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ORIGINAL ARTICLE

Subacute thyroid and SARS-CoV-2 relationship

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ABSTRACT

Background: This study aims to research the relationship of subacute thyroiditis with SARS-CoV-2. The prevailing risks of predisposition to certain diseases or organ dysfunctions even after surviving the disease are discussed more frequently each day.

Aim: Could SARS-CoV-2 be considered as a triggering factor in patients diagnosed with subacute thyroiditis? Investigating the relationship between subacute thyroiditis and SARS-CoV-2.

Methods: Thirty-three patients diagnosed with subacute thyroiditis between 01.11.2020 and 01.04.2020 were included in the study. Patients who tested positive for SARS-CoV-2 throughout the examinations performed at the time of the diagnosis for subacute thyroiditis and patients who were previously diagnosed with Covid-19, who tested positive for SARS-CoV-2, and subsequently diagnosed with subacute thyroiditis within 30 days have been included in the study. Clinical evaluation of the patient, thyroid hormone values, CRP values, sedimentation levels, and thyroid ultrasonography images were considered to diagnose subacute thyroiditis; patients whose results were compatible with subacute thyroiditis were diagnosed with subacute thyroiditis, and they were included in the study.

Results: It was found that 5 (15%) of the 33 patients included in the study had Covid-19 disease before the diagnosis of subacute thyroiditis and were isolated for the SARS-CoV-2 virus.

Conclusion: The SARS-CoV-2 virus can be considered a triggering factor for subacute thyroiditis. We believe that researching this relationship on a broader patient population will bring more clarity to the subject. Although encountered in only one of our cases, the Coronavirus vaccine and SAT relationship may shed light on future studies.

Keywords: Subacute thyroiditis, SARS-CoV-2, COVID-19

INTRODUCTION

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is found in the content of an RNA virus and causes coronavirus disease or COVID-19 disease. SARS-CoV-2 incorporates typical features of the coronavirus family, and, in this regard, it is classified in the betacoronavirus 2b class.[1] It particularly infects bronchioles and alveoli in the lung tissue.[2] When an infected person coughs, sneezes, or talks, the virus already present in respiratory secretions may be transmitted to another person through droplets. Moreover, the disease is transmitted when an infected person scatters droplets into the environment via coughing and sneezing. After touching these droplets with their hands, other people further touch the mucous membranes of their mouth, nose, or nose eyes with infected hands. Droplets are the main form of transmission. The mean incubation period of the disease has been reported as five days.[3] Three clinical stages of the virus may be outlined: Stage I – asymptomatic stage lasting an average of 3–4 days; Stage II –characterized by symptoms, such as fever, cough, malaise, nausea, and diarrhea; Stage III – severe symptoms, such as pulmonary edema, acute pulmonary failure, septic shock, multiorgan failure, and cardiac arrest are observed .[4]

Subacute thyroiditis is also known as granulomatous thyroiditis or de Quervain's thyroiditis. It is an inflammatory thyroid disease. It is thought to be triggered by a previous viral infection. In some cases, it has been reported that the patient developed subacute thyroiditis (SAT) following an infection that had occurred approximately 2–6 weeks prior. SAT is reported four times more frequently in women compared to men.[5] According to statistical analyses, the incidence of SAT is 4.9/100,000 persons.[6]

Most patients complain of neck pain that may spread to the jaw and ear. Complaints of fever up to 38.5–39 degrees are reported in most cases. In addition, weakness, fatigue, and muscle aches are observed in most cases. Laboratory findings usually indicate mild to moderate hyperthyroidism, while in most cases, anti-thyroid antibodies are found to be within normal values.[7] Erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) are usually high. While remarkable hypoechoic areas and heterogeneity are observed in thyroid ultrasonography (USG), a decrease in vascularization is observed in Doppler USG.[8] An upper respiratory tract infection is usually mentioned prior to SAT, and this infection reveals the symptoms of the viral disease. Hence, viral infections are considered to trigger SAT. The most commonly related viruses are enterovirus, coxsackievirus, mumps, measles, and adenoviruses.[9,10]

This study aims to research the relationship of subacute thyroiditis with SARS-CoV-2. The prevailing risks of predisposition to certain diseases or organ dysfunctions even after surviving the disease are discussed more frequently each day. The study investigates whether SARS-CoV-2 plays a triggering role in the formation of subacute thyroiditis.

