Case Report

SUBACUTE THYROIDITIS IN A PATIENT WITH CORONAVIRUS DISEASE 2019

Mari Des J. San Juan, MD, MBA[1]; Mary Queen V. Florencio, MD[1,2]; Mark Henry Joven, MD[1,3,4]

ABSTRACT

Objective: Subacute thyroiditis (SAT) is an inflammatory disorder of the thyroid gland that causes destructive thyrotoxicosis and is attributed to a viral or post-viral response. SARS-CoV-2 is a novel coronavirus that caused a global pandemic in 2020. We present a case that suggests that there may be a relationship between SAT and coronavirus disease 2019 (COVID-19).

Methods: We describe the clinical findings, thyroid function tests, and neck ultrasound of a patient presenting with anterior neck pain.

Results: A 47-year-old, Filipino female presented with anterior neck pain associated with neck tenderness and goiter. She did not have fever or respiratory symptoms but had right lower lobe pneumonia on chest radiograph. Thyroid function tests were consistent with subclinical hyperthyroidism with thyroid-stimulating hormone of 0.05 μIU/mL (reference range is 0.47 to 4.68 μIU/mL), free thyroxine of 1.68 pg/mL (reference range is 0.78 to 2.19 pg/mL), and total triiodothyronine of 1.4 ng/mL (reference range is 0.97 to 1.69 ng/mL). Anti-thyroid peroxidase, anti-thyroglobulin, and thyroid-stimulating hormone receptor antibodies were negative. Neck ultrasound showed heterogenous thyroid tissues with normal vascularity. Reverse transcription-polymerase chain reaction for SARS-CoV-2 using nasopharyngeal and oropharyngeal swabs were positive. The patient was diagnosed as having SAT and was treated with mefenamic acid, which was later switched to celecoxib. Ceftriaxone and hydroxychloroquine were started for COVID-19 pneumonia. Complete resolution of symptoms and primary hypothyroidism occurred after 2 months.

Conclusion: SAT may be a presenting symptom or a sequela of COVID-19. Histopathology studies and definitive documentation of the virus in thyroid tissues may be required to confirm the relationship between SAT and COVID-19. **(AACE Clinical Case Rep. 2020;6:e361-e364)**

Abbreviations:
COVID-19 = coronavirus disease 2019; **RT-PCR** = reverse transcription polymerase chain reaction; **SAT** = subacute thyroiditis; **TSH** = thyroid-stimulating hormone

INTRODUCTION

Subacute thyroiditis (SAT) is a spontaneously remitting, inflammatory disorder due to a post-viral response (1). In 2020, the novel coronavirus disease 2019 (COVID-19) caused a global pandemic resulting in numerous fatalities (2). In the Philippines, it was first reported on January 30, 2020 (3) with community transmission confirmed on March 7, 2020 (4). COVID-19 presents with mild, flu-like

Submitted for publication July 28, 2020
Accepted for publication September 21, 2020
From the [1]Section of Endocrinology, Diabetes, and Metabolism, The Medical City, Pasig City, Philippines, [2]Section of Endocrinology, Diabetes, and Metabolism, St. Luke's Medical Center, Quezon City, Philippines, [3]Faculty of Medicine and Surgery, University of Santo Tomas, Manila, Philippines, and [4]Geriatrics Center, St. Luke's Medical Center - Global City, Taguig City, Philippines.
Address correspondence to Dr. Mari Des J. San Juan, Endocrine, Diabetes, and Thyroid Center, The Medical City, Ortigas Avenue, Pasig City, Metro Manila, Philippines.
E-mail: maridessan1@gmail.com.
DOI:10.4158/ACCR-2020-0524

symptoms to sometimes severe, fatal disease (5). We present a case of SAT in a patient with COVID-19 infection, suggesting that SAT might be an atypical presentation of COVID-19.

CASE REPORT

A 47-year-old, Filipino female anesthesiologist with asthma was admitted to our institution for anterior neck pains. Seven weeks prior, she noted left-sided anterior neck pains and swelling aggravated by palpation and neck hyperextension. She denied fever, cough, colds, or hoarseness. Point-of-care ultrasound showed an enlarged right thyroid lobe with heterogenous parenchyma. She took mefenamic acid affording resolution of symptoms. Two weeks before admission, her neck pains recurred, now radiating to the right submandibular region. Oral and nasopharyngeal swabs for the virus SARS-CoV-2 via reverse transcription polymerase chain reaction (RT-PCR) were positive, hence admission.

