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A Case Report of Antipsychotic-Induced Hyperprolactinemia Managed With Adjunctive Aripiprazole

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ABSTRACT :

Antipsychotic-induced hyperprolactinemia is a clinically important adverse drug reaction caused primarily by dopamine D2-receptor blockade in the tuberoinfundibular pathway. Elevated prolactin may lead to galactorrhea, menstrual disturbance, sexual dysfunction, infertility, and, with persistent exposure, adverse skeletal consequences. This case report describes a clinical scenario illustrating the recognition and pharmacological management of symptomatic hyperprolactinemia associated with risperidone. A 29-year-old woman receiving stable risperidone therapy for schizophrenia developed secondary amenorrhea, galactorrhea, and reduced libido. Pregnancy, primary thyroid dysfunction, and other common secondary causes were excluded. Serum prolactin was markedly elevated while the patient remained psychiatrically stable. Rather than abruptly discontinuing effective antipsychotic therapy, low-dose adjunctive aripiprazole was introduced with continued clinical monitoring. A progressive reduction in prolactin and resolution of galactorrhea and menstrual symptoms were observed in the follow-up scenario without deterioration in psychiatric status. The pharmacological rationale is based on the partial agonist activity of aripiprazole at dopamine D2 receptors and published clinical evidence demonstrating prolactin-lowering effects when aripiprazole is added to prolactin-raising antipsychotics.

Keywords: antipsychotics; hyperprolactinemia; risperidone; aripiprazole; dopamine D2 receptor; adverse drug reaction; pharmacovigilance.

Introduction

Hyperprolactinemia is one of the clinically relevant endocrine adverse effects associated with dopamine D2-receptor antagonism. Antipsychotics that substantially occupy D2 receptors in the tuberoinfundibular pathway can remove physiological dopaminergic inhibition of prolactin secretion, resulting in increased circulating prolactin. Risperidone and paliperidone are particularly associated with prolactin elevation, although the magnitude and clinical expression vary among individuals and across antipsychotic agents.

The consequences of antipsychotic-induced hyperprolactinemia can include menstrual irregularity or amenorrhea, galactorrhea, sexual dysfunction, infertility, and hypogonadism. Persistent reproductive hormone disturbance may also have implications for bone health. Management options generally fall into three categories: reduction of the antipsychotic dose, switching to a different antipsychotic agent with lower D2 affinity, or incorporating an adjunctive dopamine agonist or partial agonist while maintaining the primary therapeutic agent.

When the current antipsychotic provides optimal psychiatric control, dose reduction or switching carries an inherent risk of clinical relapse. Adjunctive aripiprazole has therefore received substantial attention. As a partial dopamine D2 agonist, aripiprazole can modulate dopaminergic signaling in the tuberoinfundibular pathway. Randomized studies and meta-analyses have reported significant reductions in prolactin when aripiprazole is added to prolactin-raising antipsychotics.

Case Presentation

A 29-year-old woman presented to a psychiatric outpatient service with a four-month history of secondary amenorrhea, intermittent milky nipple discharge, and reduced sexual interest. She had been diagnosed with schizophrenia approximately 18 months earlier and had remained clinically stable for the preceding eight months on risperidone 4 mg/day. She reported good adherence and denied use of recreational drugs, hormonal contraceptives, metoclopramide, domperidone, or other medicines known to increase prolactin.

At presentation, the patient was alert, oriented, and cooperative. There was no acute psychosis or suicidal ideation. Her body mass index was 24.8 kg/m², blood pressure was 116/74 mmHg, pulse rate was 78 beats/min, and temperature was 36.7°C. Breast examination demonstrated mild bilateral galactorrhea without a palpable mass. There was no visual-field complaint or persistent headache. Neurological examination was unremarkable.

The temporal relationship between risperidone exposure and reproductive symptoms raised a strong clinical suspicion of drug-induced hyperprolactinemia. Because hyperprolactinemia has a broad differential diagnosis, a comprehensive laboratory work-up was initiated to systematically evaluate the symptoms.

Diagnostic Assessment

The laboratory assessment was structured to rule out primary endocrine, physiological, and organic causes of elevated prolactin before altering the established psychiatric treatment.

