TRIDHA
Journal of Clinical Cases & Reports
Volume 2024, Issue 2, 5 pages
https://doi.org/10.46619/joccr.2024.7-1158

CASE REPORT

Anti Thyroglobulin Interferences in TSH Measurement: A Case Report

Sajjad Bakhtiari

Department of Clinical Biochemistry, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Correspondence should be addressed to Sajjad Bakhtiari, Department of Clinical Biochemistry, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Received: 04 April 2024; Accepted: 22 April 2024; Published: 29 April 2024

ABSTRACT

Thyroglobulin (Tg) is the most expressed protein in the thyroid gland that stores iodine and produces thyroid hormones. Tg production is specific to malignant thyroid cells, making it an ideal indicator after removing thyroid tissue. As a result, it is used as a tumor marker post-surgery to assess any disease recurrence. The presence of Thyroglobulin antibody (TgAb) which is produced in autoimmune diseases can interfere with Tg value. The evaluation of plasma TSH levels is a highly sensitive diagnostic method for primary thyroid-related issues, although it can be affected by various interferences. in the present case, the high titer of TgAb interferes with TSH measurement as well as leads to unreliable Tg results.

KEYWORDS

Thyroglobulin; Anti-thyroglobulin antibodies; TSH measurement; Interference; Thyroid tumor marker

INTRODUCTION

Thyroglobulin (Tg), as the most expressed protein in the thyroid gland, is produced in the endoplasmic reticulum of the thyrocyte [1]. Its primary function is to store iodine and produce thyroid hormones [2]. Stimulation of the TSH receptor leads to Tg endocytosis from the apical membrane of thyrocytes, which is crucial for hormonogenesis. Additionally, it enhances the expression and activities of essential gene products involved in forming thyroid hormones [3]. The concentration of serum Tg is influenced by three factors that are combined: the mass of thyroid tissue present, which includes normal remnant tissue and any tumor; the effect of thyroid injury caused by biopsy, surgery, radioactive iodine therapy, or inflammation associated with thyroiditis; and the degree of TSH-receptor stimulation from endogenous TSH, recombinant human TSH, human chorionic gonadotrophin (during pregnancy), or antibodies that stimulate the TSH receptor (in hyperthyroid patients with Graves' disease [4]. Tg production is confined to well-differentiated malignant thyrocytes, making it an appropriate tumor marker after removing all healthy and pathological thyroid tissue [5]. Therefore, it is utilized

as a tumor marker for thyroid cancer and post-operatively to keep track of any recurrence of the disease [6]. The emergence of high-sensitive thyroglobulin (hsTg) assays offers better analytical sensitivity and improves detection limits. These developments have significant implications for interpreting results in current clinical practice [7]. Assays that detect anti-thyroglobulin (TgAb) have examined patients for potential antibodies that may interfere with Tg assays. These antibodies are the biggest challenge that limits the clinical utility of the Tg test and can lead to inaccurate results, either falsely positive or negative [4]. The incidence of TgAb in differentiated thyroid cancer (DTC) patients is about 20%, which is twice the rate of the general population, where it is reported to be 10% [8]. When TgAb is present, Tg can be found either free or bound to the antibody. This can affect the accuracy of thyroglobulin concentration measurements, especially when Tg concentrations are low, and most of it is bound to TgAb. In such cases, Tg concentrations may be reported as low [9]. In this article, we present a case in which high TgAb interferes with both Tg and TSH measurement.

CASE DESCRIPTION

A 32-year-old man was referred to the laboratory for post-thyroidectomy follow-up. Around three weeks ago, he had surgery to remove his thyroid gland due to DTC. The results of the laboratory tests can be found in (Table 1). The levels of serum phosphorus (4.0 mg/dl), alkaline phosphatase (153 U/L), and intact parathyroid hormone (36.1 pg/ml) were found to be within the reference range. 25-hydroxyvitamin D3 was sufficient (30.4 ng/ml), while the serum calcium level was found to be below the reference interval (7.9 mg/dl). The Tg level was undetectable (<0.04 ng/ml), while the level of TgAb was markedly increased (177.3 Iu/ml). The level of TSH was determined through the enzyme-linked fluorescent assay (ELFA) (VIDAS bioMerieux) technique and was discovered to be increased at 17.4 µIU/ml. Consequently, enzyme-linked immunosorbent assay (ELISA) (Pishtazteb Diagnostic) and chemiluminescence immunoassay (CLIA) (Atellica® SIEMENS) methods were employed to retest the TSH level which showed different results as demonstrated in (table 1).

Table 1: Laboratory findings of the patient.

