Article published online: 2025-10-28

Hyperprolactinemia-Associated Bilateral Breast Uptake in Nonlactating Breasts on Radioiodine Scans with SPECT/CT Correlation: Diagnostic Pitfalls in Patients Receiving Atypical Antipsychotic Therapy

Yeshwanth Edamadaka[1] Prathyusha Bikkina[1] Abubacker Zakir Ali[1]

[1] Department of Nuclear Medicine, Basavatarakam IndoAmerican Cancer Hospital and Research Institute, Hyderabad, Telangana, India

World J Nuclear Med

Address for correspondence Yeshwanth Edamadaka, MD, Department of Nuclear Medicine, Basavatarakam IndoAmerican Cancer Hospital and Research Institute, Banjara Hills, Road No-10, Hyderabad-500034, Telangana, India (e-mail: yeshwanthedamadaka@gmail.com).

Abstract

Hyperprolactinemia is a common endocrine disorder often induced by antipsychotic medications through dopaminergic inhibition. We report two nonlactating women on long-term atypical antipsychotics of risperidone with trifluperazine and olanzapine. They showed incidental bilateral breast uptake on radioiodine scans. One had markedly elevated serum prolactin; the other had high-normal levels. This finding reflects prolactin-mediated upregulation of the sodium/iodide symporter (NIS) in breast tissue, independent of lactation. Awareness of this mechanism is essential to avoid misinterpretation of radioiodine imaging as pathological uptake. These cases underscore the importance of correlating imaging findings with patient medication history and prolactin status in interpreting iodine scans.

Keywords

- antipsychotics
- breast iodine uptake
- false positive iodine scan
- hyperprolactinemia
- SPECT CT
- risperidone
- olanzapine

Introduction

Hyperprolactinemia is a frequent endocrine disorder with diverse etiologies, notably drug-induced cases related to psychoactive medications. We report two nonlactating women with incidental bilateral breast uptake on radioiodine scans, both on long-term atypical antipsychotic therapy. One patient exhibited overt hyperprolactinemia; the other had high-normal prolactin levels. This highlights the influence of antipsychotics on prolactin physiology and the need for careful interpretation of nuclear imaging in such contexts.[1,2]

Case History

Case 1

A 33-year-old female initially presented with slowly progressive swelling for which she underwent total thyroidectomy with nodal disease and extranodal extension. She underwent high-dose radiodine therapy with 5.5 GBq, post-therapy planar scan showed multifocal iodine-avid remnant and lymph nodes in the neck. Her follow-up evaluation revealed biochemical incomplete response with serum thyroglobulin (Tg) levels of 17 ng/mL with 131I-WBS planar scan showing residual tracer concentration in the thyroid bed and suspicious cervical lymph nodes and bilateral uptake in the thorax initially thought out to be lung metastases. But her high-resolution computed tomography (CT) showed no suspicious lung nodules. On next radioiodine therapy, intense multiple focal neck uptake and bilateral uptake in the thorax was documented diagnosed as microscopic lung disease. During her routine follow-up, we observed a decrease in trend of S Tg levels to 2.73 ng/mL with incomplete response. An empirical radioiodine therapy was administered with 3.7 GBq, post-therapy scan revealed single focal uptake in the neck and similar bilateral uptake in the thorax, which we could anatomically correlate with single-photon emission CT/CT to bilateral breasts which prompted enquiry into interaction with any of her

DOI https://doi.org/10.1055/s-0045-1812101.
ISSN 1450-1147.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

medication history shown in ►**Fig. 1**. She disclosed that she was using antipsychotic medications including trifluperazine and risperidone once daily for almost 5 years. Her serum prolactin levels were elevated 77 ng/mL (2.9–29 ng/mL).

Case 2

A 54-year-old female patient was on tablet olanzapine 5 mg once daily for generalized anxiety disorder underwent total thyroidectomy for neck swelling, postoperative histopathology report revealed invasive encapsulated follicular variant with capsular invasion of maximum dimension of 2 cm. She underwent high-dose radioiodine therapy with 3.7 GBq, post-therapy scan revealed no concentration in the neck but bilateral breast uptake in a menopausal woman with S Tg levels of 0.2 ng/mL, shown in ►**Fig. 2**. Her serum prolactin levels were in high-normal range of 17 ng/mL.

