Case Report

Graves' Thyrotoxicosis Following SARS-CoV-2 Infection

Asaf Harris, MD, Mazen Al Mushref, MD

1 Spectrum Health/Michigan State University Internal Medicine, Grand Rapids, Michigan
2 Spectrum Health Medical Group Diabetes and Endocrinology, Grand Rapids, Michigan

A R T I C L E   I N F O

Article history:
Received 27 November 2020
Accepted 3 December 2020
Available online 14 December 2020

Key words:
thyroid
Graves' disease
coronavirus
COVID-19
SARS-CoV-2

A B S T R A C T

Objective: Graves' disease is an autoimmune thyroid disease that is thought to develop following environmental exposure in patients with genetic predisposition. Our objective is to present the first report of Graves' disease onset immediately following recovery from mild coronavirus disease 2019 (COVID-19), a close temporal occurrence that should be studied further.

Methods: We describe the clinical course and laboratory features, including thyroid function studies, antibody testing, and polymerase chain reaction testing for severe acute respiratory syndrome coronavirus 2.

Results: A 21-year-old woman with prediabetes, obesity, asthma, and gastroesophageal reflux disease presented to the emergency department reporting 3 days of tachycardia, palpitations, anxiety, and shortness of breath. Laboratory investigation revealed a thyroid-stimulating hormone level of 0.01 (0.30-5.00) mcIU/mL with a free thyroxine level of 3.8 (0.6-1.6) ng/dL, prompting endocrinology consultation. On physical examination, she had mild diffuse thyromegaly without tenderness and a history, which included hypothyroidism in her mother. Antibody testing results demonstrated thyroid-stimulating immunoglobulin and thyrotropin receptor antibody levels of 2.6 (<1.3) thyroid-stimulating immunoglobulin index and 17 (0.00-1.75) IU/L, respectively. Sixteen days before presenting to the ED, she was diagnosed with COVID-19 by polymerase chain reaction test after reporting typical symptoms, including fever. Infectious symptoms resolved within 10 days. She achieved clinical and laboratory improvements with a combination of methimazole and beta blocker therapy.

Conclusion: This case documents the occurrence of Graves' thyrotoxicosis following mild symptomatic COVID-19. Whether the preceding infection is coincidental or contributed to GD development requires definitive studies. This presentation may align with the theory of a viral link in the development of autoimmune thyroid disease in those with genetic predisposition.

© 2020 AACE. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Graves' disease (GD) is an autoimmune syndrome of hyperthyroidism typically accompanied by an enlarged thyroid gland and occasionally ocular and dermatologic manifestations. The excess stimulation of thyroid-stimulating hormone (TSH) receptors by thyroid receptor antibodies generates an unregulated production and secretion of thyroid hormone, resulting in clinical thyrotoxicosis. Current research supports genetic susceptibility and epigenetic modulation as key factors in the pathogenesis of GD, with contribution from environmental factors, including exposure to iodine, medications, stress, smoking, and certain viral infections.

We describe a previously unreported case of GD development in a close temporal occurrence to coronavirus disease 2019 (COVID-19) infection.

Case Report

A 21-year-old female healthcare worker presented to the emergency department (ED) for 3 days of progressively worsening tachycardia with palpitations, anxiety, and shortness of breath. Six days prior to the ED visit, she had a complete resolution of symptoms from mild COVID-19, which included fever, cough, myalgias, and anosmia. Diagnosis had been confirmed with positive oropharyngeal swab for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). She did not require hospitalization or...
treatment for COVID-19 beyond intermittent over the counter analgesic use. Further medical history includes mild intermittent asthma, gastroesophageal reflux disease, and class-I obesity as well as prediabetes managed with lifestyle modifications. Family history includes diabetes in both parents and hypothyroidism in her mother.

ED records noted that the patient presented with a warm and flushed appearance, tachycardia at 120 to 140/min, with shortness of breath, and mild anxiety. She was afebrile. Initial blood pressure was 150/93 mm Hg, with an oxygen saturation of 100%. Electrocardiogram was obtained, which demonstrated sinus tachycardia, and interpreted as otherwise normal by attending physicians. She was given 5 mg of oral diazepam, and a stat chest x-ray was performed, and complete blood count showed white blood cell, neutrophil, hemoglobin, and platelet counts of 10.26 × 10⁹/L, 70.8% (35.0%-80.0%), 13.5 (12.0-16.0) g/dL, and 288 × 10⁹/L (140-400 × 10⁹/L), respectively. Comprehensive metabolic panel revealed glucose, sodium, potassium, and creatinine levels of 114 (70-99) mg/dL, 138 (134-146) mmol/L, 4.2 (3.4-5.0) mmol/L, and 0.50 (0.50-1.10) mg/dL, respectively. Point of care urine pregnancy test was negative. High-sensitivity troponin assay was <6 (<14) ng/L. Following the intravenous administration of a benzodiazepine as well as 2 L of normal saline and 1000 mg of acetylsalicylic acid, the patient reported improvement in symptoms; however, she remained tachycardic at 115/min. This prompted consideration for thyroid abnormalities, and thyroid function tests were obtained. Results of the thyroid studies were pending at the time of discharge from the ED and were only available the following day, demonstrating a TSH level of 0.01 (0.30-5.00) mcIU/mL with a free thyroxine (T4) level of 3.8 (0.6-1.6) ng/dL. These results were conveyed to our endocrinology practice, and she was scheduled for an urgent consultation. Notably, the patient had normal TSH results at the time of discharge from the ED and were only available the following day. Thyroid function tests 1 month later were similar with TSH (0.1 [0.30-5.00] mcIU/mL) and free T4 (3.2 [0.6-1.6] ng/dL) ng/dL, prompting an increase in the methimazole dose to 30 mg daily. Three months after the diagnosis of GD, the patient came to the office for follow-up. Clinically euthyroid on exam, her TSH level was 0.01 (0.30-5.00) mcIU/mL with a free T4 level of 1.4 (0.6-1.6) ng/dL. The patient continues to be medically managed with thionamide titration and plans a trial discontinuation of the beta blocker.