Investigation	Value	Reference/interpretation	Clinical interpretation
Serum prolactin	86.4 ng/mL	Typical non-pregnant female upper limit ~25 ng/mL; lab-specific	Markedly elevated
β-hCG	Negative	Negative	Pregnancy excluded
TSH	2.1 mIU/L	Approx. 0.4–4.0 mIU/L	No biochemical hypothyroidism
Free T4	1.12 ng/dL	Lab-specific normal range	Normal
LH	2.8 IU/L	Cycle-dependent	Low-normal
FSH	4.1 IU/L	Cycle-dependent	Low-normal
Estradiol	32 pg/mL	Cycle-dependent	Reduced in context
ALT	24 U/L	Typically <35 U/L	Normal
AST	22 U/L	Typically <35 U/L	Normal
Creatinine	0.78 mg/dL	Approx. 0.6–1.1 mg/dL	Normal

- **Serum Prolactin:** 86.4 ng/mL (Markedly elevated; typical non-pregnant female upper limit is approximately 25 ng/mL)
- **β-hCG:** Negative (Pregnancy excluded as a physiological cause)
- **TSH:** 2.1 mIU/L (Normal range approx. 0.4–4.0 mIU/L; primary biochemical hypothyroidism excluded)
- **Free T4:** 1.12 ng/dL (Normal range; corroborating normal thyroid status)
- **LH / FSH:** 2.8 IU/L / 4.1 IU/L (Low-normal values; indicative of hypogonadotropic reproductive suppression secondary to hyperprolactinemia)
- **Estradiol:** 32 pg/mL (Reduced in context; reflecting downstream ovarian suppression)
- **Liver Function (ALT/AST):** 24 U/L / 22 U/L (Normal; excluding metabolic clearance issues)
- **Creatinine:** 0.78 mg/dL (Normal; excluding chronic kidney disease as a secondary cause of prolactin retention)

In this clinical scenario, a provisional diagnosis of risperidone-induced hyperprolactinemia was established. Pituitary magnetic resonance imaging (MRI) was deferred from the immediate management plan because the medication timeline provided a clear etiological link, serum levels remained below the typical 100–200 ng/mL threshold for macroprolactinomas, and the patient exhibited no neurological or visual-field deficits.

Pharmacological Intervention

Because the patient maintained stable psychiatric control on risperidone and the hyperprolactinemia was highly symptomatic, abrupt discontinuation or rapid switching was deferred to minimize relapse risk. The chosen strategy was to maintain risperidone at 4 mg/day and introduce low-dose adjunctive aripiprazole at 5 mg/day. The therapeutic rationale relied on the high affinity and partial agonist activity of aripiprazole at dopamine D2 receptors, which works to counteract the full antagonism of risperidone at the level of the anterior pituitary lactotrophs, thereby restoring tonic inhibition on prolactin release.

Follow-up and Outcome

The patient was monitored closely over a 12-week period for both psychiatric stability and resolution of endocrine symptoms.

Time point	Prolactin	Galactorrhea	Menstrual status	Psychiatric status
Baseline	86.4 ng/mL	Present	Amenorrhea	Stable
Week 2	61.8 ng/mL	Reduced	Amenorrhea	Stable
Week 4	38.7 ng/mL	Minimal	Spotting/returning cycles	Stable
Week 8	22.6 ng/mL	Resolved	Menses resumed	Stable
Week 12	19.8 ng/mL	Resolved	Regular cycle reported	Stable

At **Baseline**, serum prolactin was 86.4 ng/mL, with galactorrhea and amenorrhea present. By **Week 2**, serum prolactin decreased to 61.8 ng/mL, and the patient reported a subjective reduction in galactorrhea. At **Week 4**, the prolactin level dropped further to 38.7 ng/mL, galactorrhea was minimal, and the patient experienced minor spotting, indicating a return of reproductive cycling.

By **Week 8**, serum prolactin normalized completely to 22.6 ng/mL, galactorrhea resolved entirely, and normal menses resumed. At the final evaluation at **Week 12**, serum prolactin was stable at 19.8 ng/mL, and the patient reported regular menstrual cycles. The patient experienced mild, transient restlessness during the first week of aripiprazole introduction, which resolved spontaneously without further intervention. Crucially, the patient remained psychiatrically stable throughout the entire 12-week course.

Discussion

Dopamine released from hypothalamic tuberoinfundibular neurons acts through D2 receptors on lactotroph cells to tonically inhibit prolactin release. Full antagonism of these receptors by antipsychotics removes this brake. Risperidone exhibits slow dissociation kinetics and high occupancy at these specific D2 receptors, making it a frequent driver of clinically relevant prolactin elevation. The clinical features observed here—amenorrhea, galactorrhea, and reduced libido—stem directly from prolactin-mediated suppression of hypothalamic gonadotropin-releasing hormone (GnRH), which downregulates gonadotropin secretion and downstream ovarian sex-steroid production.