Discussion

Hyperprolactinemia is a common endocrine condition with higher prevalence among women aged 25 to 44 years. A large retrospective cohort study in Scotland involving 32,289 individuals (1993–2013) identified drug-induced hyperprolactinemia as the most frequent nonpregnancy-related cause, accounting for 45.9% of cases, followed by pituitary disorders (25.6%), macroprolactinoma (7.5%), and hypothyroidism (6.1).[3,4] Over two decades, drug-induced cases tripled, reflecting increased use of psychoactive medications. Among these, 31% were linked to antipsychotics, 28% to

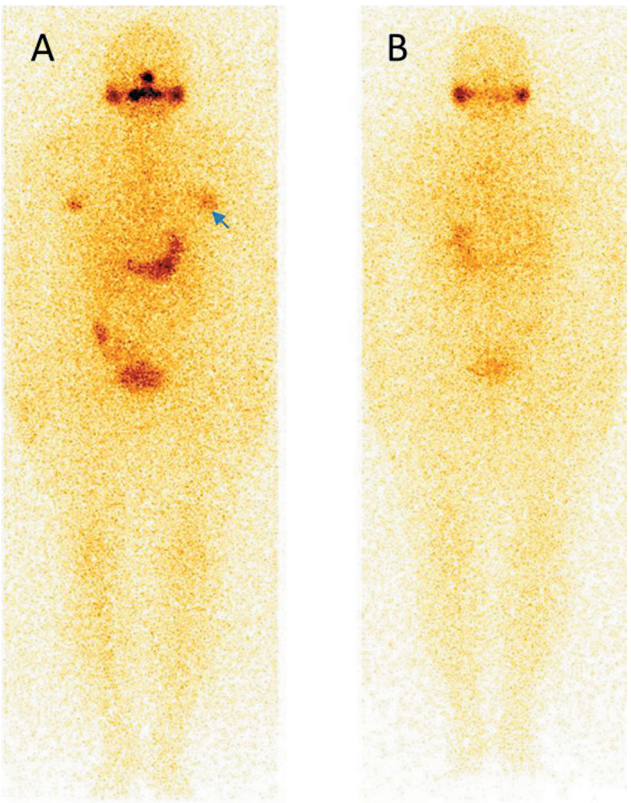

Fig. 2 (**A** and **B**) 131I-WBS anterior and posterior planar scans showing faint bilaterally symmetrical false positive uptake in breast parenchyma (arrow).

