Case Report
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Transient Elevation of CA 19-9 Due to Cessation of Levothyroxine in a Patient with Hashimoto's Thyroiditis

Hashimoto Tiroiditi Olan Bir Hastada Levotiroksinin Kesilmesi Nedeni ile Geçici CA 19-9 Yükselmesi

Arzu Or Koca, Mustafa Altay

University of Health Sciences, Keçiören Health Application and Research Center, Department of Endocrinology and Metabolism, Ankara, Turkey

Abstract

Serum CA 19-9 (carbohydrate antigen 19-9) is a tumor marker with monosialoganglioside structure. Its levels are measured frequently for screening purposes in daily practice by physicians, while its main application is in the study of tumor recurrence and the follow-up of the recurrences. Although significant elevation in the levels of CA 19-9 indicates malignancy, an underlying malignant disease may not always be determined, and benign pathologies may also be observed. A 45-year-old female patient who was undergoing a follow-up for Hashimoto's thyroiditis applied to our clinic with complaints of fatigue, tiredness, and hair loss. Elevations in the levels of both thyroid-stimulating hormone (TSH) and CA 19-9 were observed. The levels of TSH and CA 19-9 were observed to be normal after the patient was treated for hypothyroidism, and the results of the analysis conducted for malignancy were also determined to be normal. On the basis of the present case study, we propose that hypothyroidism should be considered while making a differential diagnosis for patients with elevated levels of CA 19-9.

Keywords: Hashimoto's thyroiditis; hypothyroidism; CA 19-9

Özet

Serum CA 19-9 (karbonhidrat antijeni 19-9); monosialogangliosid yapıda bir tümör belirtecidir. Günümüzde asıl kullanım amacı olan tümörün rekürrens ve nüks takibi dışında günlük pratikte hekimler tarafından sıklıkla tarama amaçlı olarak da düzeyine bakılmaktadır. Her ne kadar CA 19-9 düzeyindeki belirgin yükseklikler maligniteye yönlendirme açısından şüphe uyandırsa da her zaman altta yatan malign hastalık saptanmayıp, benign patolojiler de görülebilmektedir. Hashimoto tiroiditi ile takipli 45 yaşındaki kadın hasta; hâlsizlik, yorgunluk ve saç dökülmesi şikâyetleri ile kliniğimize başvurdu. Yapılan incelemelerde, TSH ve CA 19-9 yüksekliği olduğu görüldü. Malignite taramaya yönelik yapılan tetkik sonuçları normal saptanan hastada, hipotiroidi tedavisi sonrası normal TSH ve CA 19-9 düzeyi olduğu bulundu. Hastamızda da olduğu gibi, CA 19-9 yüksekliği saptanan bir bireyde ayırıcı tanı yapılır iken hipotiroidinin de akılda bulundurulması gerektiği düşünülmektedir.

Anahtar kelimeler: Hashimoto tiroiditi; hipotiroidi; CA 19-9

Introduction

Serum CA 19-9 (carbohydrate antigen 19-9) is a tumor marker that is expressed as a monosialoganglioside and a mucosal protein in tissues. CA 19-9, which is secreted into the blood, saliva, bronchial secretions, and in stomach and bile fluids, has found application in the follow-up of recurrence of certain malignant diseases post tumor resection, primarily in the biliopancreatic malignancies (1). However, CA 19-9 may also exhibit elevated levels in non-malignant diseases, such as biliary obstruction, chronic viral hepatitis, chronic pancreatitis, or idiopathic pulmonary fibrosis, as its specificity is not very high (2-5). Although there is no definite limit for CA 19-9 elevation that occurs in benign and malignant diseases, cer-

Address for Correspondence: Arzu Or Koca, University of Health Sciences, Keçiören Health Application and Research Center, Department of Endocrinology and Metabolism, Ankara, Turkey
Phone: +90 312 356 90 00 **E-mail:** drarzuor@hotmail.com
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tain studies have reported that the elevation values above certain thresholds are suggestive of malignant pancreatobiliary diseases (2, 6, 7). The earlier studies have revealed that CA 19-9 elevation may also occur in Hashimoto's thyroiditis in proportion to the elevation in the thyroid-stimulating hormone (TSH), even in the absence of any underlying malignant disease (8, 9). The present study was, therefore, aimed at demonstrating the relationship between the levels of CA 19-9 and thyroid function disorder in a patient undergoing a follow-up for the diagnosis of Hashimoto's thyroiditis.