MATERIAL & METHODS

Thirty-three patients diagnosed with subacute thyroiditis between 01.11.2020 and 01.04.2020 were included in the

study. Patients who tested positive for SARS-CoV-2 throughout the examinations performed at the time of the diagnosis for subacute thyroiditis and patients who were previously diagnosed with Covid-19, who tested positive for SARS-CoV-2, and subsequently diagnosed with subacute thyroiditis within 30 days have been included in the study. Clinical evaluation of the patient, thyroid hormone values, CRP values, sedimentation levels, and thyroid ultrasonography images were considered to diagnose subacute thyroiditis; patients whose results were compatible with subacute thyroiditis were diagnosed with subacute thyroiditis, and they were included in the study. Patients whose sedimentation and CRP levels were not high, whose clinical findings did not suggest subacute thyroiditis (sore throat, thyroid gland tenderness), and whose thyroid ultrasonography images did not lead to being suspicious of subacute thyroid were excluded from the study. Patients with rheumatologic diseases that may cause sedimentation and CRP levels to increase and patients with cancer were also excluded from the study. The study protocol was approved by the Human Research Ethics Committee of Sivas Cumhuriyet University, Sivas, Turkey (Registry No: 2020-10/01). The volunteers were informed about how the research would be applied and their possible risks. Then, a written contest form was requested.

SARS-CoV-2 Test Samples: For the SARS-CoV-2 tests, a study was conducted to detect SARS-CoV-2 RNA using the rt PCR method with a nasopharyngeal swab taken from patients in Sivas Cumhuriyet University Faculty of Medicine Microbiology Laboratory authorized by the General Directorate of Public Health.

Statistical analysis: SPSS 22.0 software was used for the statistical analysis. Counts were expressed as numbers (percentages) and compared using the chi-square test. Measurements were represented as mean with standard deviation and compared using independently sampled t-tests. Statistical significance was accepted with a two-tailed P value < 0.05.

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RESULTS

Of the total 33 patients included in the study, nine were male (27%), and 24 were female (77%). It was found that 5 out of 33 patients (15%) had Covid-19 disease before being diagnosed with subacute thyroiditis, and the SARS-CoV-2 virus was isolated.

Table 1: Exhibits mean age, TSH, T4, ST3, ESR, CRP, leukocyte levels of the patients included in the study.

Measure	Mean±Std.	Range
Age	47±13	58
Hemoglobin	12,4±1,6	7.7
Leukocyte	9.4±4.2	25.4
CRP	74±47.3	168.7
DVİT	31.9±21.8	90.4
ESR	70,3±34	128
FT3	5.5±1.8	6.9
FT4	2.6±1.2	4.19
TSH	0.2±0.7	3.91

Table 1 exhibits the mean age, TSH, T4, ST3, ESR, CRP, and leukocyte levels of the patients included in the study. Three of the patients whose SARS-CoV-2 virus was isolated before the diagnosis of SAT were female, and two were male. No significant difference between ESR, CRP, TSH, ST4, ST3, leukocyte values was detected when comparing the five patients whose SARS-CoV-2 virus were isolated before the diagnosis of SAT and 28 patients whose SARS-CoV-2 virus were not isolated. These findings are exhibited in Table 2.

Table 2: Comparing 5 patients whose SARS-CoV-2 virus are isolated before the diagnosis of SAT and 28 patients whose SARS-CoV-2 virus are not isolated

	COVİD				
	+ (n=5)		- (n=28)		
Measure	Mean±Std Median±IQR	Range	Mean±Std Median±IQR	Range	p
Hemoglobin	12.4±1.6	7.7	12.±1.1	2.7	0.767
Leukocyte *	8.6±3.1	3.05	8.8±2.9	2.9	0.514
CRP	72.9±50.2	168.7	80.2±29.3	71	0.756
DVİT*	25.9±18	18	28±6	6	0,880
ESR	70.9±35,6	128	67.2±26.2	70	0.829
FT3	5.6±1.7	6.9	5±2.2	5.2	0.495
FT4*	2.25±1.83	1.83	1.9±0.4	0.36	0.292
TSH*	0.01±0.03	0.03	0.01±0.02	0.02	0.413

DISCUSSION

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is found in the content of an RNA virus and causes coronavirus disease or COVID-19 disease. SARS-CoV-2 incorporates typical features of the coronavirus family, and, in this regard, it is classified in the betacoronavirus 2b class.[1] It particularly infects bronchioles and alveoli in the lung tissue.[2]