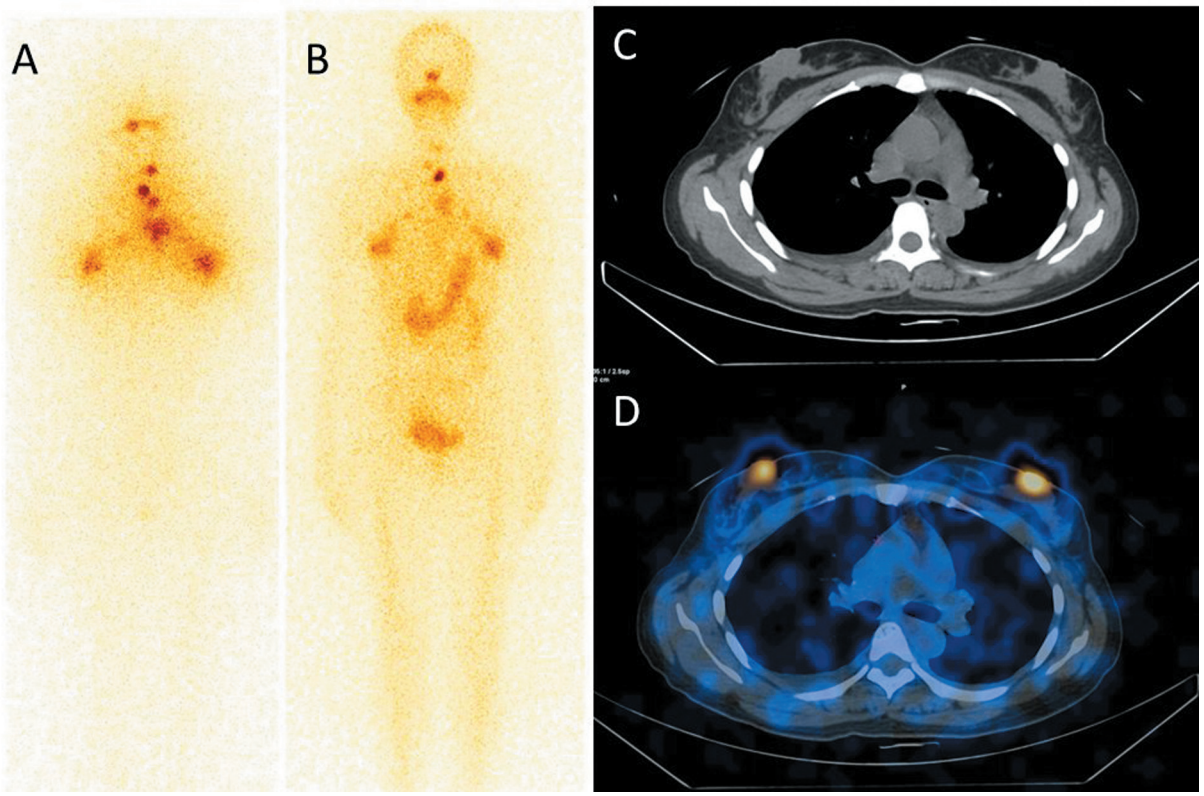

Fig. 1 (**A**) 131I- WBS posttherapy anterior planar scan showing multifocal neck uptake and bilateral symmetrical upper thorax uptake. (**B**) Persistent uptake noted in follow-up scan with documentation on empirical 131I posttherapy planar scan. (**C** and **D**) Axial computed tomography (CT) images of proliferative breast parenchyma and fusion images showing false positive iodine concentration in bilateral breast parenchyma.

neuroleptic-like agents, 26% to antidepressants, 5% to H2 receptor antagonists, and 10% to other drugs.

Prolactin, secreted by anterior pituitary lactotrophs, exhibits a circadian rhythm with peak levels during sleep. Dopamine is its principal inhibitor via D2 receptors. Drug-induced hyperprolactinemia typically arises from disruption of this dopaminergic inhibition. First-generation antipsychotics such as haloperidol and fluphenazine act as nonselective dopamine antagonists, increasing prolactin two- to threefold. While most second-generation agents cause modest (one- to two-fold) increases due to lower D2 affinity and additional 5-HT2A antagonism, exceptions include risperidone, paliperidone, and amisulpride, which significantly elevate prolactin levels.[5]

The extent of prolactin elevation also depends on the drug's interaction with the blood-brain barrier. Agents like risperidone, with high affinity for P-glycoprotein, show reduced central nervous system penetration and higher peripheral D2 antagonism at the pituitary level.[6] Serotonin further contributes by enhancing prolactin release through stimulation of prolactin-releasing factors and inhibition of hypothalamic dopamine. Aripiprazole, a partial agonist at D2 and 5-HT1A receptors and an antagonist at 5-HT2A receptors, can normalize or reduce prolactin levels.[7]

Clinically, hyperprolactinemia can suppress the gonadal axis, resulting in menstrual irregularities such as luteal phase defects, oligomenorrhea, or amenorrhea, with the latter accounting for up to 30% of secondary amenorrhea cases. Galactorrhea is a common manifestation, particularly when prolactin is markedly elevated. Mass lesions may cause additional symptoms like headaches, visual changes, and cranial nerve deficits.

