CASE REPORT OF SUBACUTE THYROIDITIS FOLLOWING SARS-COV-2 INFECTION

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Sažetak: INTRODUCTION: SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) is a single-stranded RNA virus with an envelope that causes COVID-19 infection. The disease can be accompanied by mild cold-like symptoms, but it can also have potentially severe complications, some of which can be fatal. According to recent data, the virus can also be one of the causes of subacute thyroiditis (SAT). According to available data, the period of symptom manifestation of thyroiditis (SAT) after recovering from Covid-19 infection is 29 days. The disease may pass through stages of hyperthyroidism, hypothyroidism, and then return to a euthyroid state. In 10% of cases, permanent hypothyroidism may occur, requiring levothyroxine therapy. Treatment is usually symptomatic with high doses of aspirin at 600mg 3-4 times a day or nonsteroidal anti-inflammatory drugs. Corticosteroid therapy is introduced in more severe cases. CASE REPORT: A 69-year-old female patient presented to the Covid outpatient clinic complaining of weakness, fatigue, diarrhea, difficulty swallowing, and low-grade fever around 37.5°C. In her personal history, the patient reported being treated for Hashimoto's multinodular goiter with levothyroxine replacement therapy. She tested negative for the SARS-CoV-2 virus with a rapid antigen test and subsequently had a positive PCR test of the nasopharyngeal swab. An antibiotic, cefixime 400mg once daily, was initiated along with other therapy. After three days, her symptoms worsened. She experienced intense pain in the front of the neck, difficulty swallowing, a feeling of a lump in the throat, dry cough, and a body temperature reaching 38.5°C in the evening and at night. On physical examination, a slightly swollen neck was observed, and deeper palpation revealed the thyroid gland as hard and tender. The antibiotic was changed to azithromycin 500mg and ibuprofen 800mg daily. After 15 days, the patient achieved complete clinical recovery, indicating resolution of viral thyroiditis. Hormonal status remained normal throughout, and she was well substituted with levothyroxine. CONCLUSION: General practitioners should be aware of this complication of COVID-19 disease and analyze thyroid hormone levels in their clinics. Due to the population's exposure to the SARS-CoV-2 virus, subacute thyroiditis should be considered in general practice clinics. Suspicion should arise if fever persists, neck pain worsens, and inflammatory markers persist. Laboratory tests, thyroid hormone analysis, and consultation with an endocrinologist or nuclear medicine specialist should be sought as soon as possible.
Keywords: SARS-CoV-2, subacute thyroiditis, general practitioner

INTRODUCTION

Subacute thyroiditis (SAT) is likely a benign viral disease characterized by intense general and local symptoms, transient hyperthyroidism and hypothyroidism, followed by complete recovery of the thyroid gland. Subacute thyroiditis is 40 times less common than Hashimoto's thyroiditis. It most commonly affects women between the ages of 20 and 50, and is 3-6 times less common in men. The most common causative agents are influenza viruses, coxsackievirus, hepatitis E, adenovirus, parvovirus B19, dengue virus, cytomegalovirus, HIV, rubella, mumps, as well as Q fever and malaria. According to recent reports, it is necessary to add the SARS-CoV-2 virus to this list.

Previous data show that the period of symptom manifestation of thyroiditis (SAT) after recovering from Covid-19 infection is 29 days. The SARS-CoV-2 virus is the causative agent of coronavirus disease. The disease can manifest with mild cold-like symptoms, but also with severe acute respiratory distress syndrome with numerous complications, which are often fatal. The SARS-CoV-2 virus belongs to the genus of beta-coronaviruses, single-stranded RNA viruses. The envelope plays a crucial role in the virus's pathogenicity. Viral infection can induce an excessive immune reaction in the host, known as "cytokine storm," which results in extensive tissue damage. The virus enters the cell via angiotensin-

converting enzyme 2 (ACE-2). Rotondi and colleagues discovered that ACE-2 receptors, which have affinity for RNA, are expressed most in the thyroid gland, small intestine, heart, kidneys, suggesting that the virus can infect tissues other than the lungs. It is believed that the SARS-CoV-2 virus directly destructs the target cell or acts indirectly through the action of the "cytokine storm." According to published studies, common clinical symptoms of subacute thyroiditis (SAT) after Covid-19 infection are palpitations, fatigue, fever, and neck pain radiating to the jaw.

