OPEN ACCESS

Saudi Journal of Medicine
Abbreviated Key Title: Saudi J Med
ISSN 2518-3389 (Print) | ISSN 2518-3397 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Original Research Article

Subacute Thyroiditis and the SARS-Cov-2: What Relationship?

Fadila Salmane[1*], Hafça Lahbib[1], Rayhana Rahouti[1], Mariam Benkacem[1]

[1]Department of Endocrinology, Diabetology and Metabolic Diseases, Faculty of Medicine and Pharmacy of Tangier, Abdelmalek Essaadi University, Morocco

DOI: 10.36348/sjm.2022.v07i09.003 | **Received:** 12.08.2022 | **Accepted:** 03.09.2022 | **Published:** 14.09.2022

***Corresponding Author:** Fadila Salmane
Department of Endocrinology, Diabetology and Metabolic Diseases, Faculty of Medicine and Pharmacy of Tangier, Abdelmalek Essaadi University, Morocco

Abstract

Background: De Quervain's thyroiditis is an inflammatory thyroid disorder. The new coronavirus is incriminated as the causative agent. ***Aims:*** We describe two cases of subacute thyroiditis, the first is linked to covid-19 infection, and the second is secondary to the SARS-CoV-2 vaccine. ***Methods:*** A 48-year-old female, presented with severe anterior neck pain, and thyroid dysfunction; the thyroid ultrasound showed an enlarged gland, with external hypoechoic areas. The RT-PCR was positive, the patient was treated according to the protocol of covid-19. A 49-year-old female, consulted for intense neck pain, one month after receiving the first dose of vaccination (Astrazeneca); the cervical ultrasound showed an external hypoechoic areas. ***Results:*** In first case, neck pain and other signs disappeared in one week. In second case, neck pain disappeared within two weeks. ***Conclusion:*** Clinicians should be aware of the possibility of thyroiditis in patients infected with Sars-COV-2.

Keywords: subacute thyroiditis, COVID-19, SARS-CoV-2 vaccination.

INTRODUCTION

De Quervain's subacute thyroiditis represents an inflammatory thyroid disorder in response to a viral infection [1]. Characterized by intense anterior neck pain, general signs, and thyroid dysfunction, thyroiditis is usually preceded by a viral infection of the respiratory tract [2].

The new coronavirus, is an RNA virus belonging to the family of coronaviridae, identified as the cause of severe acute respiratory syndrome, is also incriminated as the causative agent of subacute thyroiditis [3]. Recently, a few cases of thyroiditis following SARS-CoV-2 vaccination have also been reported [4].

This work aims to report two cases of subacute thyroiditis, the first is related to covid-19 infection, and the second is secondary to SARS-CoV-2 vaccine.

PATIENT AND OBSERVATION

1. First Case

A 48-year-old female patient, presented with severe anterior neck pain, dysphagia, headaches, asthenia and unquantified fever. The patient also reported anxiety, hand tremors, diarrhea and insomnia. The clinical examination found a conscious patient, hemodynamically and respiratory stable, febrile at 38°C, with an erythematous pharyngitis, and a painful tumefaction of the right lobe of the thyroid gland. Standard thyroid function test revealed elevated thyroxine (fT4), and undetectable thyroid-stimulating hormone (TSH), Further blood work demonstrated elevated levels of C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), white blood cell count were normal (Table 1).

Cervical ultrasound showed an enlarged thyroid gland, with ill-defined bilateral external hypoechoic areas, and slight glandular hyper vascularization (Figure 1).

The diagnosis of De Quervain's thyroiditis was adopted; The patient was put on anti-inflammatory drugs, and considering the context of the covid-19 pandemic, an RT-PCR was requested.

Figure 1: bilateral external hypoechoic areas

2. Second Case

A 49-year-old female patient, asthmatic, consulted for intense neck pain radiating to both ears, evolving since one month after receiving the first dose of vaccination (Astrazeneca), associated with headaches, unquantified fever, diarrhea, thermophobia and insomnia. The clinical examination found a conscious patient, tachycardic at 120BPM, with hypersensitivity of the thyroid region without a palpable nodule.

Standard thyroid function test revealed normal fT4, and suppressed TSH. Anti thyroid peroxidase receptor antibodies were negative (Table 1). Further blood work demonstrated elevated level of (CRP), white blood cells were normal.

The cervical ultrasound showed a slightly enlarged thyroid gland, with ill-defined external hypoechoic areas, and normal vascularization of the gland (Figure 2).