The patient had normal vital signs and was not in cardiorespiratory distress. The right thyroid lobe and isthmus were diffusely enlarged and tender. There was no cervical lymphadenopathy or signs of thyrotoxicosis. C-reactive protein was 5.09 mg/dL (reference range is 1.00 to 3.00 mg/dL) and lactate dehydrogenase was 251 U/L (reference range is 120 to 246 U/L), both elevated. Complete blood count, ferritin, and procalcitonin were normal. Thyroid function tests were consistent with subclinical hyperthyroidism (Table 1). Anti-thyroid peroxidase, anti-thyroglobulin, and thyroid-stimulating hormone (TSH) receptor antibodies were negative. Neck ultrasound showed a slightly enlarged right thyroid lobe, with ill-defined hypoechogenicity and normal vascularity in both lobes (Fig. 1). Thyroid uptake and scan was not done because of reagent unavailability. Chest radiograph showed right lower lobe pneumonia.

Mefenamic acid was started, but was later shifted to celecoxib due to epigastric pains. Oral hydroxychloroquine and intravenous ceftriaxone were initiated. Glucocorticoid therapy was offered, however the patient opted to continue monitoring. Repeat RT-PCR testing for SARS-CoV-2 10 days after was negative and the patient was discharged. The patient reported full resolution of symptoms a month later. Eight weeks after admission, she felt sluggish and had hair thinning but denied other symptoms of hypothyroidism. Repeat thyroid function tests showed overt hypothyroidism (Table 1) and she was started on levothyroxine supplementation.

DISCUSSION

The incidence of SAT is 4.9 cases/100,000/year with a mean age of 46 years and a female-to-male ratio of 3.5:1 (1). It presents as unilateral or bilateral neck pains radiating to the jaw or ears, and an extremely painful and tender thyroid (6). Its course can be divided into thyrotoxic, hypothyroid, and euthyroid phases. Acute inflammatory responses in the thyrotoxic phase results in suppressed TSH with elevated thyroglobulin and thyroxine, which may persist up to 6 weeks. Once thyroid stores are depleted, TSH rises to hypothyroid levels. Ninety percent of patients regain thyroid function and become euthyroid within 6 to 12 months (7). In this case, the patient was in the thyrotoxic phase at 7 weeks from the start of neck pains and transitioned to overt hypothyroidism 8 weeks later.

SAT is differentiated from other causes of thyroiditis based on elevated erythrocyte sedimentation rate, thyroglobulin, and C-reactive protein, a 24-hour radioactive iodine uptake <5% during the toxic phase, and hypoechogenic thyroid with low-to-normal vascularity on ultrasound (7). Autoantibodies are usually negative. Although histopathology confirms diagnosis, it is often unnecessary (8). The elevated C-reactive protein, the absence of thyroid autoantibodies, and characteristic neck ultrasound findings in the case suggests SAT.

Although the specific cause of SAT has not been identified, multiple studies have reported familial occurrence (9) and strong association with the antigen HLA-B35 (10,11). Viral infections are thought to trigger an inflammatory response, as SAT usually presents with viral prodrome with clustering during virus outbreaks (12). Increased antibody titers for mumps virus (13), Epstein-Barr virus (14), and influenza A virus (15) have been found during the acute phase. Pharyngeal swab PCR and viral loads were used to document co-occurrence with H1N1 influenza (16) and primary infection with human immunodeficiency virus (17).

