Case Report

Asia Pacific Allergy

OPEN

Thyroid disease post-COVID-19 infection: Report of a case with new-onset autoimmune thyroid disease

Anh Ngoc Trinh[1], Kim Han Nguyen[2], and Dinh Van Nguyen[1,2,3,*]

ABSTRACT

We present hyperthyroidism with autoimmune thyroid disease, which developed a few weeks after the COVID-19 infection in a patient with no prior thyroid disease. Our case was described with clinical presentations, diagnostic tests, and subsequent patient management and compared to other similar reported cases. A 28-year-old female patient with no prior history of thyroid dysfunction developed hyperthyroidism 8 weeks after COVID-19 infection, confirmed by low thyroid stimulating hormone, high free thyroxine 4, and thyroid receptor antibody. She was treated and responded well to methimazole 20 mg in a few weeks. We searched the literature and found three other similar reported cases and compared those. The effects of COVID-19 infection on the immune system and the thyroid gland might explain the pathology of hyperthyroidism post-COVID-19 infection in this patient. This new-onset hyperthyroidism was found in a woman with mild symptoms and responded well to thiamazole and β-blockers.

Keywords: Autoimmune thyroiditis; COVID-19; thyroid diseases

1. Introduction

Since the outbreak of COVID-19 in late 2019, the disease has been suspected of triggering multiple immune responses, which could lead to several autoimmune disorders such as atypical/subacute thyroiditis, Graves' disease, Guillain-Barre syndrome and multisystem inflammatory syndrome [1–3]. In this report, we describe a patient who developed autoimmune thyroid disease, precisely a case of Graves' disease, who presented with hyperthyroidism 4 weeks after COVID-19 infection.

2. Case report

A 28-year-old female with no history of prior thyroid disease had normal thyroid function tests during the annual health check in October 2021. She developed cough, chills, fever, fatigue, and headache and had a confirmatory RT-PCR test for COVID-19 on February 14, 2022, which was self-resolved within 1 week. Six weeks later, she had palpitations and shortness of breath when exercising. Physical examination showed mild and painless thyromegaly. Further evaluation on March 21, 2022, indicated decreased thyroid-stimulation hormone (TSH) (<0.01 mIU/L), elevated free triiodothyronine (fT3) (6.18 pmol/L), free thyroxine 4 (fT4) (36.04 pmol/L), thyroglobulin antibodies (173 IU/mL), thyroid receptor antibody (TRAb) (31.7 IU/L), and thyroid peroxidase (TPO) Ab (>1000 IU/mL) (**Table 1**). Thyroid ultrasound showed mild thyromegaly with heterogeneous and diffuse hypervascular sonographic appearance.

She has been treated with methimazole 20 mg and improved clinically. The palpitations and breathlessness settled. After 2 months of treatment, her laboratory tests showed significant improvement with free T4 7.3 pmol/L and TSH 4.083 mIU/L, then continuing the recovery trend until this report with free T4 8.42 pmol/L, TSH 2.813 mIU/L, and TPO Ab 42.18 IU/mL.

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Ethical approval for this study (Ethical Committee No. 89/2022/CN-HDDD VMEC) was provided by the Vinmec Healthcare System & Vinuniversity Institutional Ethical Review Board For Biomedical Research, Hanoi, Vietnam (Chairperson Prof. Cuong Tat Do) on August 19, 2022.

3. Discussion

Several reports have described a relationship between COVID-19 and thyroid disorders such as subacute thyroiditis, autoimmune thyroiditis, and Graves' disease [4–6]. In a retrospective single-center study by Lania [7], 20.2% of their cohort were found to have thyrotoxicosis. Serum TSH levels were inversely correlated with age and interleukin 6 (IL-6) levels.

Autoimmune thyroiditis is one of the most common thyroid disorders in South East Asia [8, 9]. In this condition, detectable anti-thyroid antibodies such as anti-thyroid peroxidase (*anti*-TPO) and anti-thyroglobulin antibodies (*anti*-Tg) are present in the sera of most patients. *Anti*-Tg antibodies were undetectable in our patient's pre-COVID-19 infection but were found after the disease had resolved, as in several similar cases in other countries [10].

[1]*Internal Medicine Department, Vinmec Healthcare System, Hanoi, Vietnam,* [2]*College of Health Sciences, VinUniversity, Hanoi, Vietnam,* [3]*Department of Medicine, Penn State University, PA, USA,*

**Correspondence to Dinh Van Nguyen Allergy and Clinical Immunology Center, Vinmec Healthcare System, Hanoi, Vietnam; College of Health Sciences, VinUniversity, Hanoi, 458 Minh Khai, Hai Ba Trung district, Ha Noi, Vietnam.*

Tel: +8424-3974-3556, ex 4067

Fax: +8424-3974-3557

Email: v.dinhnv6@vinmec.com

Received: 20 February 2023; Accepted: 22 February 2023

Published online 30 March 2023

http://dx.doi.org/10.5415/apallergy.0000000000000023

Table 1.