Discussion

We report the development of GD in a patient very recently recovered from a mild SARS-CoV-2 infection. Previous testing of thyroid function was normal, and she had no clinical signs or symptoms of hyperthyroidism prior to her illness with COVID-19. Whether COVID-19 contributes to the development of GD, or the occurrence is coincidental, requires definitive studies. The relationship between GD and viral triggers has yet to be conclusively established despite suggestive epidemiologic evidence. Studies have proposed various potential mechanisms for GD development, such as antigen exposure, molecular mimicry, cytokine release, and inflammatory response.1-6 Case reports have documented GD following subacute thyroiditis, a viral infection of the thyroid.7,8 Severe acute respiratory syndrome coronavirus, the virus responsible for severe acute respiratory syndrome, was found to cause extensive damage to the thyroid glands. Furthermore, clinicians have linked subacute thyroiditis with SARS-CoV-2, the related novel coronavirus responsible for COVID-19.9-12 Though stress related to the infection may be an independent trigger unrelated to the specific viral syndrome, this is considered less likely, given the mild nature of initial illness. Family history in this case also supports the theory of genetic predisposition with external triggers.

Conclusion

This is the first case report, of which we are aware, suggesting SARS-CoV-2 as a potential viral trigger for the development of GD. This finding reinforces the need to better elucidate the relationship between viral infection and autoimmune thyroid disease as well as the direct effects of coronavirus infections on the thyroid.

Disclosure

The authors have no multiplicity of interest to disclose.

References

1. Smith T, Hegedüs L. Graves’ disease. N Engl J Med. 2016;375(16):1552–1565.
2. Brix TH, Kyvik KO, Christensen K, Hegedüs L. Evidence for a major role of heredity in Graves’ disease: a population-based study of two Danish twin cohorts. J Clin Endocrinol Metab. 2001;86(2):930–934. https://doi.org/10.1210/jcem.86.2.7242.
3. Tomer Y. Mechanisms of autoimmune thyroid diseases: from genetics to epigenetics. *Annu Rev Pathol*. 2014;9(1):147–156.
4. Davies T. Infection and autoimmune thyroid disease. *J Clin Endocrinol Metab*. 2008;93(3):674–676.
5. Tomer Y, Davies TF. Infection, thyroid disease, and autoimmunity. *Endocr Rev*. 1993;14(1):107–120.
6. Desailloud R, Hober D. Viruses and thyroiditis: an update. *Virol J*. 2009;6(1):5.
7. Nakano Y, Kurihara H, Sasaki J. Graves’ disease following subacute thyroiditis. *Tohoku J Exp Med*. 2011;225(4):301–309.
8. Hallengren B, Planck T, Asman P, Lantz M. Presence of thyroid-stimulating hormone receptor antibodies in a patient with subacute thyroiditis followed by hypothyroidism and later Graves’ disease with ophthalmopathy: a case report. *Eur Thyroid J*. 2015;4(3):197–200.
9. Wei L, Sun S, Xu CH, et al. Pathology of the thyroid in severe acute respiratory syndrome. *Hum Pathol*. 2007;38(1):95–102.
10. Brancatella A, Ricci D, Viola N, Sgro D, Santini F, Latrofa F. Subacute thyroiditis after SARS-CoV-2 infection. *J Clin Endocrinol Metab*. 2020;105(7):1–6.
11. Asfuroğlu Kalkan E, Ates I. A case of subacute thyroiditis associated with COVID-19 infection. *J Endocrinol Invest*. 2020 Jun 5:1–2. https://doi.org/10.1007/s40618-020-01316-3.
12. Agarwal S, Agarwal SK. Endocrine changes in SARS-CoV-2 patients and lessons from SARS-CoV. *Postgrad Med J*. Epub ahead of print: June 17, 2020. https://doi.org/10.1136/postgradmedj-2020-13793