Subacute thyroiditis associated with COVID-19 affecting health professionals, a case series in high-risk population

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ABSTRACT

Background: Healthcare professionals are more vulnerable to infectious infections, especially ones that are easily transferred, such as COVID-19. Subacute thyroiditis is a self-limiting thyroid gland infection caused by a virus. SARS-CoV-2 infection increases the prevalence of subacute thyroiditis.

Objective: This case series addresses the emergence of subacute thyroiditis cases linked to SARS-CoV-2 infection, which is more common in healthcare personnel.

Methods: This study analyzed nine COVID-19 cases with neck pain symptoms. The clinical presentation, thyroid markers, ultrasound features of the thyroid gland, and its management were described in this study.

Result: There were nine cases included, and seven out of nine were experienced by healthcare professional workers. All of them were patients in the Clinic of Endocrinology Metabolism and Diabetes - Thyroid Center, Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia, from January to June 2021. Most of them presented with mild to moderate neck pain. All patients had clinical improvement within two weeks to two months after receiving treatments.

Conclusion: Subacute thyroiditis is a painful thyroid gland disease characterized by acute inflammation of the thyroid gland, which can arise during or after a viral infection such as COVID-19. This case series emphasizes the importance of physicians awareness that subacute thyroiditis could be one of many clinical spectra of SARS-CoV-2 infection that should not be missed.

Keywords: Subacute Thyroiditis, COVID-19, neck pain, healthcare workers.


INTRODUCTION

Healthcare professional workers are more susceptible to developing infectious diseases, particularly those that are easily transmitted, such as COVID-19. The prevalence of infection among medical and nursing employees calls for a heightened focus on healthcare workers. Until 11 February 2020, a very early phase of COVID-19, it was estimated that 1,716 Chinese healthcare workers were infected with COVID-19.¹

Subacute thyroiditis (SAT) is a self-limiting thyroid gland condition caused by viral infection. It is characterized by acute inflammation of the thyroid gland. Subacute thyroiditis typically develops between two and eight weeks after a viral respiratory tract infection. Neck pain or discomfort is a frequent symptom. This, however, can be masked by identical symptoms associated with a respiratory illness caused by SARS-CoV-2, the etiology of COVID-19. Clinical symptoms can range from fever to headache, myalgia and arthralgia, tiredness, and sore throat. Thyroiditis should be suspected if neck pain, thyroid gland enlargement, and soreness are present.²

Subacute thyroiditis can occur during or following a viral illness. SAT is more prevalent during and after SARS-CoV-2 infection. Numerous studies have documented an increase in SAT incidence following viral outbreaks. Additionally, previous research has demonstrated that viral infection induced by the H1N1 virus can increase the prevalence of SAT.³

This case series discusses the development of SAT cases associated with SARS-CoV-2 infection which more prevalent in health care providers. It underlines that SAT may be a clinical manifestation of SARS-CoV-2 disease and may potentially occur following SARS-CoV-2 infection, which must be appropriately managed.

METHODS

A retrospective data of patients presented at Outpatient Clinic of Endocrinology Metabolism and Diabetes - Thyroid Center, Dr. Zainoel Abidin Hospital, Banda Aceh, Aceh, Indonesia for over six months from January to June 2021. Nine patients were included in this report, six were confirmed for COVID-19, and three were probable. Demographic information, clinical manifestation, diagnostic tests, and therapy were provided. Diagnosis of COVID-19 was made by oropharynx and nasopharynx swabs.
RESULTS

Nine patients were included in this report; all were female, mostly in their thirties, most of them were healthcare providers. The most common symptom was neck pain, 50% of patients had a fever, and 30% had palpitation. Other symptoms were tenderness, weakness, fatigue, loss of appetite, weight loss, and flu-like syndrome. Laboratory results revealed leukocytosis, increased erythrocyte sedimentation rate (ESR), suppressed TSH, and elevated FT4. Thyroid ultrasound showed diffuse, hypoechoic area and minimal vascularization. A polymerase Chain Reaction (PCR) swab of the oropharynx and nasopharynx was done, and the result was confirmed positive for COVID-19 in 6 patients. In contrast, the three others had a positive result for rapid test COVID-19 antibody. Due to the COVID-19 pandemic, fine needle aspiration (FNA) was not performed on any patients. For therapy, ibuprofen in a dose of 400-1200 mg daily was used as first-line therapy in 7 patients (77.8%), but then prednisone was used as the second-line therapy in patients who did not better with ibuprofen. One patient (11.1%) was treated with prednisone 40 mg alone, and another patient has treated with only propranolol 20 mg daily as the adrenergic symptoms were prominent in this patient. All patients had clinical symptom remission after 2 to 86 weeks of therapy, and the thyroid function returned to normal. Table 1 shows the subjects demographic, symptoms, laboratory, and treatment.