Case Report

A 45-year-old female patient, who had been undergoing a follow-up for the diagnosis of Hashimoto's thyroiditis for 20 years, applied to our clinic with complaints of fatigue, tiredness, and hair loss. She had a history of smoking (five packs/year), although she had quit and been a non-smoker for the last ten years. She had no known diseases, her deceased mother had suffered from malignant esophagus neoplasm, and her father had been diagnosed with hypertension. The patient stated that she was on a replacement treatment with levothyroxine at a daily dose of 100 µg when she applied to our clinic. The findings of her physical examination were normal, except for the dry skin and frozen glance. In the laboratory analyses, it was determined that the TSH level was 17.08 µIU/mL (normal range: 0.55-4.78), serum free thyroxin level was 0.7 ng/mL (0.78-1.48), and the level of anti-thyroid peroxidase antibody was 720 U/mL (0-35). The annual routine controls conducted for screening purposes revealed high (52 U/mL) CA 19-9 levels (normal: <30.9). The CA 19-9 levels were determined to be high even on repeated measurements (Figure 1). The levels of carcinoembryonic antigen, carbohydrate antigen 15-3, carbohydrate antigen 125, alpha fetoprotein, and serum free triiodothyronine were observed to be within the normal limits, and the renal function tests and the liver function tests were also observed to be normal. She, therefore, consulted with the relevant department regarding the elevated levels of CA 19-9, following which, whole-body positron-emission tomography/computed tomography analysis was performed as the results of certain examinations such as mammography and upper gastrointestinal endoscopy were observed to be normal, and no increased metabolic activity uptake was determined for any organ. Physical examination, laboratory analyses, and imaging methods could provide no explanation for the elevated Ca-19-9 levels, and it was considered that the possible reason for the elevation in the Ca-19-9 levels was hypothyroidism.

The detailed study of the medical history of this patient with apparent hypothyroidism revealed that she had been using her medication irregularly for the last one month. Subsequently, her daily dose of levothyroxine was increased to 117.85 µg, and she was scheduled for a control visit six weeks later. Investigations in the control visit registered a significant decrease in the initial

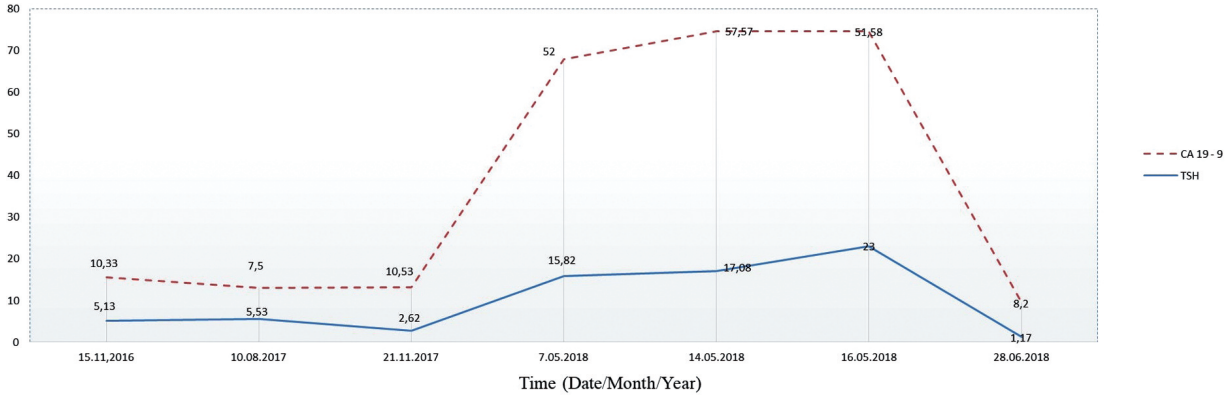

Figure 1: Patient's TSH and CA 19-9 measurements (TSH normal reference range: 0.55-4.78 µIU/mL; Ca 19-9 normal reference range: 0-30.9 U/mL).