The diagnosis of subacute thyroiditis was made and the patient was put on corticosteroid therapy for 5 days, and beta blocker for one month.

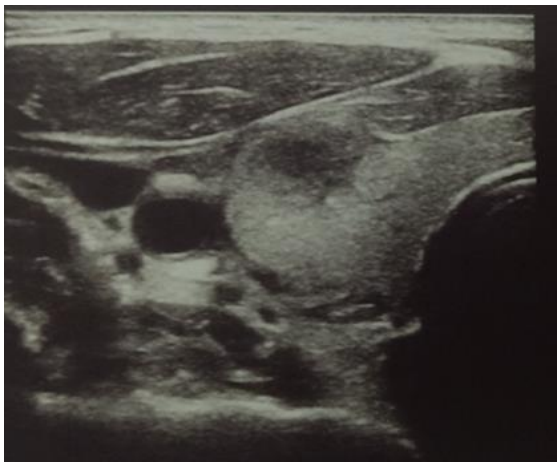

Figure 2: External hypoechoic areas

RESULTS

1. First Case

Fever disappeared in two days, neck pain and other symptoms in one week. The RT-PCR was positive, and the thoracic tomography (CT) was requested showing no parenchymal anomaly, no mediastinal adenopathy. The patient was treated at home according to the national covid-19 protocol. After one month, T4l and TSH levels were normalized, as well as biological markers of inflammation (ESR, CRP) (Table 1).

2. Second Case

Neck pain and other general symptoms disappeared in two weeks. After one month the CRP and the electrocardiogram were normalized.

Table 1: Clinical laboratory results

Measure	Reference range	Admission		Control on the 7th day		Control after a month	
		Case 1	Case 2	Case 1	Case 2	Case 1	Case 2
fT4 (pmol/L)	10--26	54,61	16,86			23,4	–
TSH (µIU/L)	0.5-4.1	0.009	0,12			2,16	–
WBC (per L)	4000-11000	5500	7400			6300	–
CRP (mg/L)	< 5	84	65	17,1	-	1,6	2,4
ESR (mm/h)	0-13	120	-			4	–

Free thyroxine (fT4); Thyroid-stimulating hormone (TSH); White blood cells (WBC); C-reactive protein (CRP); Erythrocyte sedimentation rate (ESR)

DISCUSSION

SARS-COV-2 has a marked tissue tropism causing mainly interstitial pneumonia and severe acute respiratory syndrome, inducing an inflammatory response that also involves the cardiovascular, coagulant, gastrointestinal and nervous systems. The long-term complications associated with SARS-COV-2 infection are still far from being understood and, in particular, the involvement of the thyroid gland is not yet clearly defined [3].

De Quervain's thyroiditis, also known as granulomatous thyroiditis, or Crile's thyroiditis, which represents an inflammatory state of the thyroid, reactive to a viral infection such as adenovirus, paramyxovirus, influenza virus, and enterovirus... [1]. However, a specific viral cause is not always found.

Thyroiditis predominates in women aged 30-50 years. It usually occurs seasonally (autumn - spring), is an infrequent pathology, usually with a favorable evolution, non-suppurative and non-immunizing (but rarely recurrent) [2]. A link to HLA (Human Leukocyte Antigen) B35 (more rarely B67) tissue groups that predisposes to viral diseases has been established [1].

The prevalence of subacute thyroiditis associated with the new coronavirus appears to be increasing, [5] as well as cases of subacute thyroiditis following SARS-CoV-2 vaccination have been reported recently; Iremli *et al.*, [6] reported a series of three cases who developed thyroiditis following SARS-CoV-2 CoronaVac inactivated vaccine (Sinovac Life Sciences, China).

Two other cases have been described after vaccination with the mRNA-based Comirnaty (BioNTech, Pfizer, Germany and USA) [7, 8]. Very recently Catherine *et al.*, [4] reported two cases of subacute thyroiditis, the first patient developed thyroiditis following Spikevax mRNA vaccine (Moderna Biotech, Spain), while the second patient developed thyroiditis following Vaxzevria vector-based vaccine (Astrazeneca; Sweden). One of the two cases presented in this work also developed subacute thyroiditis following Astrazeneca vaccine.