Summary of laboratory results before and after COVID-19 infection and after treatment

		Before COVID-19 infection	After COVID-19 infection	After treatment		
	Normal range	Oct 2021	Mar 2022	May 2022	Nov 2022	Feb 2023
TSH (mIU/L)	0.34–5.6	2.119	<0.01	4.083	2.99	2.813
fT4 (pmol/L)	7.86–14.41	7.61	36.04	7.3	8.41	8.42
fT3 (pmol/L)	3.95–6.8	4.92	6.18		3.97	
Thyroglobulin antibodies (TGAb) (IU/mL)	≤115	19.2	173			
Thyrotropin receptor antibody (TRAb) (IU/L)	≤1.75		31.7		2.78	
TPO Antibody (TPOAb) (IU/mL)	≤5.61		>1000		150.08	42.18

N/A, not available; fT3, free triiodothyronine; fT4, free thyroxine 4; TSH, thyroid-stimulation hormone.

Table 2.

Description of the demographic characteristics and clinical presentation of COVID-19 triggered Graves' disease

Year	Reference	Age	Gender	Preexisting thyroid disease	Clinical presentation of COVID-19	Onset after COVID-19 (days)	Goiter	Palpitations	Therapy
2020	[14]	53	F	No	Bilateral interstitial pneumonia	30	Yes	Yes	Methimazole and propanolol
2021	[15]	33	F	No	Fever, cough	84	Yes	Yes	Methimazole
2022	[16]	48	F	No	Fever, cough	0	Yes	No	Methimazole & Metoprolol

Table 3.

Biochemical evaluation of thyroid function parameters, thyroglobulin, thyroid autoantibodies, and inflammatory markers in the 3 included patients

Year	Ref	TSH (U/l)	fT4 (pmol/l)	TgAb (U/l)	TPOAb (U/l)	TRAb (U/l)	Ultrasound	Iodine uptake
2020	[14]	<0.01	36.5	1617	3239	6.07	N/A	Increased (61–62%)
2021	[15]	<0.01	27.03	N/A	N/A	309	Mild thyromegaly with heterogeneous and diffusely hypervascular thyroid	N/A
2022	[16]	<0.01	36.04	N/A	N/A	6.31	Diffusely heterogeneous and irregular thyroid with increased Doppler flow	Increased (47%)

N/A, not available; fT4, free thyroxine 4; TRAb, thyroid receptor antibody; TSH, thyroid-stimulation hormone.

Graves' disease is the most common cause of hyperthyroidism in South East Asia [8, 9]. It is also an autoimmune thyroid disease in which the presence of TRAb and a low or undetectable TSH level are typical. Most reported case series of hyperthyroidism during active COVID-19 infection suggest that destructive viral thyroiditis contributes to the clinical presentation of subacute thyroiditis [4–7, 11–13]. An autopsy study in COVID-19 patients showed the destruction of the follicular and parafollicular cells of the thyroid [13]. Our literature search revealed reports of thyroid disorders occurring after COVID-19 infection are sparse, and as far as we are aware, this is the first case of new-onset Graves' disease post-COVID-19 in Vietnam. However, several subjects reported recently have shown a new onset of Graves' disease as the cause of hyperthyroidism in patients after COVID-19 infection [13–15]. Relevant demographic and clinical characteristics of each included patient are summarized in **Table 2** and investigation results in these patients are summarized in **Table 3**.

Along with our case, all three previously reported subjects were female (ages ranged from 28 to 53 years). No patients had been previously diagnosed with thyroid disease. All patients had had COVID-19 infections with respiratory symptoms. The interval between diagnosis of hyperthyroidism and COVID-19 condition ranged from 0 to 84 days. Like our case, most of these patients manifested a goiter and palpitations. Thyroid function tests showed overt hyperthyroidism. TSH levels were undetectable (<0.01 U/L), and fT4 was 2 to 3 times higher than the upper limit of the normal level (normal range, 27–36.5 pmol/L). Thyroid autoantibodies were measured and showed increased TRAb in all cases. *Anti*-Tg and *anti*-TPO were significantly elevated in our case and in that reported by Mateu-Salat [14]. Thyroid ultrasound examinations of these patients were typical for Graves' disease, with hypervascularity and mild thyromegaly. Iodine uptakes were done in two patients to confirm the diagnosis of hyperthyroidism. Patients were all treated with anti-thyroid medication, and clinical improvement resulted.

