

# Psychosis associated with methimazole-induced hypothyroidism: a case report

*Psicose associada com hipotireoidismo induzido por metimazol: um relato de caso*

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## ABSTRACT

**Introduction:** Thyroid dysfunction has often been associated with several psychiatric manifestations. Previous case reports/series suggest the possible role played by acute alteration of thyroid status in the onset of psychotic symptoms. **Methods:** Case report and literature review. **Results:** A 45-year-old woman with no psychiatric antecedents was brought to the ER with a full-blown psychotic episode, marked by paranoid delusions, which developed gradually over two months. She had been treated elsewhere for hyperthyroidism for five years with methimazole 40 mg/d, with poor compliance. One month before the beginning of the psychotic symptoms, methimazole was raised to 60 mg/d and she started taking it correctly. Five months earlier she had TSH: 0.074 uIU/ml and free T4: 1.3 ng/dl. At admission we found a diffuse thyroid goiter, TSH: 70.9 uIU/ml and free T4: 0.03 ng/dl. Brain CT was normal. We hospitalized her with the diagnosis of a psychosis secondary to hypothyroidism, suspended methimazole, and gave her levothyroxine (up to 75 µg/d) and risperidone (2 mg/d). The patient had a quick remission and was discharged after 15 days. Within one month she had TSH: 0.7 uIU/ml and was completely recovered psychiatrically. She has been well since then, with risperidone in the first 8 months, and without it for 10 months now. **Conclusion:** This case report is a reminder of the necessity of checking thyroid status as part of clinical assessment of psychoses. It also supports the hypothesis that antithyroid drugs may have severe psychiatric consequences, especially when they lead to an acute change of thyroid status.

## Keywords

Psychotic disorders, hyperthyroidism, hypothyroidism, antithyroid agents, methimazole.

## RESUMO

**Introdução:** Disfunções tireoidianas têm sido frequentemente associadas a diversas manifestações psiquiátricas. Séries e relatos de caso sugerem o possível papel da alteração aguda do *status* tireoidiano na vigência dos sintomas psicóticos. **Métodos:** Relato de caso e revisão de literatura. **Resultados:** Uma mulher de 45 anos sem antecedentes psiquiátricos foi trazida para Unidade de Emergência Referenciada com episódio psicótico, marcado por delírios paranoides, que se desenvolveram gradualmente nos dois meses anteriores. Ela tinha sido tratada, em outro serviço, por hipertireoidismo durante cinco anos com metimazol 40 mg/d, com aderência ruim. Um mês antes do início dos sintomas psicóticos, o metimazol foi aumentado para 60 mg/d, dose que ela estava tomando corretamente. Cinco meses antes ela tinha TSH:

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## Palavras-chave

Transtornos psicóticos, hipertireoidismo, hipotireoidismo, agentes antitireoidianos, metimazol.

0,074 uUI/ml e T4 livre: 1,3 ng/dl. Na admissão, encontraram-se aumento difuso da glândula, TSH: 70,9 uUI/ml e T4 livre: 0,03 ng/dl. TC de crânio estava normal. Foi hospitalizada por diagnóstico de psicose secundária ao hipotireoidismo, suspenso o metimazol e introduzidas levotiroxina (até 75 µg/d) e risperidona (2 mg/d). A paciente teve rápida remissão e recebeu alta após 15 dias. Um mês após ela apresentava TSH: 0,7 uUI/ml, com remissão completa da psicose. Ela permaneceu bem, com risperidona nos oito meses seguintes e sem a medicação há 10 meses. **Conclusão:** Este relato de caso é um alerta para a necessidade de investigar a função tireoidiana como parte do manejo clínico da psicose. Também reforça a hipótese de que drogas antitireoidianas podem ter graves consequências psiquiátricas, especialmente quando levam à mudança aguda do *status* tireoidiano.

## INTRODUCTION

Thyroid dysfunction has often been associated with several psychiatric manifestations<sup>1</sup>. In patients with hypothyroidism, reversible cognitive impairment and depression are common occurrence. Psychotic symptoms are less prevalent but may also be present, especially in cases of myxedema (this association between hypothyroidism and insanity is known as "myxedema madness"). In hyperthyroidism, psychotic symptoms are more frequent and there is an observed association between psychoses and thyrotoxicosis (the so-called "thyrotoxic psychosis")<sup>2</sup>.

Several clinical case reports have emphasized the possible role played by acute alteration of thyroid status in the onset of psychotic symptoms<sup>3-7</sup>. These case reports present patients with hyperthyroidism who were treated with anti-thyroid drugs and had an important and sudden change in their thyroid status followed by the outbreak of a psychosis. Remission was obtained with antipsychotic medication and levothyroxine replacement regimen. We add hereby another case description to this series, reinforcing thus the hypothesis that acute fluctuation of thyroid status may lead to the onset of full-blown psychotic episode.