DISCUSSION

Healthcare professional workers are more susceptible to infectious respiratory illness since droplets easily transmit it. Nosocomial infections of infectious respiratory illnesses are frequent. It was reported that the prevalence of COVID-19 among healthcare providers was prevalent during this pandemic. The occurrence of COVID-19 in this setting was associated with the high-risk workplace, duty hours, and hand hygiene. In this study, we reported 9 cases of subacute thyroiditis related with COVID-19 which predominantly occurred in healthcare workers. Only two out of nine cases experienced by non-healthcare personnel which were a private staff and a housewife. It is caused by the high prevalence of COVID-19 which then subsequently increases the occurrence of thyroid inflammation.

Subacute thyroiditis (SAT) is a self-limiting inflammatory disease in the thyroid gland caused by a virus or a post-viral infection. It frequently manifests several weeks after viral upper respiratory tract infection. Many studies have revealed an increase in the prevalence of SAT during or after SARS-CoV-2 infection. The majority of patients in this study complained of neck pain, fever, and palpitation. Neck pain is the most common clinical symptom; it begins unexpectedly and progresses in severity. Pain may radiate to the neck or jaw area in severe cases and may worsen with neck movement and coughing. Fever, weakness, and fatigue may also be observed due to inflammation and mild hyperthyroidism. Especially in the early period of subacute thyroiditis, palpitations, sweating, and tremors may occur due to high titer of thyroid hormone in the blood. These findings usually disappear after 4 to 10 weeks, and the patient may develop asymptomatic hypothyroidism. The incidence of SAT is more common in young females than males, affects almost four times in women compared to men, and usually occurs between 18 and 60 years.

Clinical manifestations of patients in these cases were developed during and after the exposure of SARS-CoV-2. This phenomenon was in line with previous investigations which found the development of SAT following COVID-19 infection. The increased incidence of SAT during a viral outbreak supports the viral origin. It often lasts several weeks (2-8 weeks) following viral infection. Viral associated with SAT have been detected in thyroid tissue on an autopsy performed during the 2002-2003 SARS pandemic, in which severe destruction to the follicular thyroid epithelium, a histological characteristic of destructive thyroiditis, was discovered. Additionally, these glands are located close to the structures of the superior airways, which have been targeted earlier by this virus.

Moreover, there is growing evidence of a close association between SARS-CoV-2 and SAT. Brancatella et al. (2020) reported 4 cases of SAT in female patients, which developed 4 to 8 weeks after resolving from COVID-19. Other studies had reported high rates of subacute destructive thyroiditis among patients hospitalized for severe COVID-19. Some of the patients developed SAT after the typical symptoms of SARS-CoV-2 infection resolved. Therefore, it is hypothesized that SAT may occur as a viral manifestation or post-SARS-CoV-2 infection. Interestingly, thyroid involvement during COVID-19 is supported by reports that the thyroid gland’s viral receptors (ACE-2) are highly abundant.

SARS-CoV-2 enters lung cells via the ACE2 receptor. The viral and host cell membranes are activated upon binding, and viral RNA is then released into the cytoplasm and subsequently causes infection. The virus is cell-free and phagocytic macrophages that can spread to other organs and infect ACE2-expressing cells at local sites, causing multi-organ injury. Furthermore, free-cell phagocytosis-associated viruses and macrophages can spread from the lungs to other organs with high ACE2 expression through the blood circulation. The thyroid gland is an organ with a relatively high expression of ACE-2, making it a potential target for the entry of SARS-CoV-2, which will then cause inflammation.