complaints of fatigue, tiredness, and hair loss. Laboratory analysis determined that she was euthyroid. A decrease in the levels of CA 19-9, which reached 8.2 U/mL, was observed to accompany this improvement in the thyroid function (Figure 1).

Discussion

The American Association of Clinical Oncology has suggested that tumor markers should not be used in research on malignancies as even though they are relatively high in sensitivity, they exhibit low specificity (8). Tumor markers are nonetheless studied frequently with the belief that the unusually high values of the markers may assist in identifying malignancies. However, elevation in the levels of CA 19-9 (a tumor marker) may also be observed in benign diseases, as occurred in the case reported in the present study. Such a situation may cause anxiety to both the clinician and the patient, and may lead to unnecessary screening analyses. In the case reported in the present study, the reduced levels of CA 19-9 post the treatment for hypothyroidism demonstrated that the elevated value observed initially was not a result of any underlying malignancy. The literature indicates that thyroiditis may increase the levels of CA 19-9, Hashimoto's thyroiditis may elevate the CA 19-9 levels without disturbing the thyroid function tests, and an increase in the CA 19-9 levels may also occur in benign or malignant thyroid diseases (8, 10-15). However, contrary data were also reported suggesting that there was no relationship between Hashimoto's thyroiditis and CA 19-9 levels. In a study conducted in 2009 by Sezer et al., 71 patients with a diagnosis of Hashimoto's thyroiditis were examined, and no statistically significant difference was observed in the levels of CA 19-9 between the euthyroid and hypothyroid subjects. However, the number of patients included in that study was not reported, and no correlation was addressed between the serum CA 19-9 levels and TSH levels (16). Although the influence of thyroid diseases on CA 19-9 elevation has not been elucidated to date, it is commonly believed to be multifactorial (9). A previous study used immunohistochemical staining to demonstrate that the inflamed thyroid tissue produced CA 19-9 (11). However, CA 19-9 elevation could not be demonstrated in all the cases of inflammatory thyroid disease. The association between thyroid diseases and CA 19-9 levels remains a mystery due to a number of reasons, such as lack of CA 19-9 elevation in certain cases of thyroiditis, the observed elevations not always being in proportion to thyroid function disorder, and the complete absence of CA 19-9 elevation in certain malignant thyroid diseases (16). Therefore, it is suggested that screening for thyroid diseases in addition to the routine screening parameters would serve as a suitable approach to diagnosis for the patients exhibiting CA 19-9 elevations. In addition, further studies investigating the association between CA 19-9 and thyroid diseases are required to elucidate the details of this association.

Informed consent of the patient was obtained for the case report.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Arzu Or Koca, Mustafa Altay; Design: Arzu Or Koca, Mustafa Altay; Control/Supervision: Arzu Or Koca, Mustafa Altay; Data Collection and/or Processing: Arzu Or Koca, Mustafa Altay; Analysis and/or Interpretation: Arzu Or Koca, Mustafa Altay; Literature Review: Arzu Or Koca, Mustafa Altay; Writing the Article: Arzu Or Koca, Mustafa Altay; Critical Review: Arzu Or Koca, Mustafa Altay; References and Fundings: Arzu Or Koca, Mustafa Altay; Materials: Arzu Or Koca, Mustafa Altay.