Diagnostic evaluation should begin with a detailed history including medication use, menstrual status, galactorrhea, and sexual dysfunction. In suspected drug-induced cases, cessation or substitution of the offending agent is recommended, with reassessment of prolactin levels within 3 days to 2 to 3 weeks.[8] Persistent elevation or discordant timing necessitates pituitary magnetic resonance imaging to exclude structural causes. Early identification is vital to prevent complications such as infertility, osteoporosis, and hypopituitarism.[9]

The sodium/iodide symporter (NIS), a transmembrane glycoprotein is essential for the active transport of iodide into cells particularly in the thyroid gland where it facilitates thyroid hormone synthesis. NIS is also physiologically expressed in other tissues, most notably in the lactating mammary gland. During lactation, NIS expression is markedly upregulated in mammary epithelial cells. This process is hormonally regulated, primarily through prolactin which induces transcriptional activation of NIS in breast tissue.[10] The upregulation of NIS during lactation ensures that iodide is efficiently secreted into breast milk, supporting thyroid hormone synthesis in the neonate, which is vital for normal neurodevelopment. Further research demonstrated functional NIS expression using immunohistochemistry in human lactating breast tissue.[11] These findings underscore the importance of considering physiological NIS expression in the breast when interpreting radioiodine scans.

To summarize, we identified incidental bilateral breast uptake in two nonlactating women who were on long-term atypical antipsychotic medications of risperidone and trifluperazine in case 1 and olanzapine in case 2. None of the patients had any symptoms pertaining to iodine uptake in bilateral breasts and were correlated with almost threefold raise in serum prolactin levels in case 1 as expected. Interestingly, in the other patient, despite serum prolactin levels being in high-normal range bilateral breast uptake was visualized requiring caution in the interpretation of scan findings. Similar to our case, Ronga et al[12] reported a case with false positive radioiodine uptake in bilateral breasts due to risperidone. We also documented bilateral breast uptake at normal prolactin levels in patient on long-term history of atypical antipsychotics.

Conclusion

Incidental bilateral iodine uptake in breasts can occur in patients with long-term history of drug-induced prolactinemia. Image interpretation requires clinical context to avoid diagnostic pitfalls in patients receiving atypical antipsychotic therapy.

Conflict of Interest

None declared.

References

1 Hammami MM, Bakheet S. Radioiodine breast uptake in non-breastfeeding women: clinical and scintigraphic characteristics. J Nucl Med 1996;37(01):26–31
2 Hu LH, Wang SJ, Liu RS. Hyperprolactinemia-related ^{131}I uptake in nonlactating breasts. Clin Nucl Med 2012;37(03):e57–e58
3 Kamberi I, Li D, McNeill A. Trends and causes of hyperprolactinemia in a Scottish cohort. Endocr Connect 2016;5:93–101
4 Peveler RC, Branford D, Citrome L, et al. Antipsychotics and hyperprolactinaemia: clinical recommendations. J Psychopharmacol 2008;22(02):98–103
5 Haddad PM, Wieck A. Antipsychotic-induced hyperprolactinaemia: mechanisms, clinical features and management. Drugs 2004;64(20):2291–2314
6 Takeuchi H, Suzuki T, Remington G, Uchida H. Antipsychotic-induced hyperprolactinemia: pathophysiology and clinical consequences. CNS Drugs 2010;24:561–576
7 Yoon YB, Um YH, Sohn IK. Adjunctive aripiprazole for antipsychotic-induced hyperprolactinemia. Clin Psychopharmacol Neurosci 2016;14:354–362
8 Molitch ME. Evaluation and treatment of hyperprolactinemia. J Clin Endocrinol Metab 2023;108:1–12
9 Melmed S, Kaiser UB, Lopes MB, et al. Clinical biology of the pituitary adenoma. Endocr Rev 2022;43(06):1003–1037
10 Tazebay UH, Wapnir IL, Levy O, et al. The mammary gland iodide transporter is expressed during lactation and in breast cancer. Nat Med 2000;6(08):871–878
11 Wapnir IL, van de Rijn M, Nowels K, et al. Immunohistochemical profile of the sodium/iodide symporter in thyroid, breast, and other carcinomas using high density tissue microarrays and conventional sections. J Clin Endocrinol Metab 2003;88(04):1880–1888
12 Ronga G, Bruno R, Puxeddu E, et al. Radioiodine uptake in nonlactating mammary glands: evidence for a causative role of hyperprolactinemia. Thyroid 2007;17(04):363–366