Assay	Result	Reference Interval
Ca	7.9	8.5 mg/dl - 10.5 mg/dl
Ph	4	2.6 mg/dl - 4.5 mg/dl
ALP	153	80 U/L - 306 U/L
25 (OH) D	30.4	30 ng/ml - 100 ng/ml (sufficient)
iPTH	36.1	18.5 pg/ml - 88 pg/ml
Tg	<0.04	3.5 ng/ml - 77 ng/ml
Tg-Ab	177.3	0 Iu/ml - 4.11 Iu/ml
TSH	17.4	0.25 µIU/ml - 5 µIU/ml (ELFA)
	3.7	0.32 µIU/ml - 5.2 µIU/ml (ELISA)
	2.8	0.55 µIU/ml - 4.78 µIU/ml (CLIA)

Ca: Calcium; Ph: Phosphorus; ALP: Alkaline Phosphatase; 25 (OH) D: 25-Hydroxy Vitamin D; iPTH: Intact Parathormone; Tg: Thyroglobulin; TgAb: Thyroglobulin Antibody; TSH: Thyroid Stimulating Hormone

DISCUSSION

The measurement of plasma TSH is the most widely used and sensitive screening test for primary thyroid disorders. This is because even slight changes in the levels of free thyroid hormones can cause significant changes in the secretion of the pituitary gland [10]. There are several methods to determine the levels of TSH in the serum or plasma. Among non-isotope methods that are not usually used currently is the Enzyme Immunoassay (EIA),

which is sensitive and effective. In this method, an antigen or antibody is linked to an enzyme, which triggers a color reaction whose intensity is dependent on the concentration of the antigen or antibody. The concentration is then determined using spectrophotometric methods [11]. Enzyme-linked fluorescence assay (ELFA) is similar to ELISA, but in this method, the substrate produces a fluorescent product as a result of the enzyme's action [12]. Chemiluminescent immunoassay (CLIA) is a type of immunoassay method that uses luminescent molecules as a label [13]. CLIA offers advantages over other immunoassays, including high sensitivity, wide linear range, and reduced sample volume requirements [14]. (Figure 1) illustrates a schematic comparison between these three different methods.

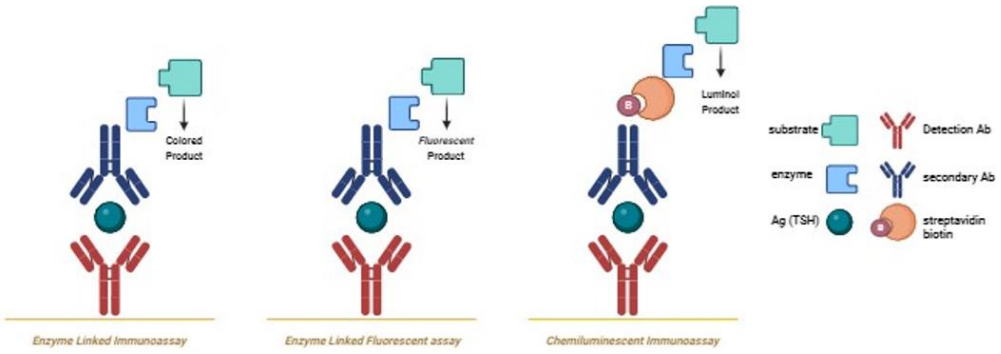

Figure 1: Comparison of TSH measurement with three different sandwich techniques.

Current available TSH determination methods are highly sensitive (≤0.001 μIU/ml). However, TSH levels can be affected by drugs, substances, and pathologic conditions [10]. Cross-reactivity, heterophil antibodies, human anti-animal antibodies (HAAA), autoantibodies, and hook effects are among the most important interfering factors in TSH measurement which may cause erroneous high or low results [15]. In accordance with current protocols, it is crucial to include TgAb with every Tg test sample. The TgAb result's qualitative aspect (positive or negative) affects the risk of Tg assay interference, while the quantitative TgAb level functions as a substitute tumor marker [16].

It is widely accepted that thyroid autoimmune diseases are primarily characterized by the production of thyroid antibodies, which originate in intrathyroidal lymphocytes. It is noteworthy that even after thyroid removal, TgAb can remain present for years without any apparent ongoing health issues [17]. In the present case, TgAb significantly impacts the Tg value, making it unsuitable as a dependable indicator of tumor recurrence. Furthermore, we believe that elevated levels of TgAb could interfere with TSH measurements when using the ELFA technique. Nevertheless, it is crucial to consider the potential interference of TgAb in ELISA and CLIA tests, particularly given the inconsistencies between the results of these two methods, which need further investigation. Although efforts are made to counteract interference through the development of multisite immunoassays incorporating chosen monoclonal antibodies, it seems that immunoassay interference challenges persist, necessitating further attempts.