CASE REPORT

A 69-year-old female patient presented to the Covid clinic due to weakness, fatigue, diarrhea, and a low-grade fever of around 37.5°C. In her medical history, the patient reported treatment for hypertension (Prilenap H® 10mg+25mg once daily along with Bisprol® 5mg once daily), Hashimoto's multinodular goiter (Euthyrox® 50mcg for 3 days, then 25mcg for 4 days), and type 2B hyperlipidemia. She tested negative for the SARS-CoV-2 virus with a rapid antigen test initially, but a subsequent PCR test of the nasopharyngeal swab was positive. Symptomatic therapy was initiated with vitamin D, vitamin C, zinc, analgesics, and antipyretics. At the scheduled follow-up after seven days, the patient reported no improvement, with difficulty swallowing and a low-grade fever persisting. Cefixime 400mg once daily was added to her therapy regimen. Three days later, her symptoms worsened, with severe neck pain, difficulty swallowing, sensation of a lump in the throat, dry cough, and fever peaking at 38.5°C in the evenings and nights. On physical examination, she had a visibly swollen neck, and the thyroid gland was palpable during swallowing, feeling firm and tender on deeper palpation. Both sternocleidomastoid muscles were tender and very firm. Blood pressure was 124/83 mmHg with a pulse rate of 72 beats per minute. Oxygen saturation remained around 98%-99% throughout. An ECG was unremarkable, and chest auscultation revealed no abnormalities. Laboratory tests showed elevated inflammatory markers (CRP 113.1 mg/l; ESR 115mm/h), and a complete blood count indicated lymphopenia, monocytosis, and signs of anemia (HGB 104g/l, RBC 3.32, MCV 98.5, MCH 31.3, MCHC 318 g/l) with platelets within normal limits. Thyroid hormone levels after 14 days from the onset of illness were within reference ranges (TSH 1.35μIU/ml, FT3 3.37pmol/l, FT4 12.5pmol/l). Chest X-ray was normal. The patient was referred to an endocrinologist, where thyroid ultrasonography revealed significantly enlarged thyroid lobes, with a thickened isthmus measuring 10.2 mm. The lobes were predominantly hypoechoic and vascularized. The right lobe measured 40.4mm x 21.1mm x 16.2 mm, with a large hypoechoic nodule approximately 21.4mm x 11.9mm in the midsection. The left lobe measured 40.8mm x 19.6mm x 26.4 mm, showing clear hypoechoic areas suggestive of nodules. Inflammatory lymph nodes were visible around both neck muscles. The neck muscles appeared structurally altered and elevated due to enlarged lobes from the inflammatory viral process. The patient's therapy was adjusted, with azithromycin 500mg added to the existing cefixime regimen once daily, along with a probiotic, zinc, and selenium supplements before lunch, Vigantol® (vitamin D) drops (10 drops) after meals, and ibuprofen 800mg daily. After 15 days of this therapy, the patient's pain decreased, and she discontinued ibuprofen. On physical examination, the thyroid gland was palpable but non-tender. Skin moisture was normal, and tremor was very discreet, with a pulse rate of 71/min and blood pressure of 134/84mmHg. After one month from the onset of illness, laboratory tests showed a decrease in inflammatory parameters (CRP 6.5), while mild anemia persisted in the blood count (RBC 3.85x1012/l, HGB 109 g/l). Other findings were within reference values. A follow-up ultrasound was not performed, and the patient's hormonal status remained normal throughout. She was clinically well-substituted with levothyroxine, leading to recovery from viral thyroiditis.

DISCUSSION AND CONCLUSION

This case illustrates that any viral upper respiratory tract infection can be complicated by subacute thyroiditis (SAT). Several cases of SAT following Covid infection have been reported worldwide. SAT may manifest as described in our case, with fever, general symptoms of illness, difficulty swallowing, neck pain radiating to the jaw, and transient vocal cord paralysis, nervousness, tachycardia, increased sweating, and tremor. Symptoms may peak on the third and fourth days of illness, then gradually diminish and disappear within one week. However, in most cases, symptoms develop gradually over one to two weeks, with fluctuations in severity and prevalence over the next 3-6 weeks. Some patients may experience worsening symptoms for several months before complete recovery. Recovery from subacute

thyroiditis may be accompanied by transient hypothyroidism in a quarter of patients, with less than 10% experiencing permanent hypothyroidism.

A pathognomonic sign for SAT in the acute phase is transient elevation of FT3 and FT4 due to thyroid cell destruction, suppressed TSH, and increased erythrocyte sedimentation rate and other serum inflammatory markers (CRP, fibrinogen). Therefore, serum thyroglobulin concentration is elevated, while anti-thyroglobulin and anti-TPO antibodies are usually negative. Thyroid scintigraphy will show reduced radioactive iodine fixation <5% and technetium pertechnetate. Liver enzyme elevation may be present in serum in half of the patients and may persist for several months. Some patients may not require any medication therapy. Sometimes, aspirin at a dose of 600mg every 4-6 hours or nonsteroidal anti-inflammatory drugs (NSAIDs) may be necessary to reduce pain. In cases of severe symptoms, corticosteroid therapy is initiated with prednisone at a daily dose of 40mg, gradually reduced by 5mg every 7 days over 6 weeks. In the event of permanent hypothyroidism following an episode of SAT, levothyroxine replacement therapy is indicated.

Due to the prevalence of SARS-CoV-2 infection in the population, general practitioners should consider subacute thyroiditis as a complication of the disease. Suspect it if fever persists, neck pain intensifies, and inflammatory markers persist. Conduct laboratory tests, analyze thyroid hormone levels, and seek consultation with an endocrinologist or nuclear medicine specialist.

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