1. Pathophysiology of the Association

Subacute thyroiditis associated with SARS-COV- 2 infection is considered to be similar to the association with other viral infections, and is an inflammatory response focused on the thyroid in genetically susceptible people. Covid-19, uses angiotensin converting enzyme 2 (ACE2) as the principal cellular receptor to enter the host cell. More recent studies in 2020 showed that ACE2 expression levels were higher in the thyroid among other organs, such as small intestine, kidney, heart, and adipose tissue, providing insight into the pathophysiological mechanism of thyroiditis in COVID-19 [9]. Therefore, SARS-COV-2 will be responsable for the destruction of follicular cells, dysfunction and fibrosis of the thyroid gland, with the histopathological characteristics of thyroiditis [3].

Vaccinations could trigger thyroid alterations in susceptible patients, mediated by an immune response comparable to the T-cell response to viral agents. These alterations might be independent of the mechanism of action of the SARS-CoV-2 vaccination, because patients described in the literature have received mRNA-based vaccines as well as inactivated SARS-CoV-2 and vector-based vaccines. Furthermore, the development of subacute thyroiditis following other types of vaccinations such as influenza or hepatitis B has also been described in the literature; five cases of thyroiditis following influenza vaccination and one case following hepatitis B vaccination have been published so far [4]. However, the mechanism of development of post-vaccination subacute thyroiditis remains unknown.

2. Clinical Presentation

Two to six weeks after a nasopharyngeal infectious episode, which may have gone unremarked, anterior cervical pain often appears, radiating to the ears, and cervical muscles, often accompanied by dysphagia. Mostly, there is a febrile context, asthenia, clinical signs of thyrotoxicosis, whereas clinical hypothyroidism is rare [1]. However, 35% of patients may be asymptomatic [6]. The thyroid is diffusely hypertrophied, sometimes asymmetric, firm and painful to palpation.

3. Biological Presentation

In the initial phase, there is an intense biological inflammatory syndrome, with marked elevation of inflammatory markers (ESR and CRP). Most of the patients have an evident thyrotoxicosis [2], which is followed by a period of intense and prolonged hypothyroidism, then a return to euthyroidism [1], this thyroid dysfunction usually persists for three months [10]. Sequential hypothyroidism is sometimes described. Anti-TSH receptor antibodies (TRAK) and anti-thyroperoxidase antibodies (anti-TPO) are usually undetectable [5]. The absence of thyroid antibodies differentiates this condition from autoimmune thyroiditis [11].

4. Radiological Presentation

Thyroid ultrasound reveals an hypertrophied gland with hypoechoic areas and poor vascularity. Thyroid scintigraphy (iodine 123 or technetium 99m) is white, showing reduced or no tracer uptake [2].

5. Treatment

Treatment aims to limit inflammatory and painful phenomena, most often with anti-inflammatory drugs in moderate forms, more rarely with corticosteroids in severe or rebellious forms. B-blockers are sometimes useful if the thyrotoxicosis is not tolerated. Transitory thyroid hormone substitution may be necessary in the hypothyroid phase [2]. However, some patients become hypothyroid and they will need to remain on hormone therapy indefinitely [11]. In our experience, the administration of anti-inflammatory drugs during the acute phase is associated with a faster resolution of symptoms. Indeed, in the first week of treatment, we achieved a complete recovery of symptoms. While the second case required the administration of corticosteroids for 5 days, with the achievement of a complete recovery of symptoms in two weeks. We reported a case of SARS-COV-2 revealed by subacute thyroiditis, emphasizing the importance of being aware of the possibility of thyroiditis in patients infected by SARS-COV-2. And given the high prevalence of asymptomatic patients with covid-19, any patient with subacute thyroiditis

should be tested for Sars-COV-2 [5]. We have also described a case of thyroiditis secondary to the Sars-COV-2 vaccine (Astrazeneca), however, early reviews of different vaccinations against SARS-CoV-2 have shown a satisfactory efficacy against the virus emphasizing the importance of mass vaccination and the continuation of vaccination programs worldwide. The rare side effects such as subacute thyroiditis are reasonable compared to the risk of infection with Covid-19, which has caused millions of deaths. Therefore, the importance of vaccination against this devastating disease outweighs the minor risks of vaccination against SARS-CoV-2.

CONCLUSION

Subacute thyroiditis is a rare complication of COVID-19, so clinicians should be aware of the possibility of this clinical manifestation related to SARS-CoV-2 infection. Based on the presented cases and data on other cases reported in the literature, thyroiditis should be considered a possible side effect of SARS-CoV-2 vaccination.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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