



Subacute Thyroiditis Associated with COVID-19 Infection: Two Case Reports

COVID-19 Enfeksiyonu ile İlişkili Subakut Tiroidit: İki Olgu Sunumu

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Abstract

Subacute thyroiditis (SAT) is granulomatous thyroiditis of the thyroid gland that usually occurs after a viral infection. Coronavirus disease-2019 (COVID-19) infection has led to a pandemic that has affected the whole world since late 2019. The virus has been reported to cause different extrapulmonary clinical symptoms. Few cases in the literature have reported SAT after COVID-19 viral infection. In this article, 2 cases were diagnosed, where SAT was presented after COVID-19 infection. Using these cases, we aimed to emphasize that patients who present with pain and tenderness in the anterior neck region after COVID-19 infection may develop SAT, whose diagnosis can be missed.

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

Özet

Subakut tiroidit (SAT), genellikle bir viral enfeksiyondan sonra ortaya çıkan tiroid bezinin granülatöz bir tiroiditidir. Koronavirüs hastalığı-2019 [coronavirus disease-2019 (COVID-19)] enfeksiyonu, 2019 yılının sonundan beri tüm dünyayı etkileyen bir pandemiye yol açmıştır. Ekstrapulmoner birçok farklı klinik tabloya yol açtığı bildirilmiştir. COVID-19 viral enfeksiyonu sonrasında SAT bildirilen olgular literatürde az sayıdadır. Bu yazıda, COVID-19 enfeksiyonu sonrası SAT tanısı olan 2 olgu sunuldu. Bu olgular ile birlikte COVID-19 enfeksiyonu sonrası özellikle ön boyun bölgesinde ağrı ve hassasiyet gelişen olgularda atlanabilen bir tanı olarak SAT gelişebileceğini vurgulamak istemekteyiz.

Anahtar kelimeler: Subakut tiroidit; COVID-19; SARS-CoV-2

Introduction

Subacute (granulomatous, de Quervain's) thyroiditis (SAT) is defined as an inflammatory, granulomatous and painful thyroiditis and is usually developed after an upper respiratory viral infection (1). It has also been reported after many other viral infections (2). Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) has

lead to coronavirus disease-2019 (COVID-19) since late 2019 (3). The first case of SAT after SARS-CoV-2 infection was reported by Brancatella et al. in 2020 (4). SAT after COVID-19 infection has been reported in few literature cases until now (5). Here, we reported two cases of SAT in patients affected by COVID-19 infection.

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Case Reports

Case 1

A 56-year-old man with no history of thyroid disease was presented to the endocrinology clinic with severe pain and swelling on the right anterior side of his neck for two weeks, which radiated to the right ear. He had fatigue and myalgia for one week. Four weeks before the onset of symptoms, he had a fever (38°C), cough, and myalgia. The patient's nasopharyngeal reverse transcriptase-polymerase chain reaction (RT-PCR) test revealed positivity for SARS-CoV-2 while the computed tomography scanning of his chest was normal. The patient reported that his symptoms improved after a 5-day use of oral favipiravir and paracetamol. However, four weeks after his initial symptoms, the patient was presented to us with severe anterior neck pain. The patient's thyroid gland was painful, tender, and palpable. His blood test results showed elevated erythrocyte sedimentation rate (ESR) (78 mm/h) and C-reactive protein (CRP) (45 mg/L) but normal complete blood cell count. Thyroid function tests (TFTs) revealed a low thyroid-stimulating hormone (TSH) with normal free T3 and free T4. Anti-Tg and anti-TPO were tested negative. Thyroid Tc99m scintigraphy scan showed no uptake. Thyroid ultrasound revealed the right lobe of the thyroid gland to be heterogeneous with hypoechoic areas, suggestive of SAT. The left lobe of the thyroid gland was focally heterogeneous, and there was no cervical lymphadenopathy. The demographic features along with clinical, laboratory, and radiographic findings of patients with SAT after COVID-19 infection are shown in Table 1. After the patient was diagnosed with SAT, he was started on 550 mg of oral naproxen sodium twice a day. His pain disappeared within two days, while the remaining symptoms were relieved within ten days. Later, the naproxen sodium treatment was continued for four weeks while the patient was being followed up as an outpatient. After the treatment, TFTs and inflammatory markers (ESR, CRP) were tested to be normal (Table 2).

Case 2

A 38-year-old woman with no history of thyroid disease was presented to the endocrinology clinic with an abnormal level of TSH. She was presented with fatigue, myalgia, back

Table 1. Demographic features along with clinical, laboratory, and radiographic findings of patients with SAT after COVID-19 infection.