## CASE REPORT

A 45-year old woman, without any previous psychiatric history, was admitted at the emergency unit of a university general hospital with paranoid and self-reference delusions. These symptoms had been present for the last two months and she was acting on them. Throughout this period, the patient had been suspicious of her bosses and other employees of the house at which she worked as a maid. She insisted they intended to harm her somehow, claiming also that there were hidden cameras in the house that allowed strangers to observe her. She talked about how people in the streets judged her, laughed at her and turned their backs as she went by. She was brought to the hospital by her family relatives due to aggravating agitation and insomnia and looked bewildered and paranoid on arrival. A full-blown psychotic

episode was diagnosed and then she was hospitalized at the psychiatric ward for further evaluation and treatment.

Investigation showed that she had been in medical follow-up due to arterial hypertension and hyperthyroidism for the past five years, being prescribed captopril (75 mg/d) and methimazole (40 mg/d), with poor compliance. One month before the beginning of the psychotic symptoms, methimazole was raised to 60 mg/d and she started taking it correctly. During physical examination a diffusely enlarged thyroid was detected. The patient also mentioned treatment for deep venous thrombosis (DVT) the year before and had with her exam results that showed TSH: 0.074 uUI/ml, free T4: 1.3 ng/dl from five months earlier and TSH: 60.162 uUI/ml, free T4 < 0.4 ng/dl from 15 days before her arrival at our hospital.

During the hospitalization, the results obtained were: TSH: 70.9 uUI/ml, free T4: 0.03 ng/dl. Body temperature and heart rate were within the normal range. There was no myxedema. Brain CT was normal. Two diagnoses were made: hypothyroidism due to methimazole and associated psychotic syndrome. Methimazole was suspended and levothyroxine treatment was introduced – reaching the dose of 75 µg in a period of five days – together with risperidone (2 mg/d). Significant improvement regarding the psychotic symptoms was then observed within the next few days. At the day 10 of levothyroxine (75 µg/d), she had TSH: 19.2 uUI/ml, and it fell to normal levels within a month (TSH: 0.7 uUI/ml). The patient was discharged from the hospital with partial insight of the situation after 15 days of medical treatment.

When the patient came to her first follow-up appointment in the psychiatric outpatient clinic, she was asymptomatic and showed enough insight as to acknowledge the circumstances that had led to her being hospitalized. After eight months of her discharge, as she remained well, the antipsychotic medication was gradually suspended. There was no return of the psychiatric symptoms in the 10 months that elapsed since then and her functioning is normal. She has been seen at the internal medicine outpatient clinic, and has continued taking the levothyroxine, maintaining TSH levels around 0.01 uUI/ml.

## DISCUSSION

We describe here an acute psychotic episode apparently precipitated by a methimazole-induced hypothyroidism during the treatment of hyperthyroidism. Even though psychotic reactions are relatively uncommon in thyroid dysfunction, it is known that this condition itself can present a variety of neurologic or psychiatric symptoms<sup>1,2</sup>.

Rathi described the case of 47-year old woman with no previous history of psychiatric illness who received the diagnosis of Graves' thyrotoxicosis and was treated aggressively with propylthiouracil leading to hypothyroidism, which was then treated with levothyroxine. Shortly after, she presented with extreme agitation, plus visual and olfactory hallucinations. The psychiatric symptoms improved after thyroid function stabilization<sup>3</sup>. Brewer and Herridge and Abey-Wickrama also reported cases where anti-thyroid drug therapy (carbimazole in both cases) for thyrotoxicosis has led to a hypothyroid state with the exhibition of psychotic features<sup>4,5</sup>. Benvenga *et al.* described a case of psychosis in a patient with hypothyroidism that was due to overtreatment with methimazole<sup>8</sup>.

The close temporal connection between aggressive treatment for thyrotoxicosis and the appearance of psychiatric symptoms suggest rapid change of thyroid hormone to be a common trigger for developing psychotic episodes<sup>6</sup>. That is thought to happen regardless of whether thyroid function remains high or is moving downward. In the retrospective study of thyrotoxic patients with associated psychosis, sixteen cases occurred in untreated thyrotoxicosis and two developed psychosis within weeks of commencing antithyroid medication when thyroid hormone levels were falling<sup>9</sup>.

Bewsher *et al.* describes a patient who developed mental illness at a time when she was euthyroid<sup>7</sup>. Her thyroid status, however, had undergone a rapid transition from fairly severe overactivity to normal in a period of four weeks. Our patient had a previous follow-up for hyperthyroidism and prescription of methimazole. After an increase of the dose and the patient started taking it correctly, hypothyroidism developed and she presented with evident psychotic behavior that only improved after recovery of thyroid status and a short use of risperidone.

## CONCLUSION

We believe this case report should interest psychiatrists and general clinicians alike. For psychiatrists, it is a reminder of the necessity of checking thyroid status as part of clinical assessment of psychoses. For general clinicians, the message conveyed is that antithyroid drugs may have severe psychiatric consequences, especially when they lead to an acute change of thyroid status.

## AUTHORS' CONTRIBUTIONS

**Priscila Lazaro and Claudio Banzato** – Were responsible for the psychiatric care of the patient.

**Priscila Lazaro, Julia Loureiro and Claudio Banzato** – Analyzed and interpreted the clinical data, performed the literature review and jointly prepared the manuscript.

All authors approved the final version of the manuscript.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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