

CASE REPORT

A Case of Pseudo Prolactin Elevation Caused by Medication

Hong-Gang Sun¹, Li-Qin He², Lan-Bing Liu²

¹Department of Medical Laboratory, Shaoxing People's Hospital, Shaoxing, Zhejiang Province, China

²Department of Geriatrics, Shaoxing People's Hospital, Shaoxing, Zhejiang Province, China

SUMMARY

Background: After the patient had a long course of disease and symptoms of bilateral breast milk secretion, the doctor first considered that the patient had breast cancer. After screening and excluding the breast, he found that the patient had high prolactin, and suspected that the patient had a pituitary tumor. After breast cancer and pituitary adenoma were excluded, the doctor suspected that there might be interference of macroprolactin. After PEG treatment, we also excluded the interference of macroprolactin. After repeated communication with doctors and patients, we found that the patient had gone to a psychiatric hospital for treatment and taken the antidepressant drug Deanxit (Flupentixol and Melitracen tablets).

Methods: Flupentixol acts by antagonizing hypothalamic prolactin releasing inhibitory factors, reducing dopamine release, leading to hyperprolactinemia.

Results: The patient's examination found that prolactin was 3,172.9 mIU/L (normal range 108.80 - 557.10 mIU/L), and after PEG treatment, it was 2,692.86 mIU/L. Patient stopped using Deanxit for one month, and prolactin levels were 302.8 mIU/L.

Conclusions: Only effective communication between laboratory and clinical departments can make laboratory results more accurate and provide strong guarantees for clinical diagnosis and treatment.

(Clin. Lab. 2025;71:xx-xx. DOI: 10.7754/Clin.Lab.2024.240834)

Correspondence:

Lan-Bing Liu

Department of Geriatrics

Shaoxing People's Hospital

Shaoxing, Zhejiang Province, 312000

China

Phone: +86 0575-88559463

Email: 13454519668@163.com

KEYWORDS

pseudo prolactin elevation, medication, interference

INTRODUCTION

Prolactin is a peptide hormone secreted by cells in the anterior pituitary gland, which promotes the growth and development of the mammary gland, maintains milk production and secretion [1]. Hyperprolactinemia is a type of hypothalamic pituitary reproductive endocrine disorder syndrome caused by multiple factors, mainly characterized by elevated serum prolactin levels and related clinical manifestations [2]. The laboratory test results of prolactin are important diagnostic indicators and basis. The serum prolactin levels in women significantly increase during pregnancy and lactation. Under stress conditions such as emotional tension, cold, exercise, and low blood sugar, prolactin levels may temporarily increase, typically lasting less than an hour [3,4]. But if there is a sustained increase in prolactin in elderly wom-

en, they should be alert to pituitary tumors.

CASE PRESENTATION

The patient is a 61-year-old female with a history of renal insufficiency and kidney tumors for over 5 years. She was admitted to the hospital with a fever for three days. Physical examination upon admission revealed lactation in both breasts of the patient.

The patient was admitted due to recurrent urinary system infections. Admission examination showed a blood creatinine level of 440 $\mu\text{mol/L}$. She underwent dialysis and her condition has recurred. The patient's examination revealed 3,172.9 mIU/L of prolactin (normal range 108.80 - 557.10 mIU/L), and after PEG treatment, 2,692.86 mIU/L. The patient's head MRI examination did not reveal any pituitary tumors. No abnormalities were found in the bilateral breast ultrasound.

We inquired about the patient's self-reported tendency towards depression. She has sought medical attention at a psychiatric hospital. The psychiatrist prescribed a new version of Deanxit (Flupentixol and Melitracen tablets), 2 tablets per day; one tablet in the morning and one tablet at noon regularly for one month.

The patient stopped using Daixin for one month, and prolactin levels were 302.8 mIU/L.

DISCUSSION

There are various factors that can cause an increase in serum prolactin levels, including physiological, pharmacological, and pathological factors.

There are three main forms of prolactin in human blood, namely small molecule prolactin monomers, large molecule prolactin, and macroprolactin that binds to IgG. The proportion of prolactin monomers with a size of 23 kD is the highest, reaching over 80% [5]. Prolactin monomers can bind to target cell prolactin receptors through capillary walls and exert biological activity. However, the molecular weight of macroprolactin generally exceeds 100 kD, making it difficult to pass through the blood vessel wall and having low biological activity [6].

When more than 60% of the prolactin in the peripheral blood circulation is composed of macroprolactin, it is called macroprolactinemia. The incidence of hyperprolactinemia in the general population is 3% - 4%, but it accounts for 10% - 25% in patients with hyperprolactinemia [7]. Macroprolactinemia is considered a normal variant, usually without typical clinical manifestations, and generally does not require treatment.

Although macroprolactin cannot exert biological activity, it maintains partial or complete immunoreactivity to prolactin antibodies in immunoassay reagents. Therefore, the presence of macroprolactin can cause an erroneous overestimation of serum prolactin levels, leading to over examination and unnecessary treatment. Our

laboratory's main method for detecting prolactin is PEG precipitation. The PEG precipitation method is easy to operate and suitable for routine implementation. PEG is an inert molecule that can absorb bound water, reduce protein solubility, precipitate immunoglobulin and its complexes, and achieve the effect of separating prolactin through serum pretreatment. Traditionally, it is believed that a prolactin monomer recovery rate of less than 40% after precipitation is indicative of macroprolactinemia. However, when true prolactin and macroprolactin molecules coexist, relying solely on the recovery rate may lead to misdiagnosis.