Case	Age (year)	Sex	Symptoms of COVID-19	Time from diagnosis of COVID-19 (weeks)	Thyrotoxicosis Symptoms	Findings of thyroid USG	Findings of Thyroid Tc99m scintigraphy	Treatment
1	56	M	Mild	Initial symptoms: 4 weeks Diagnosis: 6 weeks	Subclinical Anterior neck pain, myalgia, fatigue	Heterogenous thyroid, hypoechoic areas, decreased vascularity (unilateral- right lobe)	No uptake	Naproxen sodium, (NSAID)
2	38	F	Mild	Initial symptoms: 4 weeks Diagnosis: 9 weeks	Anterior neck pain, myalgia, fatigue, back pain, headache	Heterogenous thyroid, hypoechoic areas, decreased vascularity bilateral)	-	Naproxen sodium, (NSAID)

SAT: Subacute thyroiditis; USG: Ultrasonography; NSAID: Nonsteroidal anti-inflammatory drug.

pain, headache, and anterior neck pain for five weeks. Four weeks before the onset of symptoms, the patient experienced a sore throat. The patient's nasopharyngeal RT-PCR test was positive for SARS-CoV-2. She reported that her symptoms improved after oral favipiravir treatment. Four weeks after her initial symptoms, she was presented with severe back pain and myalgia. Initially, paracetamol and myorelaxant were administered to the patient considering it as a COVID-19 related pain. Later, chest X-ray examination, thoracic tomography, and D-Dimer tests were requested by the pulmonologist, whose results were evaluated as normal. Physical therapy was applied to the patient, and she was further consulted with a neurology doctor. The diagnosis of fibromyalgia led to the administration of Duloxetine. As the patient started complaining of pain in the anterior neck region and throat while swallowing and an increase in headache, antibiotic treatment was initiated by the otolaryngologist. However, the patient's complaints did not disappear, and she was applied to general surgery. Later, she was referred to endocrinology due to suppressed TSH levels (0.1 µIU/mL) and unresolved complaints. Physical examination of the patient revealed a painful, tender, and large thyroid gland. Also, the laboratory test results showed elevated ESR (68 mm/h) and CRP (18.4 mg/L). The patient's thyroid function tests and whole blood count were normal. Anti-Tg and anti-TPO were negative. Bilateral and diffuse hypoechoic areas were detected during thyroid ultrasound (Table 1). SAT was diagnosed, and the patient was started with 550 mg of oral naproxen sodium twice a day, after which, the patient's neck pain disappeared within two days. Later, naproxen sodium treatment was continued for four weeks. After the treatment, TFTs and inflammatory markers (ESR, CRP) were found to be normal (Table 2).

The patients consent was obtained for this case study.

Discussion

SAT is granulomatous thyroiditis, which usually occurs due to a viral infection in genetically predisposed patients (6). The etiopathogenesis of SAT has not been fully known (7). SAT is usually developed after a viral upper respiratory tract infection (1). Different studies have found its associations with coxsackievirus (groups A & B), echovirus, mumps, measles, influenza, cytomegalovirus, rubella, Epstein Barr, enterovirus, adenovirus, and other viruses (6,8-10). In literature, a small series of patients and clinical cases have reported the occurrence of SAT after COVID-19 infection (4,11-14). Another review of literature also evaluated 22 patients with SAT after COVID-19 infection, which showed that 81.8% of the patients were female while the average age of patients was 39. It was emphasized that SAT's clinical symptoms emerged approximately 21±11 days after COVID-19 infection (5). In our study, the patients were a 56-year-old male and a 38-

Table 2. Laboratory findings of the cases before and after the treatment.

	TSH (µIU/mL) (date of diagnosis) (N: 0.35-4.94)	TSH (µIU/mL) (4 weeks after treatment) (N: 0.35-4.94)	Free T4 (ng/dl) (date of diagnosis) (N: 0.7-1.48)	Free T4 (ng/dL) (4 weeks after treatment) (N: 0.7-1.48)	ESR (mm/h) (date of diagnosis)	ESR (mm/h) (4 weeks after treatment)	CRP (mg/L) (date of diagnosis)	CRP (mg/L) (4 weeks after treatment)
1	0.139	3.8	1.39	0.82	78	5	45	<2
2	0.99	2.30	1.02	1.02	68	23	18.4	<2

TSH: Thyroid-stimulating hormone; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein.