CONCLUSION

In conclusion, this case study highlights the interference of high levels of TgAb with both Tg and TSH measurements. The presence of TgAb can lead to inaccurate results, affecting the reliability of Tg as a tumor marker for thyroid cancer, especially when Tg concentrations are low. Additionally, elevated levels of TgAb can

interfere with TSH measurements, particularly when using the ELFA technique. Further investigation is needed to understand the possible interference of TgAb on different TSH determination methods.

ACKNOWLEDGMENT

None

ETHICAL APPROVAL

Ethical approval is not applicable for this article.

STATEMENT OF INFORMED CONSENT

The patient agrees to use his personal information, medical history, and treatment details in a case report article. he understands that his identity will be kept confidential, and the purpose is to contribute to medical knowledge. He has the right to withdraw his consent at any time.

FUNDING

The author received no financial support for the research, authorship, and/or publication of this article.

DATA AVAILABILITY STATEMENT

Data will be made available on request.

REFERENCES

1. Citterio CE, Targovnik HM, Arvan P (2019) The role of thyroglobulin in thyroid hormonogenesis. Nature Reviews Endocrinology 15(6): 323-338.
2. Di Jeso B and Arvan P (2016) Thyroglobulin from molecular and cellular biology to clinical endocrinology. Endocrine Reviews 37(1): 2-36.
3. Marsili A, Zavacki AM, Harney JW et al. (2011) Physiological role and regulation of iodothyronine deiodinases: A 2011 update. Journal of Endocrinological Investigation 34: 395-407.
4. Spencer CA and LoPresti JS (2008) Technology insight: Measuring thyroglobulin and thyroglobulin autoantibody in patients with differentiated thyroid cancer. Nature Clinical Practice Endocrinology & Metabolism 4(4): 223-233.
5. Giovanella L, D'Aurizio F, Algeciras-Schimnich A et al. (2023) Thyroglobulin and thyroglobulin antibody: An updated clinical and laboratory expert consensus. European Journal of Endocrinology 189(2): R11-R27.
6. Krahn J and Dembinski T (2009) Thyroglobulin and anti-thyroglobulin assays in thyroid cancer monitoring. Clinical Biochemistry 42(4-5): 416-419.
7. Algeciras-Schimnich A (2018) Thyroglobulin measurement in the management of patients with differentiated thyroid cancer. Critical Reviews in Clinical Laboratory Sciences 55(3): 205-218.
8. Görges R, Maniecki M, Jentzen W et al. (2005) Development and clinical impact of thyroglobulin antibodies in patients with differentiated thyroid carcinoma during the first 3 years after thyroidectomy. European Journal of Endocrinology 153(1): 49-55.
9. Kastrup J, Feldt-Rasmussen U, Bartram HR et al. (1985) An enzyme linked immunosorbent assay (ELISA) for measurement of human serum thyroglobulin. Evaluation of the influence of thyroglobulin auto-antibodies. Scandinavian Journal of Clinical and Laboratory Investigation 45(5): 471-476.

10. Matyjaszek-Matuszek B, Pyzik A, Nowakowski A et al. (2013) Diagnostic methods of TSH in thyroid screening tests. Annals of Agricultural and Environmental Medicine 20(4).
11. Ma LN, Zhang J, Chen HT et al. (2011) An overview on ELISA techniques for FMD. Virology Journal 8: 1-9.
12. Yolken RH and Stopa PJ (1979) Enzyme-linked fluorescence assay: Ultrasensitive solid-phase assay for detection of human rotavirus. Journal of Clinical Microbiology 10(3): 317-321.
13. Cinquanta L, Fontana DE, Bizzaro N (2017) Chemiluminescent immunoassay technology: What does it change in autoantibody detection?. Autoimmunity Highlights 8: 1-8.
14. Azim MAU, Hasan M, Ansari IH et al. (2015) Chemiluminescence immunoassay: Basic mechanism and applications. Bangladesh Journal of Pharmacology 18(2).
15. Ward G, Simpson A, Boscato L et al. (2017) The investigation of interferences in immunoassay. Clinical Biochemistry 50(18): 1306-1311.
16. Chung JK, Park YJ, Kim TY et al. (2002) Clinical significance of elevated level of serum antithyroglobulin antibody in patients with differentiated thyroid cancer after thyroid ablation. Clinical Endocrinology 57(2): 215-221.
17. Chiovato L, Latrofa F, Braverman LE et al. (2003) Disappearance of humoral thyroid autoimmunity after complete removal of thyroid antigens. Annals of Internal Medicine 139(5_Part_1): 346-351.