The doctor first considered the patient's breast cancer after the patient was older and had a long course of disease with bilateral lactation symptoms. After screening and excluding the breast, he found that the patient had high prolactin, and suspected that the patient had pituitary tumor. After breast cancer and pituitary adenoma were excluded, the doctor suspected that there might be interference of macroprolactin. After PEG treatment, he also excluded the interference of macroprolactin. After repeated communication with doctors and patients, he found that the patient had gone to a psychiatric hospital for treatment and taken the antidepressant drug Deanxit (Flupentixol and Melitracen tablets). The two main ingredients of Deanxit are Flupentixol and Melitracen. Flupentixol is a type of antipsychotic drug that works by blocking dopamine receptors in the midbrain limbic and midbrain cortical systems. It has an antagonistic effect on dopamine D2 receptors in the brain and has anti-anxiety and anti-depression effects at low doses [9].

Adverse reactions of Deanxit often occur within the 8- to 30-day medication period. The more common symptoms involve the central and peripheral nervous systems, including extrapyramidal symptoms (increased muscle tone, tremors in both hands, balance dysfunction), inability to sit still, dizziness, Parkinson's syndrome, and mental disorders (delirium, hallucinations), as well as sleep disorders, restlessness, agitation, gastrointestinal discomfort, etc. It should be noted that the longer the medication time, the higher the incidence rate, and the various manifestations are not easy to identify.

Many drugs like fluoxetine can cause hyperprolactinemia by antagonizing hypothalamic prolactin release inhibitory factors and reducing dopamine release, resulting in hyperprolactinemia. Generally, hyperprolactinemia caused by drugs has serum prolactin levels below 100 $\mu\text{g/L}$, but there are also reports that long-term use of some drugs can increase serum prolactin levels up to 500 $\mu\text{g/L}$, causing massive lactation and amenorrhea [8, 9]. However, such high prolactin levels in this patient are even rarer.

If clinically significant hyperprolactinemia, milk leakage, amenorrhea, or sexual dysfunction occurs, dose reduction or discontinuation of medication should be considered. In general, after discontinuing the medication, the effects of the medication are reversed. The patient's prolactin levels decrease to normal after discontinuing

the medication, and clinical symptoms improve.

The elevation of prolactin caused by Deanxit is a rare case in clinical practice. The tolerance and side effects of drugs vary greatly among different organisms. Effective communication between laboratory doctors and clinical doctors is required for unexplained test results, including detailed medical history inquiry, identification of clues, thorough investigation to uncover the truth, and treatment to relieve pain.

In the process of clinical laboratory work, there are often situations where the test results are inconsistent with the patient's clinical symptoms. If communication is not done well and in a timely manner, misunderstandings may arise. This requires us to coordinate with each other, strengthen communication, and identify the reasons that led to the result.

The organic combination of laboratory medicine and clinical medicine is an important measure for the level of medical diagnosis and treatment. Due to differences in expertise, there are certain barriers in communication, exchange, and mutual learning between laboratory personnel and medical staff, which is not conducive to improving medical standards. If communication can be strengthened in all aspects, misunderstandings between testing and clinical practice can be reduced. If communication can be strengthened with the testing personnel regarding the patient's medical history, medication use, etc., it can ensure standardized specimen collection and submission, thereby ensuring the correctness of the test results and the accuracy of diagnosis. Strengthening communication between laboratory personnel and clinical doctors can help clinical doctors deepen their understanding and reevaluate the clinical significance of laboratory items, contributing to the correct diagnosis and treatment as well as the continuous improvement of laboratory technology level.

CONCLUSION

Laboratory medicine and clinical medicine are closely related and inseparable as a whole. Only effective communication between laboratory and clinical departments can make laboratory results more accurate and provide strong guarantees for clinical diagnosis and treatment.

Sources of Support:

This work was supported by the Shaoxing City Science and Technology Bureau Grant (2023A14022).

Declaration of Interest:

All authors declare that they have no conflict.

References:

1. Cabrera-Reyes EA, Limon-Morales O, Rivero-Segura NA, Camacho-Arroyo I, Cerbon M. Prolactin function and putative expression in the brain. *Endocrine* 2017;57(2):199-213. (PMID: 28634745)
2. Mah PM, Webster J. Hyperprolactinemia: etiology, diagnosis, and management. *Semin Reprod Med* 2002;20(4):365-74. (PMID: 12536359)
3. Vilar L, Vilar CF, Lyra R, Freitas M. Pitfalls in the Diagnostic Evaluation of Hyperprolactinemia. *Neuroendocrinology* 2019;109(1):7-19. (PMID: 30889571)
4. Melmed S, Casanueva FF, Hoffman AR, et al. Diagnosis and treatment of hyperprolactinemia: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2011;96(2):273-88. (PMID: 21296991)
5. Biagetti B, Ferrer Costa R, Alfayate Guerra R, et al. Macroprolactin: From laboratory to clinical practice. *Endocrinol Diabetes Nutr (Engl Ed)* 2022;69(1):63-9. (PMID: 35232561)
6. Saparamadu A, Lam C, Lim LC, Lee J. Prolactin Assay Interference by Macroprolactin. *Clin Lab* 2021;67(7). (PMID: 34258986)
7. Taipale H, Solmi M, Lahteenvuo M, Tanskanen A, Correll CU, Tiihonen J. Antipsychotic use and risk of breast cancer in women with schizophrenia: a nationwide nested case-control study in Finland. *Lancet Psychiatry* 2021;8(10):883-91. (PMID: 34474013)
8. Carvalho AF, Sharma MS, Brunoni AR, Vieta E, Fava GA. The Safety, Tolerability and Risks Associated with the Use of Newer Generation Antidepressant Drugs: A Critical Review of the Literature. *Psychother Psychosom* 2016;85(5):270-88. (PMID: 27508501)
9. Eckman A, Dobs A. Drug-induced gynecomastia. *Expert Opin Drug Saf* 2008;7(6):691-702. (PMID: 18983216)