There are two theories on how the SARS-CoV-2 virus can infect the thyroid gland. The first is through direct infection to the thyroid gland, and the second is through the hypothalamus-pituitary axis. The expression of ACE-2 is relatively high in the thyroid gland, as reported by Rotondi, Coperchini (2020), who found that the RT-PCR analysis showed the expression of ACE-2 mRNA at a reasonably high level in follicular cells of the thyroid gland. In addition, ACE-2 is also expressed by all cells in the human body, including the hypothalamus and pituitary. So that it can cause interference with the hypothalamic-pituitary-thyroid axis signals so that as a result, thyroid gland disconnection can occur.
Table 1. Data demographic, symptoms, laboratory, and treatment of patients.

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Occupation</th>
<th>The first clinical state comes</th>
<th>COVID-19 status</th>
<th>Lab results</th>
<th>Thyroid ultrasound</th>
<th>Therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>36</td>
<td>Midwife</td>
<td>Neck pain, tenderness, fever, palpitations, and weakness</td>
<td>Confirm</td>
<td>WBC 22,000</td>
<td>Bilateral diffuse goiter, hypoechoic, and no vascularization</td>
<td>Prednisone 40 mg OD</td>
<td>Improved in 2 weeks</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>62</td>
<td>Housewife</td>
<td>Fever, mild pain in the neck accompanied by tenderness, fatigue, palpitations, often sweating more than usual.</td>
<td>Probable</td>
<td>ESR 80</td>
<td>Diffuse hypoechoic with minimal vascularization</td>
<td>Ibuprofen 400mg BID</td>
<td>Improved in 1.5 months</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>40</td>
<td>Housewife</td>
<td>Mild neck pain, tenderness, fever, weakness, and no appetite</td>
<td>Confirm</td>
<td>WBC 15,000</td>
<td>Hypoechoic with minimal vascularization</td>
<td>Ibuprofen 400 BID</td>
<td>One month later, the response to treatment was good.</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>32</td>
<td>Doctor</td>
<td>Pain in the neck, tenderness, fever, fatigue, weakness, and no appetite</td>
<td>Confirm</td>
<td>WBC 14,000</td>
<td>Right segmental hypoechoic with minimal vascularization</td>
<td>Ibuprofen 400mg TID, the pain worsened, then replaced with prednisone 40 mg OD.</td>
<td>Better clinical outcome after a 1-month therapy. Thyroid function returned to normal. Clinical symptoms disappear after one month after therapy, normal thyroid function,</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>34</td>
<td>Nurse</td>
<td>Mild pain in the neck, tenderness, fever,</td>
<td>Confirm</td>
<td>WBC 20,000</td>
<td>Segmental hypochoic left and right with minimal vascularization.</td>
<td>Ibuprofen 400 mg BID, the symptoms worsened, then replaced with prednisone 40 mg OD.</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>38</td>
<td>Midwife</td>
<td>Mild pain in the neck, tenderness, palpitations, weight loss</td>
<td>Confirm</td>
<td>WBC 17,000</td>
<td>Bilateral diffuse hypochoic with minimal vascularization</td>
<td>Ibuprofen 400 mg TID, then replace with prednisone 40 mg OD</td>
<td>Ibuprofen stopped due to allergy, then continued with prednisone. Good response two months later.</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>37</td>
<td>Private</td>
<td>No neck pain, no tenderness either. Palpitation. Decreased appetite and weight loss of 20 kg for five weeks.</td>
<td>Probable</td>
<td>WBC 12,300</td>
<td>Normal</td>
<td>Propranolol 2 x 10 mg</td>
<td>Thyroid function is normal and clinical symptoms improve after two weeks of treatment.</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>52</td>
<td>Housewife</td>
<td>Neck pain right lobe One week later, radiated to the left lobe</td>
<td>Confirm</td>
<td>WBC 13,100</td>
<td>Normal</td>
<td>Ibuprofen 400 BID then switch to prednisone 40 mg OD</td>
<td>Thyroid function and clinical symptoms improve after four weeks</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>34</td>
<td>Nurse</td>
<td>Mild neck pain, flu-like syndrome</td>
<td>Probable</td>
<td>WBC 12,300</td>
<td>Normal</td>
<td>Ibuprofen 200 mg BID</td>
<td>Thyroid function is normal and clinical symptoms have improved.</td>
</tr>
</tbody>
</table>

