

Post-COVID-19 Subacute / de Quervain's Thyroiditis

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ABSTRACT

Subacute thyroiditis is a self-limiting clinical condition manifesting as an acute phase of hyperthyroidism followed by hypothyroidism that eventually resolves on its own but sometimes leads to permanent hypothyroidism. This is usually preceded by a viral infection, and in this case, it was a COVID-19 infection. The authors report a case of a 42-year male who developed subacute thyroiditis as a result of a COVID-19 infection. He presented to the emergency room with complaints of severe headache, sore throat, and fever. Thyroid function tests revealed hyperthyroidism, and radiological investigations indicated retropharyngeal abscess formation. Treatment with antibiotics and analgesics resulted in incomplete symptomatic resolution. Total thyroidectomy and neck exploration were planned. On microscopy, a diagnosis of subacute thyroiditis with micropapillary carcinoma was rendered.

Key Words: Subacute thyroiditis, de Quervain thyroiditis, Post-COVID-19.

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INTRODUCTION

Subacute thyroiditis is a clinical condition that is usually self-limiting. This condition mainly manifests clinically and biochemically as an acute phase of hyperthyroidism followed by hypothyroidism and eventually returns to an euthyroid state in the majority of cases. This term was first coined by Fritz de Quervain in 1904.¹ The most frequent cause of a painful thyroid gland is subacute granulomatous thyroiditis, being the most frequent pathology behind thyroid gland discomfort. Migratory thyroiditis, painful subacute thyroiditis, and de Quervain's thyroiditis are all terms used to describe this disease.¹ It is widely known to be associated with viral infections. It is uncommon to see viral particles inside the thyroid, but it is often associated with dropping post-convalescent viral titers of many viruses, including coxsackievirus, mumps, influenza, and adenovirus.¹

A hereditary predisposition to the development of subacute granulomatous thyroiditis is well known. Patients with human leucocyte antigen (HLA)-Bw35 have a six-fold increased risk of acquiring the disease than the general population.² In most cases, it is resolved in 6-8 weeks. Only about 1% of total cases end up having thyroid dysfunction, i.e., hypothyroidism. Many reports have recently discovered that coronavirus disease (COVID-19) may cause subacute thyroiditis in some patients.³⁻⁵ The authors present a case of SARS-CoV-2 induced subacute (de Quervain's) thyroiditis. To the authors' knowledge, this is the second case being reported from Pakistan.

CASE REPORT

A 42-year male presented to the Emergency Department (ED) of the Shifa International Hospital in March 2021 with complaints of severe headache, sore throat, and fever for the past three days. He had recovered from a COVID-19 infection in December 2020. During that time, a nasopharyngeal swab tested via reverse transcriptase-polymerase chain reaction for SARS-CoV-2 was positive. He recovered from symptoms without morbidity after a week of conservative therapy. He is a known diabetic and hypertensive on regular medication. There was no previous history of intravenous contrast, lithium, amiodarone, radiation, trauma, or other disorders.

On examination, he was febrile (99°C) with a pulse rate of 104 beats/min. His respiratory rate was 18 bpm, blood pressure was 124/78 mm Hg, oxygen saturation was 99% on room air, and random capillary blood glucose was 117 mg/dL. There was an ill-defined swelling in the anterior neck. His pertinent laboratory investigations were decreased thyroid stimulating hormone (TSH) and raised T3 and T4. C-reactive protein (CRP) and white blood cells (WBCs) were raised, as shown in Table I. Serum uric acid, creatinine, urea, random glucose, sodium, potassium, bicarbonate, chloride, and liver function tests were all normal.

Magnetic resonance imaging (MRI) and computed tomography (CT) scan of the neck and soft tissue with contrast showed retropharyngeal/prevertebral collection/abscess (Figure 1A-C). Antibiotics and analgesics were given; however, his symptoms did not resolve completely. Neck exploration was planned based on radiological suggestion of prevertebral abscess and consistently deranged thyroid function tests. Peroperatively, the retropharyngeal abscess was found along with diffuse thyroid swelling. Total thyroidectomy was performed, and the specimen was sent for histopathological examination.

