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Hypothyroidism and Schizophrenia: Causal Link and Therapeutic Challenge – A Case Report

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Abstract **Case Report**

Schizophrenia is a chronic disabling psychosis characterized by thought disorganization, positive symptoms such as hallucinations and delusions, and negative symptoms including apathy and social withdrawal. Among the many pathophysiological hypotheses proposed, endocrine disturbances—particularly thyroid dysfunction—have attracted increasing attention. We report the case of a 28-year-old man with schizophrenia in whom a severe hypothyroidism was diagnosed during the course of illness. This case highlights important clinical considerations regarding the interaction between these two conditions and their therapeutic implications. Based on this observation and a comprehensive literature review, we explore the possible pathophysiological links, the iatrogenic impact of antipsychotic treatments on thyroid function, and propose adapted therapeutic strategies for managing this dual pathology. Keywords: Schizophrenia, hypothyroidism, antipsychotics, autoimmunity, hormone replacement therapy, thyroid dysfunction.

Keywords: Schizophrenia, Hypothyroidism, Antipsychotics, Thyroid dysfunction, Comorbidity.

INTRODUCTION

Schizophrenia affects approximately 1% of the global population, with peak incidence between the ages of 18 and 25 [1]. Despite advances in neuroscience, its etiology remains multifactorial, involving genetic, neurodevelopmental, environmental, and increasingly, endocrine factors [2]. Thyroid dysfunctions, once considered peripheral metabolic issues, are now recognized to interact with central nervous system pathways implicated in psychosis. In particular, hypothyroidism may cause a wide range of neuropsychiatric manifestations, from mood disorders to severe psychotic states referred to as myxedema psychosis [3, 4]. This association raises important questions regarding shared pathophysiological mechanisms, the endocrine effects of antipsychotic treatment, and the complexities of managing coexisting psychiatric and thyroid disorders.

Objectives

This work aims to analyze the potential interactions between severe hypothyroidism and schizophrenia based on a clinical case, to explore the impact of antipsychotics on thyroid function, and to propose tailored therapeutic strategies for managing this comorbidity.

MATERIALS AND METHODS

This report is based on a detailed clinical observation of a patient hospitalized for psychotic symptoms, supplemented by a systematic literature review conducted via PubMed, ScienceDirect, and the Cochrane Library (2000–2023). The keywords used were "schizophrenia AND hypothyroidism," "antipsychotics AND thyroid dysfunction," and "autoimmune thyroiditis AND psychosis." Inclusion criteria comprised observational studies, systematic reviews, and case reports published in English or French.

Clinical Observation

The patient was a 28-year-old unemployed single man from a socioeconomically disadvantaged background. He had a history of chronic tobacco use (10 pack-years) and a family history of schizophrenia affecting two first-degree relatives. His psychiatric symptoms had begun insidiously at age 25, including progressive social withdrawal, threatening auditory hallucinations, and behavioral disorganization. The diagnosis of schizophrenia was established according to DSM-5 criteria. On clinical examination, the patient exhibited positive symptoms (auditory hallucinations, paranoid delusions), marked negative symptoms (apathy, anhedonia, poor hygiene), disorganized speech, and

motor stereotypies. First-line treatment with haloperidol (10 mg/day) and chlorpromazine (300 mg/day) was initiated. However, the patient rapidly deteriorated, developing fever, profound asthenia, and elevated creatine phosphokinase levels (up to 2,627 IU/L), suggestive of neuroleptic malignant syndrome. Concurrent blood tests revealed profound hypothyroidism, with a TSH level of 296.6 µIU/mL and a free T4 below 5.15 pmol/L. Thyroid ultrasound showed hypoplastic glands with hypoechoic nodules classified as EU-TIRADS 3, suggestive of autoimmune thyroiditis, although anti-TPO antibodies could not be measured due to financial constraints. Management included hormone replacement therapy with levothyroxine (50 µg/day, taken on an empty stomach), discontinuation of typical antipsychotics, and initiation of risperidone (4 mg/day). Psychiatric and endocrine follow-up was coordinated throughout the course of care.

DISCUSSION

The association between hypothyroidism and schizophrenia is increasingly seen as reflecting complex pathophysiological interactions. Three main mechanisms are typically invoked: immuno-hormonal, neurodevelopmental, and iatrogenic. From an immuno-hormonal perspective, several studies have reported a higher prevalence of thyroid autoantibodies, particularly anti-TPO, in patients with schizophrenia [5]. These markers, characteristic of Hashimoto's thyroiditis, have been associated with more severe clinical presentations, including pronounced negative symptoms and impaired social functioning [6]. In the present case, although antibodies were not measured, ultrasound findings and the clinical picture strongly suggested an autoimmune etiology. Moreover, thyroid hormones play a regulatory role in the dopaminergic and glutamatergic systems involved in psychosis [2]. Their deficiency can thus contribute to the emergence or worsening of psychiatric symptoms through impaired neurotransmission and increased neuroinflammation. From a neurodevelopmental standpoint, thyroid hormones are critical for fetal brain development. Maternal hypothyroxinemia—even if subclinical—can impair neuronal migration, synaptogenesis, and myelination [7]. A Finnish birth cohort study demonstrated a significant association between maternal thyroid hormone deficiency during early pregnancy and increased risk of schizophrenia in offspring [8]. This supports the idea that perinatal thyroid dysfunction may serve as a nonspecific risk factor for neurodevelopmental disorders, including schizophrenia, autism spectrum disorder, and bipolar disorder. Iatrogenic mechanisms also deserve attention. Several antipsychotic drugs—especially second-generation agents such as quetiapine and olanzapine—have been associated with reduced free T4 levels, possibly through increased hepatic metabolism or hypothalamic pituitary–thyroid axis interference [9, 10]. Although often subclinical, this effect may contribute to overt hypothyroidism in susceptible individuals. Moreover, classical neuroleptics may indirectly disrupt thyroid function via chronic hyperprolactinemia. In the current case, the patient's severe hypothyroidism may have increased his sensitivity to haloperidol, precipitating a neuroleptic malignant syndrome. Similar cases have been reported in the literature, where unrecognized hypothyroidism exacerbated antipsychotic toxicity [11]. Managing this dual pathology requires an integrated approach. Routine thyroid screening should be included in the assessment of patients with new-onset or treatment-resistant psychosis [12]. Collaborative care involving psychiatrists, endocrinologists, primary care providers, and nutritionists is critical for optimal treatment planning. The simultaneous initiation of levothyroxine and an atypical antipsychotic, as in our case, allowed for a more rapid clinical response while limiting metabolic side effects. Careful titration of psychotropic drugs is essential, particularly in hypothyroid patients, due to altered pharmacokinetics. Treatment adherence is another crucial factor. Contrary to common misconceptions, structured follow-up and caregiver support can result in good adherence to hormone replacement therapy among patients with schizophrenia [13]. Additionally, some preliminary reports suggest that triiodothyronine (T3) may be considered as an adjunctive strategy in resistant or depressive subtypes, though evidence in schizophrenia remains limited [14].

CONCLUSION

This clinical case illustrates the need for systematic thyroid function assessment in patients with psychosis. The coexistence of autoimmune hypothyroidism and schizophrenia reveals complex interactions between hormonal and neuropsychiatric systems. Rather than a mere coincidence, this association requires careful diagnostic consideration and multidisciplinary therapeutic coordination. Further research should clarify the role of thyroid autoimmunity, evaluate combined therapeutic strategies, and propose clinical algorithms to guide management of this dual diagnostic challenge.

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