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Subacute Granulomatous Thyroiditis Occurring after SARS-CoV-2 Infection: A Case Report

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Abstract **Case Report**

Subacute thyroiditis is a rare self-limited thyroid inflammatory condition characterized in the majority of cases by sudden onset of neck pain. It seems to be mostly linked, directly or indirectly, to viral infections. During the COVID-19 pandemic, several cases of thyroiditis were reported in the literature, occurring during or after infection by the SARS-CoV-2, suggesting that this virus is also linked to subacute thyroiditis. Therefore, knowledge of a possible association between these two entities is of the most importance. Several hypotheses explaining the mechanism of action of SARS-CoV-2 on the thyroid gland have been put forward. Clinical symptoms do not appear to be very typical, and thyroid hormonal dysfunction may not be present. Treatment is essentially based on corticosteroids and NSAIDs. The prognosis remains favorable. We report the case of a 46-year-old woman who presented with subacute thyroiditis 25 days after SARS-CoV-2 infection. Her workup showed elevated CRP, multinodular goiter, normal thyroid function and negative antibodies. She was treated with corticosteroids that resulted in improvement of her symptoms.

Keywords : Thyroiditis, Granulomatous, De Quervain, COVID-19.

INTRODUCTION

Subacute thyroiditis also known as granulomatous or de Quervain thyroiditis is a thyroid inflammatory disease characterized by sudden onset of neck pain, general malaise, and thyroid dysfunction. This entity is rare, it accounts for less than 5% of symptomatic thyroid pathology and its incidence is 4.9 per 100,000. It is more frequent in women between 30 and 50 years of age [1].

The cause of this entity is not well established yet. It seems to be linked, directly or indirectly, to numerous viruses of the upper respiratory tract such as Coxsackievirus, influenza virus, adenovirus, etc [2]. Evidence for this association includes previous upper respiratory tract infection, multiple antibodies to certain viruses, seasonal patterns and clusters of cases [3].

COVID-19 caused by the SARS-CoV-2 virus, was a pandemic that affected millions of people around the world. Multiple cases of subacute thyroiditis associated with the SARS-CoV-2 infection has been described in the literature. SARS-CoV-2 invades the cells through the Angiotensin-converting enzyme 2 receptor, which is expressed in many tissues among which the thyroid gland. COVID-19 can also affect thyroid function through other mechanisms, among which the autoimmune effects on the thyroid mediated by cytokine storm [4].

This case emphasizes a case of subacute thyroiditis declared right after a SARS-CoV-2 infection.

CASE REPORT

A 46-year-old diabetic woman with no other known personal or family history reports, except having had a PCR-confirmed SARS-CoV-2 infection classified as moderate.

The patient presented to the emergency department, 25 days after the start of the SARS-CoV-2 infection, with severe neck pain and dyspnea, in a context of asthenia, thermophobia, palpitations, diarrhea and weight loss. The initial workup showed an enlarged and nodular thyroid on ultrasound. TSH was in the lower half of the normal range at 1.6 mUI/L. Patient was discharged with acetaminophen prescription, and was programmed for surgery for the thyroid nodules later.

Faced with increasing pain and dyspnea, the patient consulted a second time. On clinical examination, her heart rate was 93, she had no fever, she had a grade 2 goiter firm in character and non-beating, and she had no signs of Grave's ophthalmopathy or any skin lesions.

The new assessment showed always a normal TSH level 1.1 mUI/L. T3 and free T4 were normal. TPOAb and TRAb antibodies were negative, as was the Calcitonin. Her CRP was slightly elevated at 46 mg/L. The second cervical ultrasound showed a multinodular goiter without signs of hyper vascularization, with nodules classified as Eu-Tirads 3.

Treatment with corticosteroids was decided in view of the suspicion of subacute thyroiditis occurring on a nodular goiter after the SARS-CoV-2 infection she had. The patient took the treatment with an adaptation of her antidiabetic treatment. She had complete disappearance of symptoms after a few months, and the treatment was stopped after 6 months.

The patient subsequently underwent surgery for the multi-nodular goiter. Histology confirmed subacute granulomatous thyroiditis without signs of malignancy.