year-old female. As per our case 1, SAT clinical symptoms emerged approximately four weeks after COVID-19 infection. But, case 2 was diagnosed with SAT after five weeks of the patient's initial symptoms. Patients may present with pain in the anterior neck region radiating to the jaw or ear region, fever, myalgia, fatigue, weakness, and signs of thyrotoxicosis (palpitations, hyperhidrosis, etc.) (1,5). Our cases had symptoms similar to the cases found in the literature (pain in the anterior neck region radiating to the ear, fatigue, and myalgia) and examination findings (painful, tender, and enlarged thyroid gland). Laboratory, ultrasonography, and scintigraphy findings of SAT cases reported after COVID-19 were similar to typical SAT findings (4,11-14). Also, laboratory findings of our cases (increased CRP and ESR, a low TSH level, diffuse heterogeneity and focal hypoechoic areas without hypervascularization during color Doppler ultrasonography, low uptake on thyroid scintigraphy) were similar to the SAT cases after COVID-19 in the literature as well. SAT is treated with aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), or corticosteroids. If there are symptoms of thyrotoxicosis, beta-blocker therapy can be used (1). Of the 22 SAT cases compiled after COVID-19, 50% used corticosteroids, 9.09% used aspirin, 4.55% used only NSAIDs, 4.55% used only beta-blockers, while 18.18% cases used blockers with other drugs, and 27.27% did not receive any treatment (5). In our study, both the cases recovered with NSAID therapy. In both cases, no clinical picture of symptomatic thyrotoxicosis was observed, and thus, no beta-blockers were used. Unlike the literature, our cases were treated with NSAID drugs, and complete recovery was achieved.

In the review evaluating SAT cases, 72.73% of the patients had mild COVID-19 symptoms, 13.64% had an asymptomatic disease, while 13.64% developed pneumonia (5). However, both our cases had mild symptoms during the COVID-19 infection. Our cases support the hypothesis that SAT may occur after a mild COVID-19 episode, which was also consistent with the literature.

No significant increase was observed between SAT cases after different viral infec-

tions following COVID-19 infection. Although this relationship has not been clearly proven, it is clinically associated with COVID-19 (15). The hypothesis that supports the relationship between SAT and COVID-19 is based on the angiotensin-converting enzyme 2 (ACE-2) receptor. The receptor for cellular entry of SARS-CoV-2 is ACE-2, which is involved in the renin-angiotensin pathway (16). ACE-2 receptor has been observed in different tissues of humans (17). In the study of Rotondi et al., the ACE-2 receptor gene was shown to be used by SARS CoV-2 to enter the cell and was also expressed in thyroid tissue. ACE-2 is reported to be present in the thyroid follicular cells (18). SARS-CoV-1 causes destruction of the follicular epithelium through thyroid follicular cell dysfunction, spillage of epithelial cells into the follicle, and the spread of fibrosis following the acute phase (19). Similar to SARS-CoV-1, SARS CoV-2 also causes inflammatory changes such as lymphocytic infiltration in the interstitial space of the thyroid tissue (15).

In conclusion, many different extra-pulmonary involvements may occur following COVID-19 disease. With different clinical pictures being reported in the literature about COVID-19, many new clinical manifestations are also defined related to COVID-19. We aimed to contribute to these few case reports in the literature by presenting two cases that developed SAT following COVID-19. We wish to draw attention to the fact that SAT may develop as one of the little-known and rare extra-pulmonary involvements of COVID-19, and we also emphasize that patients presenting with pain and tenderness in the anterior neck region after COVID-19 infection may develop SAT, whose diagnosis can be missed.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Mustafa Ünüböl, Zehra Erdemir, Engin Güney, Mustafa Gökhan Ünsal; Design: Mustafa Ünüböl, Engin Güney, Mustafa Gökhan Ünsal; Control/Supervision: Mustafa Ünüböl, Zehra Erdemir, Gökhan Çolak; Data Collection and/or Processing: Mustafa Ünüböl, Zehra Erdemir, Gökhan Çolak, Mustafa Gökhan Ünsal, Engin Güney; Analysis and/or Interpretation: Mustafa Ünüböl, Engin Güney, Gökhan Çolak; Literature Review: Mustafa Ünüböl, Zehra Erdemir, Mustafa Gökhan Ünsal; Writing the Article: Mustafa Ünüböl, Gökhan Çolak, Zehra Erdemir, Engin Güney, Mustafa Gökhan Ünsal; Critical Review: Mustafa Gökhan Ünsal, Engin Güney, Mustafa Ünüböl, Gökhan Çolak; References and Fundings: Mustafa Ünüböl, Zehra Erdemir, Gökhan Çolak; Materials: Mustafa Ünüböl, Zehra Erdemir.

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