References

1. Ventrucci M, Pozzato P, Cipolla A, Uomo G. Persistent elevation of serum CA 19-9 with no evidence of malignant disease. Dig Liver Dis. 2009;41:357-363. [Crossref] [PubMed]
2. Kim MS, Jeon TJ, Park JY, Choi J, Shin WC, Park SE, Seo JY, Kim YM. Clinical interpretation of elevated CA 19-9 levels in obstructive jaundice following benign and malignant pancreatobiliary disease. Korean J Gastroenterol. 2017;70:96-102. [Crossref] [PubMed]
3. Bertino G, Ardiri AM, Calvagno GS, Malaguarnera G, Interlandi D, Vacante M, Bertino N, Lucca F, Madeddu R, Motta M. Carbohydrate 19.9 antigen serum levels in liver disease. Biomed Res Int. 2013;2013:531640. [Crossref] [PubMed] [PMC]
4. Fania C, Pezzilli R, Melzi d'Eril G, Gelfi C, Barassi A. Identification of small proteins and peptides in the differentiation of patients with intraductal mucinous neoplasms of the pancreas, chronic pancreatitis and pancreatic adenocarcinoma. Dig Dis Sci. 2018;63:920-933. [Crossref] [PubMed]
5. Romero Estarlich V, González-Senac NM, Yulissa Peña Lora D, Vidán Astiz MT, Serra Rexach JA. [Progressive elevation of CA 19-9 tumour marker in a nonagenarian with advanced idiopathic pulmonary fibrosis]. Rev Esp Geriatr Gerontol. 2018;53:360-361. [Crossref] [PubMed]
6. Kim HJ, Kim MH, Myung SJ, Lim BC, Park ET, Yoo KS, Seo SK, Min YI. A new strategy for the application of CA19-9 in the differentiation of pancreaticobiliary cancer: analysis using a receiver operating characteristic curve. Am J Gastroenterol. 1999;94:1941-1946. [Crossref] [PubMed]
7. Morris-Stiff G, Teli M, Jardine N, Puntis MC. CA19-9 antigen levels can distinguish between benign and malignant pancreaticobiliary disease. Hepatobiliary Pancreat Dis Int. 2009;8:620-626. [PubMed]
8. Parra JL, Kaplan S, Barkin JS. Elevated CA 19-9 caused by Hashimoto's thyroiditis: review of the benign causes of increased CA 19-9 level. Dig Dis Sci. 2005;50:694-695. [Crossref] [PubMed]
9. Jamaludin AZ, Metassan MM, Zainal-Abidin Z, Chong VH. Elevated serum CA 19-9 in association with Hashimoto's thyroiditis. Singapore Med J. 2010;51:e143-145. [PubMed]
10. Takahashi N, Shimada T, Ishibashi Y, Oyake N, Murakami Y. Transient elevation of serum tumor markers in a patient with hypothyroidism. Am J Med Sci. 2007;333:387-389. [Crossref] [PubMed]
11. Tekin O. Hypothyroidism-related CA 19-9 elevation. Mayo Clin Proc. 2002;77:398. [Crossref] [PubMed]
12. Hashimoto T, Matsubara F. Changes in the tumor marker concentration in female patients with hyper-, eu-, and hypothyroidism. Endocrinol Jpn. 1989;36:873-7879. [Crossref] [PubMed]
13. Kamoshida S, Ogane N, Yasuda M, Muramatsu T, Bessho T, Kajiwara H, Osamura RY. Immunohistochemical study of type-1 blood antigen expressions in thyroid tumors: the significance for papillary carcinomas. Mod Pathol. 2000;13:736-741. [Crossref] [PubMed]
14. Ogawa M, Hori H, Hirayama M, Kobayashi M, Shiraishi T, Watanabe Y, Komada Y. Anaplastic transformation from papillary thyroid carcinoma with increased serum CA19-9. Pediatr Blood Cancer. 2005;45:64-67. [Crossref] [PubMed]
15. Leaes CG, Sperb D, Garcia E, Barra MB, Lima JP, da Oliveira MC. Elevated CA 19-9 associated with thyroid follicular adenoma. Endocrinologist. 2008;18:176-177. [Crossref]
16. Sezer K, Cakal E, Ozkaya M, Yaman E, Akbay E. Normal CA 19-9 levels in Hashimoto's thyroiditis. Asian Pac J Cancer Prev. 2009;10:315-318. [PubMed]