalance in tyrosine hydroxylase, altered serotonergic neurotransmission, or increased T₃ receptor density in the amygdala and hippocampus [7]. Nevertheless, thyroid hormone replacement therapy — sometimes augmented with antipsychotics — remains the cornerstone of treatment.

There are documented cases in which psychotropic medications were not used, or were only prescribed for brief periods, particularly when hypothyroidism was identified and treated early [11, 12]. Symptomatic improvement typically occurs between one week and several months following the initiation of thyroid hormone replacement therapy [13]. Notably, the severity of thyroid dysfunction does not appear to correlate directly with the presence or intensity of psychiatric symptoms [14].

The clinical literature reflects high heterogeneity in reported cases, as demonstrated in two systematic reviews. Krüger et al. reported 52 cases, noting complete remission of psychotic symptoms in 82.7% of them; 40.4% of patients did not receive antipsychotic treatment [5]. The most frequently reported symptoms were delusions, perceptual disturbances, and formal thought disorders.

In contrast, Mohamed et al. reviewed 75 cases, with a mean age of 42 years and a female-to-male ratio of 2:1. Delusional thinking, especially paranoid and persecutory delusions, was the most common clinical presentation. Antipsychotics were used in 92% of cases, typically for a median duration of 1.8 weeks, and 93% of patients achieved remission. Only two of those cases underwent treatment lasting more than 9 months [7]. To the best of our knowledge, this is the clinical case with the longest reported antipsychotic treatment duration, totaling 12 months.

Establishing causality in cases of secondary psychosis can be challenging. However, three key elements are

considered helpful in this process: atypicality, temporality, and explicability. These criteria involve: (1) recognizing atypical features such as late-onset psychosis or unusual symptoms; (2) identifying a temporal association between psychotic symptoms and an underlying medical condition; and (3) excluding primary psychotic disorders as more likely explanations. Our patient met all three criteria.

A thorough diagnostic evaluation during the first episode is essential. This includes comprehensive history-taking, careful physical examination, and appropriate laboratory and imaging studies [15]. Certain symptom patterns may also suggest secondary psychosis. A systematic review and meta-analysis reported a significant association between visual hallucinations and secondary psychosis (OR 3.0, $p < 0.001$; I^2 70%) [16].

Accurate diagnosis relies on diligent clinical investigation. Gama Marques (2020) retrospectively assessed 200 patients initially diagnosed with schizophrenia and found that 25% (50 patients) were later reclassified with a diagnosis of “organic psychosis”. The average delay to correct diagnosis was 12 years [17]. Secondary psychosis is estimated to account for approximately 11% of psychosis cases, with roughly 10 patients needing to be evaluated to detect one such case. Approximately 5% of cases are due to an underlying non-psychiatric medical condition [18].

The patient shared the following regarding his experience with treatment: *“I’m doing very well with the treatment. Thank God I’m feeling better. So far, everything has gone well. I’ve been following the treatment to the letter”*.

CONCLUSION

This clinical case illustrates the crucial need for ruling out underlying non-psychiatric medical causes of psychiatric symptoms. We believe that our case report can help clinicians in recognizing the potential risk of relapses, the need for individualized care, and the value of long-term follow-up — particularly in rare conditions such as this one, where formal guidelines or standardized management protocols are lacking and reported cases show high variability.

Article history

Submitted: 18 Apr. 2025

Accepted: 03 Oct. 2025

Published Online: 24 Dec. 2025

Acknowledgements: The authors are deeply grateful to Dr. Rodrigo Morales-García and Dr. Yleana Teresa

López-Delfin, psychiatrists, for providing scientific advice and administrative support for the case.

Authors’ contribution: All the authors made a significant contribution to the article, checked and approved its final version prior to publication.

Funding: The research was carried out without additional funding.

Conflict of interest: The authors declare no conflicts of interest.

Generative AI use statement: Nothing to disclose.

For citation:

López-Villa JE, Martín-Escoto DP. Hypothyroidism-Induced Psychotic Disorder with Prolonged Antipsychotic Treatment: A Case Report. *Consortium PSYCHIATRICUM*. 2026;7(1): CP15671. doi: 10.17816/CP15671

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