REVISTAPORTUGUESADE PSIQUIATRIA ESAÚDEMENTAL
2026; 12(2): 76-79; https://doi.org/10.51338/rppsm.689

CASO CLÍNICO /CASE REPORT

Delusion of Pregnancy Secondary to Antipsychotic-Induced Hyperprolactinemia: A Case Report

Delírio de Gravidez Secundário a Hiperprolactinémia Induzida por Antipsicóticos: Caso Clínico

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ABSTRACT

We report the case of a 33-year-old woman diagnosed with schizophrenia, with 4 previous psychiatric hospitalizations. After her last hospitalization, at the age of 33 years old, she was stable under treatment with long-acting injectable paliperidone palmitate 150 mg monthly. Six months after discharge, she presented with delusion of pregnancy and somatic hallucinations. Laboratory tests results showed hyperprolactinemia (185 ng/mL) and a negative hCG. Aripiprazole 5 mg was initiated, resulting in remission of psychotic symptoms within one month.

RESUMO

Descrevemos o caso clínico de uma mulher de 33 anos de idade, com o diagnóstico de esquizofrenia e quatro internamentos prévios em serviços agudos de Psiquiatria. Após o seu último internamento, aos 33 anos, a doente encontrava-se estável sob terapêutica com injetável de longa duração de palmitato de paliperidona 150 mg mensal. Seis meses após a alta, a doente apresentou um quadro caracterizado por delírio de gravidez e alucinações somáticas. Os resultados dos testes laboratoriais demonstraram hiperprolactinémia (185 ng/mL) e valores negativos de hCG. Foi iniciada terapêutica com aripiprazol 5 mg, que resultou na remissão de sintomas psicóticos ao fim de um mês.

Keywords: Antipsychotic Agents; Aripiprazole; Delusions; Hyperprolactinemia; Pregnancy

Palavras-chave: Antipsicóticos; Aripiprazol; Delírios; Gravidez; Hiperprolactinémia

INTRODUCTION

Delusion of pregnancy may be described as a persistent belief of being pregnant despite clear evidence to the contrary. It is a rare psychiatric condition that may develop within the spectrum of schizophrenia or other psychotic conditions, neurological or endocrine disturbances.[1-4] Its etiology is heterogeneous, with biological and psychological factors implicated in its genesis.[1-5] One important factor that may contribute to this delusion is hyperprolactinemia, which can have several causes, one of them being antipsychotic medication.[1-3,6,7] The elevation of prolactin above levels considered within the normal range can cause amenorrhea, galactorrhea, breast enlargement, abdominal distension and other symptoms of pregnancy.[3,7-9] However, delusions

Recebido/Received: 2025-12-20
Aceite/Accepted: 2026-06-08
Publicado Online/Published Online: 2026-06-20
Publicado/Published: 2026-09-07

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of pregnancy have been reported even in the absence of such symptoms.[1,3,5] Given the clinical complexity of this phenomenon and the implications for treatment, it is essential to understand the role of hyperprolactinemia. In this report, we aim to explore the pathophysiological mechanisms that link antipsychotic use, hyperprolactinemia and the development of a delusion of pregnancy. Additionally, we highlight the role of aripiprazole as a therapeutic option.

CASE REPORT

We present the case of a 33-year-old woman from Guinea-Bissau, who has lived in Portugal since the age of 14 and has recently returned to Portugal after living for 1 year in Guinea-Bissau. She speaks Guinea-Bissau Creole and Portuguese, with some difficulty, and is married and mother of an 11-month-old infant. Her past medical history is remarkable for significant hearing loss secondary to meningitis at the age of 8. The patient has a diagnosis of schizophrenia and was admitted to the psychiatry ward 4 times in the past. She was admitted twice, at the age of 21, due to behavioral changes, mystical and persecutory delusional ideation and auditory hallucinations. She was discharged after improvement with olanzapine 10 mg per day. Due to recurrence of psychotic symptoms in the context of treatment non-compliance, she was hospitalized again at the age of 26, where she was medicated with injectable haloperidol 100 mg monthly. The patient maintained irregular compliance with treatment and at the age of 29 she moved to Guinea-Bissau, abandoning medication and follow-up.

At the age of 31, after a few months in Portugal, while in the immediate postpartum period and during hospitalization at the obstetrics ward, she developed persecutory delusional ideation with substantial behavioral and functional impairment towards relatives and healthcare professionals, believing they intended to harm her baby, also presenting with delusional misidentification and food refusal. The patient was transferred to the psychiatry inpatient unit, where she was involuntarily admitted and was not able to breastfeed. At the psychiatry ward she was treated with oral risperidone, increased to 6 mg/day, resulting in remission of psychotic symptoms. Medication was switched to monthly long acting injectable paliperidone palmitate 150 mg, and she was subsequently discharged. Psychiatric assessments were conducted using written communication, with the support of professionals trained in sign language and assistance from family members due to difficulties in communication. Owing to insufficient family support and socioeconomic hardship, her daughter was placed in institutional care.