F, female; TSHs, thyrotropin serum; FT4, free thyroxine; WBC, white blood cells; ESR, Erythrocyte sedimentation rate; OD, once daily; BID, twice a day; TID, thrice daily. The normal range for leukocytes 3.800-10.600 /mm3; ESR 0-20 mm/hr; serum FT4 0.93 – 1.71 ng/dL, TSHs 0.27 – 4.2 IU/mL.
A combination made the diagnosis of SAT in this study of clinical manifestations, physical examination, laboratory, and ultrasound examination as also performed by scholars in a recent study of subacute thyroiditis subjects. The most common clinical manifestations include pain in the neck and palpation of the thyroid gland. Other symptoms that can appear are symptoms of thyrotoxicosis. The usual investigations are thyroid examination (FT4 and TSH), ESR, and C-reactive protein. Elevated ESR and CRP levels, along with mild leukocytosis, are commonly found in SAT. FT3 and FT4 are elevated, and TSH decreases due to hormonal release into the circulation from the inflamed thyroid gland. The thyroid function in SAT will go through many episodes over several weeks to months. It will initially become hyperthyroid, followed by a brief euthyroid period. Then, it will go to a hypothyroid phase before recovering to normal thyroid function. In this situation, hyperthyroidism is induced by cytotoxic T lymphocytes attacking follicular cells, releasing significant amounts of T4 and T3 into circulation. For weeks, patients will remain hyperthyroid until their thyroid stores are depleted.

Ultrasound examination of the thyroid gland has a high sensitivity in diagnosing SAT. The ultrasound feature will show a normal or enlarged thyroid, hypoechogenic, and minimal vascularization on color Doppler.

The principle of SAT treatment is to provide anti-inflammatory. Salicylates or NSAIDs can be used for patients with mild or moderate disease. For more severe cases, corticosteroids may be started at doses ranging from 15 to 20 mg daily, reduced over 4 to 6 weeks. Patients who experience bothersome symptoms of hyperthyroidism such as palpitations, anxiety, or tremors may be given a beta-blocker such as propranolol (40-120mg). Thionamides should not be used.

Subacute thyroiditis usually resolves on its own, with the patient returning to the euthyroid within a few months. Recurrence is rare but can occur in up to 2% of patients. Contact transmission is one of the SARS-CoV-2’s primary pathways. Transmission from patients to health providers typically occurs as a result of contamination of the providers’ hands after contacting either patients or fomites, despite the fact that hand cleanliness is widely regarded as the most important preventive practice for healthcare-associated infections. This finding suggests hand hygiene is necessary after interacting or caring for COVID-19 patients to lower the amount of viruses or bacteria on the hands.

CONCLUSION

This case series emphasizes the necessity of being aware of the broad variety of differentials in a COVID-19 patients who work as healthcare providers and develop neck pain, palpitation, sore throat, and thyroid dysfunctions, which eventually manifested in our case. It is important to thoroughly evaluate the thyroid gland as subacute thyroiditis can be one of the many clinical spectrums of SARS-CoV-2 infection that should not be missed.

CONFLICT OF INTEREST

The authors state that the manuscript has no conflicts of interest.

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AUTHOR CONTRIBUTION

All authors contributed equally to data collection, manuscript preparation, and review.

ETHICAL APPROVAL

Ethical approval for this study was obtained from Institutional Review Boards of Faculty of Medicine at Universitas Syiah Kuala and Dr. Zainoel Abidin General Hospital (RSUZA), Banda Aceh (KEPPKN of Faculty of Medicine at Universitas Syiah Kuala). Ethical approval for this study was obtained from Institutional Review Boards of Faculty of Medicine at Universitas Syiah Kuala and Dr. Zainoel Abidin General Hospital (RSUZA), Banda Aceh (KEPPKN Registration number: 1171012P, No. 010/EA/FK-RSUDZA/2021).

REFERENCES


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