Subacute thyroiditis is also known as granulomatous thyroiditis or de Quervain's thyroiditis. It is an inflammatory thyroid disease. It is thought to be triggered by a previous viral infection. In some of the cases, it has been reported that the patient developed subacute thyroiditis (SAT) following an infection that had occurred approximately 2–6 weeks prior. SAT is reported four times more frequently in women compared to men.[5] Most patients clinically complain of neck pain that may spread to the jaw and ear. Complaints of fever up to 38.5–39 degrees are reported in most cases. In addition, weakness, fatigue, and muscle aches are observed in most cases. Laboratory findings usually indicate mild to moderate hyperthyroidism, while in most cases, anti-thyroid antibodies are found to be in normal values.[7] Erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) are usually high. Viral infections are considered to trigger SAT. It is known that the most common associated viruses are enterovirus, coxsackievirus, mumps, measles, and adenoviruses.[9,10] Some studies reported a high incidence of SAT during echovirus and coxsackievirus outbreaks in the summer.[11,12] In addition, many viruses, such as adenovirus, Epstein-Barr virus, cytomegalovirus, dengue fever, and rubella, have been reported to be associated with SAT.[13,14,15]

Thyroid tissue damage was detected in a thyroid gland autopsy performed during the SARS-CoV infection epidemic in 2002.[16] The relationship of coronavirus infection with SAT is not known so far. Because viruses are a triggering factor in the formation of SAT disease, in this study, we aimed to find an answer as to whether the

SARS-Cov-2 virus, a pandemic in the world, could be a triggering factor for subacute thyroiditis. For this purpose, 33 patients diagnosed with SAT between 1.11.2020 and 1.4.2021 were evaluated. Patients who tested positive for SARS-CoV-2 throughout the examinations performed at the time of the diagnosis for subacute thyroiditis and patients who were previously diagnosed with Covid-19, who tested positive for SARS-CoV-2, and subsequently diagnosed with subacute thyroiditis within 30 days have been included in the study.

As a result of this study, it was determined that five of our patients had Covid-19 disease, and the SARS-CoV-2 virus was isolated before being diagnosed with SAT. Our first case, a 26-year-old male patient, had Covid-19 14 days before being diagnosed with SAT. Our second case, a 33-year-old female patient, had Covid-19 16 days before being diagnosed with SAT; our third case, a 31-year-old female patient, had Covid-19 19 days before being diagnosed with SAT; our fourth case, a 31-year-old female patient, had Covid-19 17 days before being diagnosed with SAT and our fifth case, a 41-year-old male patient, had Covid-19 20 days before being diagnosed with SAT 5.

We could not isolate the SARS-CoV-2 virus at the time of diagnosis in any of our patients diagnosed with SAT. However, our 35-year-old female nurse working in a hospital was diagnosed with Covid-19 15 days after being diagnosed with SAT. Again, interestingly, we found out that the Sinovac vaccine was administered to our 84-year-old female patient 12 days before being diagnosed with SAT. In five of our cases with Covid-19, the clinical findings of SAT were moderate[21]. We started treatment with 32 mg of methylprednisolone for these patients and administered the same dose for ten days. Then we reduced the dose by 4 mg every three days. When we reached 4 mg/dose, we continued the treatment for another ten days and then terminated the medicine. None of these five cases relapsed, and the thyroid functions of the patients regressed to normal values.

As a result of our study, we isolated the pandemic infection SARS-CoV-2 virus in 15% of the patients before the diagnosis of SAT. Case reports confirm this relationship in the literature. Ippolito et al., Brancatella et al., and Ruggeri et al.[17,18,19] think that the pathophysiological relationship between SAT and SARS-CoV-2 is similar to other viral infections. Müller et al. suggest that the affinity of SARS-CoV-2 for thyroid cells is mediated by ACE2 receptors, which are more common than lung cells.[20] In the light of the case reports examined in the literature review and as a result of the research study presented, it has been concluded that the SARS-CoV-2 virus may play a triggering role in patients with SAT. In addition, the incidence of SAT has been reported as 4.9/10000.[12] Although the number of cases with SAT that we need to detect on an annual average is 30, we detected 33 cases in our 5-month study. This increase in the prevalence of SAT can be explained by the fact that SARS-CoV-2 is a triggering factor in SAT disease. Therefore, we suggest the clinicians keep in mind that the SARS-CoV-2 virus, which causes a pandemic infection, may be a triggering factor in patients diagnosed with SAT and consider the possibility of SARS-CoV-2 as an underlying factor in patients with SAT.

Additional studies involving a larger patient series are needed to confirm the relationship between SAT and SARS-CoV-2 further. Therefore, we recommend that this relationship be further investigated in a larger patient series. Although encountered in only one of our cases, the Coronavirus vaccine and SAT relationship may shed light on future studies.

CONCLUSION

The fact that the SARS-CoV-2 virus may be a triggering factor in patients diagnosed with subacute thyroiditis has posed a question that should be kept in mind in light of the results obtained from our study. We believe that researching this relationship on a broader patient series will bring more clarity to the subject. In line with the results of our study, we would like to suggest that the relationship between SAT and Coronavirus vaccine may be the subject of additional research.

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