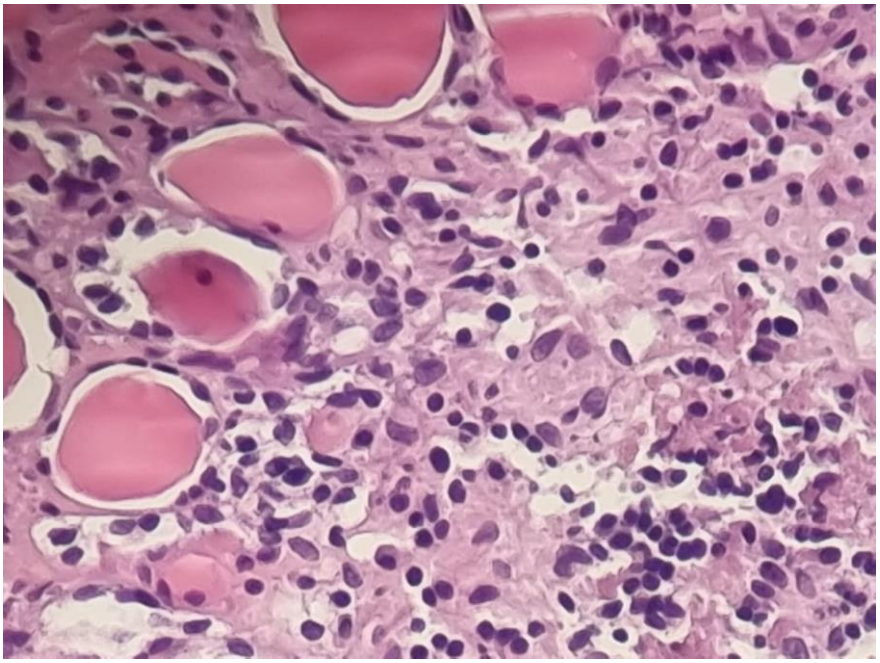

Fig-1: Histological image showing granulomatous reaction with presence of neutrophils and histiocytes.

DISCUSSION

Thyroid dysfunction was reported in some patients during the COVID-19 pandemic, suggesting that SARS-CoV-2 may have damaged the thyroid, during or after the infection [4]. Subacute thyroiditis is more commonly linked to viral infections, in particular those of the upper respiratory tract, such as coronaviruses, compared to other subtypes of thyroiditis [5].

Thyrotoxicosis, hypothyroidism, and sick euthyroid syndrome were the common thyroid complications among the effects of SARS-CoV-2 on the thyroid gland [6].

SARS-CoV-2 has the potential to destroy multiple tissues including the thyroid directly or indirectly. Multiple hypotheses were discussed; the most accepted mechanism involves direct viral damage through transmembrane serine protease 2 and angiotensin-converting enzyme 2 receptors, which are present on the surface of the thyroid follicular cells [7]. In addition, other mechanisms, such as indirect immune mediated responses and medicines prescribed for COVID-19, are also thought to be responsible for thyroid damage [5].

Another hypothesis explaining the relation between SARS-CoV-2 and subacute thyroiditis is molecular mimicry; an in-vitro investigation revealed that antibodies against SARS-CoV-2 antigens may cross-react with TPO. This mechanism is a potential pathogenic trigger of immune-mediated adverse events following SARS-CoV-2 infection and immunization [8].

The time elapsed between the onset of COVID-19 infection and the appearance of subacute thyroiditis symptoms ranged from zero to 168 days. The clinical symptoms might not be typical. The asymptomatic patients and those with severe COVID-19 symptoms had similar subacute thyroiditis presentations. The most prevalent symptom was neck pain (69%), followed by fever (54%); other symptoms were asthenia and palpitation [4].

The ESR is increased in the majority of cases (99%), and the CRP in 85% of cases. Regarding the hormonal status, TSH levels are low during the early phase of the illness in 60% of cases reported in the literature, with high free T3 and free T4 levels [4].

The thyroid dysfunction in the subacute thyroiditis is characterized by three phases: thyrotoxicosis, hypothyroidism, and euthyroidism [2].

The classic sonographic findings of De Quervain thyroiditis include bilateral or unilateral, localized or multifocal, and poorly defined hypoechoic regions. Radionuclide uptake in the thyroid gland ranges from very low or absent in the hyperthyroid phase to a normal appearance in the late recovery phase [9].

A previously firm thyroid nodule can rapidly develop in the setting of subacute thyroiditis. Clinicians should therefore be aware that subacute thyroiditis may present as a suspicious nodular lesion on ultrasound and may require thyroid FNA, which is rarely used in diagnostic workups. However, one study has suggested that margin, vascularity and echogenicity can help differentiate the features of subacute thyroiditis from those of a malignant tumor, reducing the need for FNA [4, 10].

The majority of studies reveal normal thyroid antibody levels. Some studies reported positive transient results of anti-TPO, anti-Tg, and TRAb in subacute thyroiditis, suggesting that immunological hyperactivity in COVID-19 might have led to the formation of these antibodies [4].

Histological findings in subacute thyroiditis vary according to the time of diagnosis. Thyroid vesicles are edematous in the early phase, then destroyed and replaced by an inflammatory infiltrate dominated by neutrophils. It can form true micro-abscesses in some cases. Then lymphocytes become more abundant, and multinucleated giant cell granulomas appear. Fibrosis occurs later [1, 2].

According to the literature, glucocorticoids are the preferred treatment for subacute thyroiditis secondary to COVID-19, with beta-blockers and NSAIDs as the other drugs prescribed respectively. The time from symptomatic improvement to complete recovery varies from two days to three months in the literature [4, 5].

Around 10% of individuals may develop persistent hypothyroidism [6]. Therefore, a follow-up period of up to twelve months is encouraged to prevent potential adverse effects.

CONCLUSION

SARS-CoV-2 infection is currently considered as a multifocal disease, affecting several organs, and we still have a lot to learn about its clinical manifestations. Thyroid involvement, for example, needs to be taken into account, as it can go undetected since symptoms can be non-specific in some cases. Similarly, SARS-CoV-2 must be considered as a possible causal agent of the thyroiditis cases we observe in our clinical practice. Knowledge of a possible association between these two entities is therefore of the most importance.

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