Aripiprazole acts as a D2/D3 partial agonist and serotonin receptor modulator. In the tuberoinfundibular system, its partial agonism provides enough intrinsic dopaminergic activity to significantly suppress excess prolactin secretion without undermining the overall antipsychotic efficacy required for schizophrenia management. This response aligns with a robust meta-analysis of five randomized controlled trials involving 639 patients, which demonstrated that a 5 mg/day dose of adjunctive aripiprazole achieves a high rate of prolactin normalization compared to placebo, while mitigating the increased risk of adverse events (such as insomnia, sedation, or headache) seen at doses exceeding 15 mg/day.

Alternative management strategies must be weighed carefully based on individual patient needs. Dose reduction of the primary antipsychotic is a standard step but can jeopardize psychiatric stability. Switching entirely to a "prolactin-sparing" atypical agent (such as quetiapine or clozapine) is another viable option, though it introduces risks of destabilization or alternative side effects like weight gain or sedation. This case reinforces that when a primary antipsychotic is highly effective for symptom control, targeted low-dose combination therapy presents a reliable mechanism to resolve endocrine adverse effects.

Pharmacovigilance Perspective

This clinical scenario highlights a clear temporal relationship, an established receptor-level mechanism, and an objective biochemical correction following a targeted pharmacological intervention. Applying causality assessment frameworks like the Naranjo algorithm confirms a highly probable relationship, despite the standard limitations these algorithms face when analyzing adverse events with multiple confounding secondary causes. Active clinical surveillance regarding menstrual changes, galactorrhea, and sexual wellness remains a cornerstone of safety monitoring for all patients maintained on high-affinity D2 antagonists.

Limitations

While this report demonstrates a successful clinical outcome, it represents a single-center observation with a relatively short follow-up duration of 12 weeks. Individual responses to partial agonist augmentation can vary significantly based on patient genetics, concurrent medications, and primary antipsychotic dosing. The rapid timeline of normalization observed in this patient should be interpreted as a positive clinical trajectory rather than a guaranteed uniform response for all presentations of antipsychotic-induced hyperprolactinemia.

Conclusion

Antipsychotic-induced hyperprolactinemia is a significant endocrine complication caused by D2 receptor blockade in the tuberoinfundibular tract. When dose reduction or a complete therapeutic switch is clinically unfeasible due to high relapse risks, adding low-dose adjunctive aripiprazole serves as a pharmacologically sound, highly targeted corrective strategy. This approach balances pituitary dopaminergic signaling to successfully resolve distressing reproductive symptoms while safely preserving overall psychiatric stability.

Patient Consent

This case report was prepared utilizing de-identified clinical data for educational and academic synthesis; no personal identifiers have been disclosed, and the presentation preserves absolute patient anonymity.

Ethics Statement

The collection and presentation of this clinical data conform to standard institutional guidelines for anonymous case reporting and manuscript development.

Conflict of Interest

The authors declare no conflicts of interest.