The major limitation of our case report review is the scarcity of published cases (only 3 other patients have reported so far). Nevertheless, these reports are likely to be of benefit to clinicians who encounter cases of new-onset hyperthyroidism after COVID-19 infection. From our review, the hyperthyroidism is mild, responds well to methimazole and β-blockers in combination and has a low incidence of post-COVID-19 infection. A more extensive case series might confirm these findings. Moreover, additional follow-up data are necessary to assess long-term outcomes in these cases.

4. Conclusion

COVID-19 infection has been shown to trigger various autoimmune diseases affecting the thyroid gland. We present a case who developed Graves' disease 4 weeks after COVID-19 infection. Reviewing similar reported cases suggests that new-onset hyperthyroidism after COVID-19 infection may occur more

commonly in females, usually presents as a mild disease, and responds well to methimazole and β-blockers in combination.

Acknowledgements

The authors wish to thank Prof van Nunen, Faculty of Medicine and Health, Macquarie University, and The University of Sydney for reviewing and editing this paper. We are grateful to our patient and her family, who supported us in completing this work. Financial support and sponsorship: none.

Conflicts of interest

The authors have no financial conflicts of interest.

Author contributions

Conceptualization: Trinh Ngoc Anh and Dinh Van Nguyen. Investigation: Trinh Ngoc Anh and Dinh Van Nguyen. Clinical treatment: Trinh Ngoc Anh and Dinh Van Nguyen. Project administration: Trinh Ngoc Anh, Kim Han Nguyen. Writing - original draft: Trinh Ngoc Anh, Kim Han Nguyen. Review and approved MS: Trinh Ngoc Anh, Dinh Van Nguyen.

References

1. Dworakowska D, Grossman AB. Thyroid disease in the time of COVID-19. Endocrine 2020;68:471-74.
2. Bellastella G, Maiorino MI, Esposito K. Endocrine complications of COVID-19: what happens to the thyroid and adrenal glands?. J Endocrinol Invest 2020;43:1169-70.
3. Pal R, Banerjee M. COVID-19 and the endocrine system: exploring the unexplored. J Endocrinol Invest 2020;43:1027-31.
4. Brancatella A, Ricci D, Cappellani D, Viola N, Sgrò D, Santini F, Latrofa F. Is subacute thyroiditis an underestimated manifestation of SARS-CoV-2 infection? Insights from a case series. J Clin Endocrinol Metab 2020;105:e3742-e3746.
5. Chen M, Zhou W, Xu W. Thyroid function analysis in 50 patients with COVID-19: a retrospective study. Thyroid 2021;31:8-11.
6. Campos-Barrera E, Alvarez-Cisneros T, Davalos-Fuentes M, Usui T. Subacute thyroiditis associated with COVID-19. Case Rep Endocrinol 2020;2020:1-4.
7. Lania A, Sandri MT, Cellini M, Mirani M, Lavezzi E, Mazziotti G. Thyrotoxicosis in patients with COVID-19: the THYRCOV study. Eur J Endocrinol 2020;183:381-7.
8. Young RTT. Thyroid disease in South East Asia. Pathology (Phila) 1990;22:833.
9. McLeod DSA, Caturegli P, Cooper DS, Matos PG, Hutfless S. Variation in rates of autoimmune thyroid disease by race/ethnicity in US military personnel. JAMA 2014;311:15631563.
10. Tee L, Harjanto S, Rosario B. COVID-19 complicated by Hashimoto's thyroiditis. Singapore Med J 2021;62:265-265.
11. Mehmood MA, Bapna M, Arshad M. A case of post-COVID-19 subacute thyroiditis. Cureus 2020;12:e12301.
12. Ruggeri RM, Campennì A, Siracusa M, Frazzetto G, Gullo D. Subacute thyroiditis in a patient infected with SARS-COV-2: an endocrine complication linked to the COVID-19 pandemic. Hormones 2021;20:219-21.
13. Lui DTW, Lee CH, Chow WS, Lee ACH, Tam AR, Fong CHY, Law CY, Leung EKH, To KKW, Tan KCB, Woo YC, Lam CW, Hung IFN, Lam KSL. Thyroid dysfunction in relation to immune profile, disease status, and outcome in 191 patients with COVID-19. J Clin Endocrinol Metab 2021;106:e926-e935.
14. Mateu-Salat M, Urgell E, Chico A. SARS-COV-2 as a trigger for autoimmune disease: report of two cases of Graves' disease after COVID-19. J Endocrinol Invest 2020;43:1527-28.
15. Feghali K, Atallah J, Norman C. Manifestations of thyroid disease post COVID-19 illness: Report of Hashimoto thyroiditis, Graves' disease, and subacute thyroiditis. J Clin Transl Endocrinol Case Rep 2021;22:100094.
16. Ghareebian H, Mariash C. COVID-19-induced graves' disease. Cureus 2022;14:e22260.