During outpatient psychiatric follow-up, she initially remained clinically stable and compliant to treatment. Six months after discharge, however, the patient developed delusional ideas of pregnancy and somatic hallucinations, believing she was pregnant and claiming to feel fetal movements. Laboratory tests revealed hyperprolactinemia (185 ng/mL) and negative human chorionic gonadotropin levels. Other routine laboratory parameters were unremarkable. The patient did not exhibit additional clinical features suggestive of hyperprolactinemia (e.g., galactorrhea or amenorrhea) either at this time or before developing delusional ideas of pregnancy. We did not have access to baseline serum prolactin levels or any measurements before this time. A brain magnetic resonance was not performed due to service-related constraints, which did not allow for the exam to be scheduled before the patient transferred care to a different hospital. Given the temporal association with antipsychotic treatment and the absence of laboratory findings suggestive of alternative causes, the hyperprolactinemia was interpreted as most likely antipsychotic-induced. Considering the severity of the illness, with several previous episodes and the need for multiple adjustments during follow-up, the decision was made to maintain paliperidone palmitate 150 mg and add aripiprazole 5 mg. After one month, remission of the psychotic symptoms was achieved. Blood tests were repeated and prolactin value reduced to 64.6 ng/mL. The patient remained clinically stable, without recurrence of psychotic symptoms, and later transferred care to a different hospital due to reorganization of geographical areas of responsibility.

DISCUSSION

Delusion of pregnancy has been documented across various clinical settings and is believed to result from the combination of psychological, cultural, and biological factors. Among biological factors, hyperprolactinemia, particularly in the setting of antipsychotic treatment, has been proposed as an important one.[1-7]From a neurobiological perspective, dopaminergic pathways play a central role in both psychotic symptoms and neuroendocrine regulation. Four major dopaminergic circuits have been described: the mesolimbic, mesocortical, nigrostriatal and tuberoinfundibular pathways.[10] While hyperdopaminergia in the striatum is considered a key substrate for positive psychotic symptoms, such as delusions and hallucinations, hypodopaminergia in the prefrontal cortex has been linked to negative and cognitive symptoms.[11,12] Antipsychotic drugs exert their therapeutic effects primarily through dopamine-2 (D2) receptor modulation, particularly by reducing excessive dopaminergic transmission in striatal regions, which underlies their efficacy in controlling positive symptoms.[11,12] However, this action is not pathway-specific. Excessive D2 blockade in the nigrostriatal pathway is associated with extrapyramidal symptoms, highlighting the narrow therapeutic window of dopaminergic antagonism.[12] Similarly, antipsychotic drugs may have an undesirable effect on the tuberoinfundibular pathway.[10]

Thus, antipsychotic-induced hyperprolactinemia may be explained by their effect on D2-receptors blockage, particularly in the tuberoinfundibular tract. Prolactin secretion is under tonic inhibition by hypothalamic dopamine, which acts to reduce both synthesis and release.[3,6,8,13] Antipsychotic drugs inhibit dopamine in the tuberoinfundibular pathway, resulting in increased prolactin secretion from the anterior pituitary.[3,7,14]

Hyperprolactinemia is usually more common with typical antipsychotics, such as haloperidol and chlorpromazine, however, atypical antipsychotics such as risperidone and

paliperidone also show a high potential to elevate prolactin.[3,6,7,9,13] Higher levels of prolactin result from longer exposure to a higher dosage of antipsychotic and usually younger women within the reproductive age may be more susceptible.[6,9,14] Notably, as it has been confirmed in some case reports, treatment of hyperprolactinemia resolves the delusion of pregnancy, reinforcing this causal link.[1,5-7,15] Treatment of antipsychotic-induced hyperprolactinemia includes different strategies: dose reduction, drug switch or augmentation with a prolactin-sparing antipsychotic.[6,14,16] Partial D2-receptors agonists introduce a stabilizing effect, acting as functional antagonists in hyperdopaminergic states while preserving dopaminergic tones in pathways where it is deficient.[12] This mechanism may explain both its antipsychotic efficacy and its favorable endocrine profile, particularly in reversing antipsychotic-induced hyperprolactinemia.[10,12] Aripiprazole, being one example of such antipsychotics and therefore considered a prolactin-sparing antipsychotic, may be associated with the reduction of prolactin levels, as it has been shown in both meta-analyses and case series.[4,15-18] Furthermore, an umbrella review by Jiang *et al* (2024),[19] concluded that adjunctive aripiprazole is among the most evidence-supported treatments for antipsychotic-induced hyperprolactinemia. Low doses of aripiprazole (5-10 mg/day) seem to be effective and possibly correspond to the optimal dosage, while also being safe and well-tolerated.[16,17,19] In this case, delusional pregnancy emerged alongside marked hyperprolactinemia during paliperidone treatment and remitted after prolactin reduction with adjunctive low-dose aripiprazole, without switching the primary antipsychotic. Clinicians should consider checking prolactin levels when pregnancy-related delusions arise under prolactin-elevating antipsychotics, as simple targeted management may help address both endocrine adverse effects and associated psychotic content, potentially avoiding unnecessary therapeutic escalation.

RESPONSABILIDADES ÉTICAS

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.
Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.
Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.
Consentimento: Consentimento do doente para publicação obtido.
Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

ETHICAL DISCLOSURES

Conflicts of Interest: The authors have no conflicts of interest to declare.
Financing Support: This work has not received any contribution, grant or scholarship.
Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of patient data.
Patient Consent: Consent for publication was obtained.
Provenance and Peer Review: Not commissioned; externally peer-reviewed.

DECLARAÇÃO DE CONTRIBUIÇÃO

BSF e ACN: Contribuíram igualmente para este trabalho e devem ser consideradas co-primeiras autoras.
Todos os autores contribuíram de forma substantiva para a conceção do trabalho, aquisição, análise e interpretação dos dados, redação e/ou revisão crítica do manuscrito, aprovaram a versão final e assumem responsabilidade pelo seu conteúdo, cumprindo os critérios de autoria do ICMJE.

CONTRIBUTORSHIP STATEMENT

BSF and ACN: Contributed equally to this work and should be considered co-first authors.
All authors made substantial contributions to the conception of the work and to the acquisition, analysis and interpretation of data, drafting and critical revision of the manuscript, approved the final version, and take responsibility for the content, meeting the ICMJE authorship criteria.

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