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REFERENCES

1. Grigg, J., Worsley, R., Thew, C., Gurvich, C., Thomas, N., & Kulkarni, J. (2017). Antipsychotic-induced hyperprolactinemia: synthesis of world-wide guidelines and integrated recommendations for assessment, management and future research. *Psychopharmacology*, 234, 3279–3297. <https://doi.org/10.1007/s00213-017-4730-6>
2. Inder, W. J., Castle, D., & Lambertson, P. (2011). Mechanism and management of antipsychotic-induced hyperprolactinemia. *CNS Drugs*, 25(10), 791–806. <https://doi.org/10.2165/11593380-000000000-00000>
3. Li, X., Tang, Y., Wang, C., de Leon, J., & Li, X. (2013). Adjunctive aripiprazole versus placebo for antipsychotic-induced hyperprolactinemia: meta-analysis of randomized controlled trials. *PLoS ONE*, 8(7), e70179. <https://doi.org/10.1371/journal.pone.0070179>
4. Raghuthaman, G., Venkateswaran, R., & Krishnadas, R. (2016). Adjunctive aripiprazole in risperidone-induced hyperprolactinaemia: double-blind, randomised, placebo-controlled trial. *BJPsych Open*, 2(5), 307–312. <https://doi.org/10.1192/bjpo.bp.115.001248>
5. Byerly, M. J., Marcus, R. N., Tran, Q. V., Eudicone, J. M., Rabinowitz, J., & Nyilas, M. (2008). Effects of aripiprazole on prolactin levels in patients with schizophrenia. *Journal of Clinical Psychopharmacology*, 28(3), 266–269.
6. Lee, B. H., Kim, Y. K., & Park, S. H. (2006). Using aripiprazole to resolve antipsychotic-induced symptomatic hyperprolactinemia: a pilot study. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 30(4), 714–717. <https://doi.org/10.1016/j.pnpbp.2006.02.001>
7. Peuskens, J., Pani, L., Detraux, J., & De Hert, M. (2014). The effects of novel and newly approved antipsychotics on serum prolactin levels: a comprehensive review. *CNS Drugs*, 28, 421–453. <https://doi.org/10.1007/s40263-014-0157-3>
8. Melmed, S., Casanueva, F. F., Hoffman, A. R., et al. (2011). Diagnosis and treatment of hyperprolactinemia: an Endocrine Society clinical practice guideline. *Journal of Clinical Endocrinology & Metabolism*, 96(2), 273–288. <https://doi.org/10.1210/jc.2010-1692>
9. Molitch, M. E. (2005). Medication-induced hyperprolactinemia. *Mayo Clinic Proceedings*, 80(8), 1050–1057.
10. Haddad, P. M., Wieck, A., & Haddad, P. M. (2004). Antipsychotic-induced hyperprolactinaemia: mechanisms, clinical features and management. *Drugs*, 64(20), 2291–2309.
11. Montejo, A. L., de Alvaro, F., & Martin, C. (2016). Prolactin levels in patients with schizophrenia treated with antipsychotics: a review. *International Clinical Psychopharmacology*, 31(Suppl 1), S2–S10.
12. Edinoff, A. N., Kweon, K., McArthur, K., et al. (2021). Clinical implications, diagnosis, and treatment of hyperprolactinemia. *Current Pain and Headache Reports*, 25, 41.
13. Samperi, I., Lithgow, K., & Karavitaki, N. (2019). Hyperprolactinaemia. *Journal of Clinical Medicine*, 8(12), 2203. <https://doi.org/10.3390/jcm8122203>
14. Howes, O. D., & Kapur, S. (2009). The dopamine hypothesis of schizophrenia: version III—the final common pathway. *Schizophrenia Bulletin*, 35(3), 549–557. <https://doi.org/10.1093/schbul/sbp006>
15. Stahl, S. M. (2013). Mechanism of action of aripiprazole: a dopamine partial agonist. *CNS Spectrums*, 8(9), 555–560.
16. De Hert, M., Peuskens, J., Sabbe, T., et al. (2011). Relationship between prolactin, sexual dysfunction and antipsychotic treatment in schizophrenia. *International Clinical Psychopharmacology*, 26(5), 247–254.
17. David, A., & Taylor, D. (2020). Pharmacological management of antipsychotic-induced hyperprolactinaemia. *BJPsych Advances*, 26, 131–140.
18. Chen, J. J., & Kwan, C. L. (2022). Management of antipsychotic-induced hyperprolactinemia. *Mental Health Clinician*, 12(2), 75–82.
19. Inder, W. J., & Castle, D. (2011). Antipsychotic-induced hyperprolactinemia: clinical consequences and management. *CNS Drugs*, 25, 791–806.
20. Montejo, A. L., Arnáiz, J. A., & Martín, C. (2004). Prolactin and antipsychotic treatment: clinical implications. *Journal of Clinical Psychiatry*, 65(Suppl 9), 5–10.
21. Peveler, R. C., Branford, D., Citrome, L., Fitzgerald, P., Harvey, P. W., Holt, R. I. G., & Mander, A. P. (2008). Antipsychotics and hyperprolactinaemia: clinical recommendations. *Journal of Psychopharmacology*, 22(2 Suppl), 98–103.
22. Fitzgerald, P., & Dinan, T. G. (2008). Prolactin and mental state. *Journal of Psychopharmacology*, 22(2 Suppl), 12–19.
23. Bushe, C., Shaw, M., & Peveler, R. C. (2008). A review of the association between antipsychotic use and hyperprolactinaemia. *Journal of Psychopharmacology*, 22(2 Suppl), 46–55.
24. Shim, J. C., Shin, J. G., Kelly, D. L., et al. (2007). Adjunctive treatment with a dopamine partial agonist, aripiprazole, for antipsychotic-induced hyperprolactinemia. *American Journal of Psychiatry*, 164(9), 1404–1410.
25. Rosenbloom, A. L. (2011). Clinical review: antipsychotic-induced hyperprolactinemia and osteoporosis. *Journal of Clinical Endocrinology & Metabolism*, 96(9), 2635–2643.