The receptor-binding domains of SARS-CoV-2 is recognized by human angiotensin-converting enzyme-2 receptor (18). Apart from the lungs, gene expression profiling revealed high expression of angiotensin-converting

Table 1
Thyroid Function Tests

	Upon admission	After 8 weeks	Reference range
Thyroid-stimulating hormone (μIU/mL)	0.05	94.30	0.47-4.68
Free thyroxine (pg/mL)	1.68	0.23	0.78-2.19
Total triiodothyronine (ng/mL)	1.40	--	0.97-1.69
Free triiodothyronine (pg/mL)	--	1.20	2.77-5.27

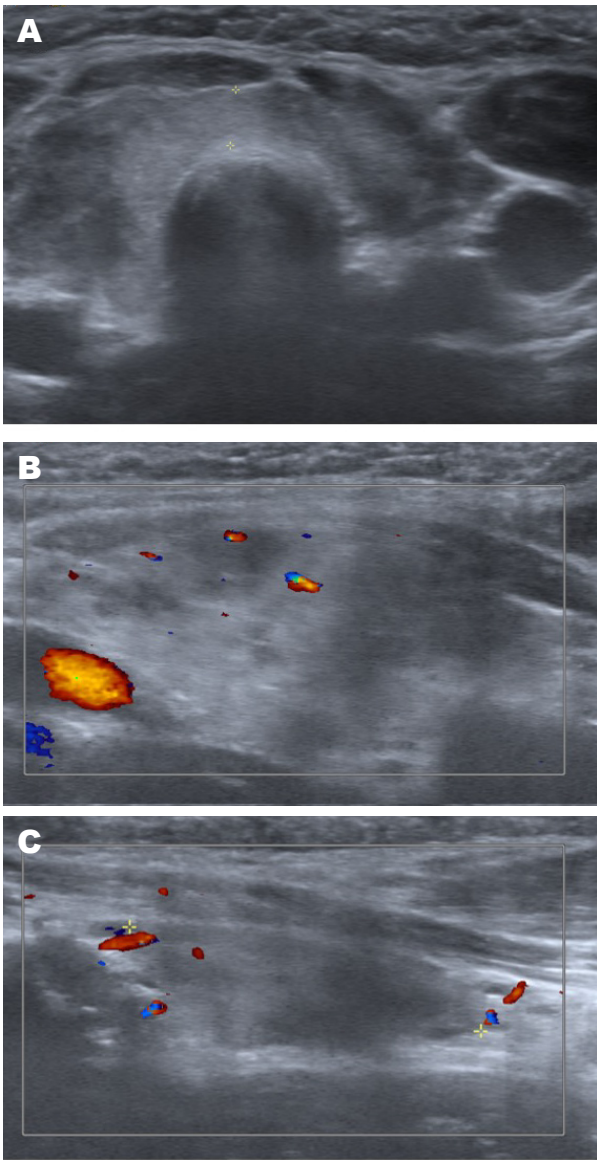

Fig. 1. (*A*) Transverse view of neck ultrasound showed slightly enlarged right thyroid lobe (4.72 × 1.78 × 2.11 cm) and a normal-sized left thyroid lobe (3.18 × 1.26 × 1.18 cm), with heterogenous echogenicity of both lobes. (*B*) Sagittal view of right thyroid lobe with Doppler studies revealing normal vascularity. (*C*) Sagittal view of left thyroid lobe with Doppler studies revealing normal vascularity.

enzyme-2 receptors in the thyroid and other tissues (19), suggesting possible SARS-CoV-2 infection of the thyroid. At present, there are no studies that document the presence of SARS-CoV-2 in thyroid tissues. A case report from Italy described an 18-year-old female who presented with mild upper respiratory and thyrotoxic symptoms, elevated inflammatory markers, and ultrasound findings consistent with SAT 15 days after a positive SARS-CoV-2 RT-PCR oropharyngeal swab (20). Since the relationship between COVID-19 and SAT is unknown, a high index of suspicion for COVID-19 may be necessary in patients presenting with SAT to identify patients who may require early isolation to prevent transmission of SARS-CoV-2.

CONCLUSION

To our knowledge, this is one of the earliest reported cases of SAT in a patient with confirmed COVID-19 without respiratory manifestations. Symptoms, physical examination findings, and laboratory results appear similar to the usual course of disease. SAT may be a presentation or sequela of COVID-19. Histopathology studies with definitive documentation of the virus in thyroid tissues is required to confirm the relationship.

ACKNOWLEDGMENT

We thank the staff of the Endocrine, Diabetes, and Thyroid Center, The Medical City, Pasig City, Philippines for their support.

DISCLOSURE

The authors have no multiplicity of interest to disclose.

REFERENCES

1. **Fatourechi V, Aniszewski JP, Fatourechi GZE, Atkinson EJ, Jacobsen SJ.** Clinical features and outcome of subacute thyroiditis in an incidence cohort: Olmsted County, Minnesota, study. *J Clin Endocrinol Metab*. 2003;88:2100-2105.
2. **Rothan HA, Byrareddy SN.** The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *J Autoimmun*. 2020;109:102433.
3. Department of Health, Philippines. DOH confirms first 2019-nCoV case in the country; assures public of intensified containment measures. Available at: https://www.doh.gov.ph/doh-press-release/doh-confirms-first-2019-nCoV-case-in-the-country. Accessed November 8, 2020.
4. Department of Health, Philippines. DOH reveals more negative 2019-nCoV cases; confirms first nCoV ARD death in PH. Available at: https://www.doh.gov.ph/press-release/DOH-reveals-more-negative-2019-nCoV-cases-confirms-first-nCoV-ARD-death-in-PH. Accessed November 8, 2020.
5. **Ge H, Wang X, Yuan X, et al.** The epidemiology and clinical information about COVID-19. *Eur J Clin Microbiol Infect Dis*. 2020;39:1011-1019.
6. **Guimarães VC.** Subacute and Riedel's thyroiditis. In: Jameson JL, De Groot LJ, eds. *Endocrinology: Adult and Pediatric*. 7th ed. Philadelphia, PA: Elsevier; 2015: 1528-1539.
7. **Samuels MH.** Subacute, silent, and postpartum thyroiditis. *Med Clin North Am*. 2012;96:223-233.
8. **Prajapati S, Hernandez-Prera JC.** Putting all the pieces together: clinical, macroscopic and microscopic characteristics of subacute thyroiditis. *Head Neck Pathol*. 2019;13:231-234.
9. **Zein EF, Karaa SE, Megarbane A.** Familial occurrence of painful subacute thyroiditis associated with human leukocyte antigen-B35. *Presse Med*. 2007;36:808-809.
10. **Tamai H, Goto H, Uno H, et al.** HLA in Japanese patients with subacute (De Quervain's) thyroiditis. *Tissue Antigens*. 1984;24:58-59.
11. **Kramer AB, Roozendaal C, Dullaart RP.** Familial occurrence of subacute thyroiditis associated with human leukocyte antigen-B35. *Thyroid*. 2004;14:544-547.
12. **Desailloud R, Hober D.** Viruses and thyroiditis: An update. *Virol J*. 2009;6:5.

13. **Eylan E, Zmucky R, Sheba C.** Mumps virus and subacute thyroiditis; evidence of a causal association. *Lancet*. 1957;272:1062-1063.
14. **Espino Montoro A, Medina Pérez M, González Martín MC, Asencio Marchante R, López Chozas JM.** Subacute thyroiditis associated with positive antibodies to the Epstein-Barr virus [in Spanish]. *An Med Interna*. 2000;17:546-548.
15. **Cunha BA, Berbari N.** Subacute thyroiditis (de Quervain's) due to influenza A: presenting as fever of unknown origin (FUO). *Heart Lung*. 2013;42:77-78.
16. **Dimos G, Pappas G, Akritidis N.** Subacute thyroiditis in the course of novel H1N1 influenza infection. *Endocrine*. 2010;37:440-441.
17. **Bouillet B, Petit JM, Piroth L, Duong M, Bourg JB.** A case of subacute thyroiditis associated with primary HIV infection. *Am J Med*. 2009;122:e5-e6.
18. **Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R.** COVID-19 infection: origin, transmission, and characteristics of human coronaviruses. *J Adv Res*. 2020;24:91-98.
19. **Ziegler CGK, Allon SJ, Nyquist SK, et al.** SARS-CoV-2 receptor ACE2 is an interferon-stimulated gene in human airway epithelial cells and is detected in specific cell subsets across tissues. *Cell*. 2020;181:1016-1035.e19.
20. **Brancatella A, Ricci D, Viola N, Sgrò D, Santini F, Latrofa F.** Subacute thyroiditis after Sars-COV-2 infection. *J Clin Endocrinol Metab*. 2020;105:dgaa276.