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The total thyroidectomy specimen weighed 45 grams, and the dimensions were 6.0 × 5.0 × 3.5 cm. Microscopically, there was an effacement of normal architecture. There was marked folliculosis, with atrophic follicles. There were multiple epithelioid granulomas with foreign body-type giant cells (Figure 2).

The granulomas were centred in the follicles, and multinucleated giant cells were seen around the colloid. The stroma showed a lymphoplasmacytic infiltrate with areas of fibrosis. Hyperplastic follicles lined by tall columnar epithelium were evident. Scalloping of the colloid was seen in hyperplastic follicles. A focus of papillary microcarcinoma was also seen, measuring 1.0 cm. The focus displayed nuclear features of papillary thyroid carcinoma, i.e. nuclear membrane irregularity, nuclear enlargement, clearing of nuclear chromatin, and overlapping of nuclei. In the lumen of neoplastic follicles, a hypereosinophilic colloid was seen which was quite dense. Based on these features, a final diagnosis of de Quervain's thyroiditis with a focus on papillary microcarcinoma was rendered.

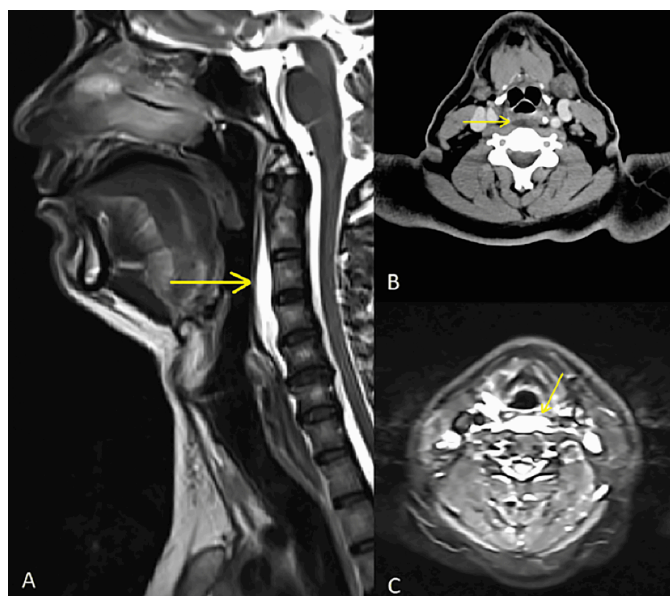


Figure 1: MRI with contrast, sagittal, and transverse views (A and C). CT scan transverse view (B). All of the images show the neck and soft tissues showing retropharyngeal/prevertebral collection/abscess.

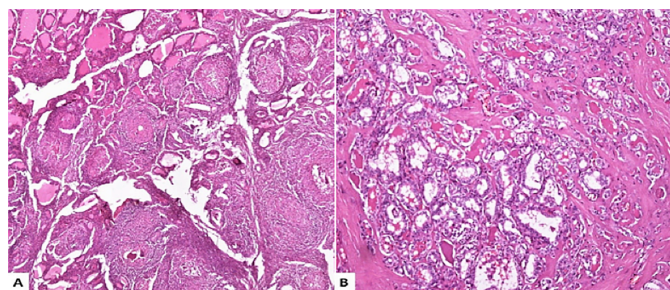


Figure 2: (A) Subacute thyroiditis: Multiple epithelioid granulomas centred in follicles with few multinucleated giant cells engulfing colloid (H&E, ×4). (B) Micropapillary carcinoma (H&E, ×4).

Table 1: Summary of laboratory tests of the patient.

Laboratory investigations	Results	Reference ranges
Thyroid-stimulating hormone	<0.01	0.5 to 5.0 mIU/L
T3	276 ng/dL	80 to 220 ng/dL
T4	16.35 ng/dL	5.0 to 12.0 ng/dL
C-reactive protein	319.75 mg/dL	upto 5.0 mg/L
White blood cells	18560/L	4000 to 11000/L
Erythrocyte sedimentation rate	215.33 mm/1 st hour	1-13 mm/1 st hour

DISCUSSION

Subacute or de Quervain's thyroiditis is a self-limiting condition of the thyroid gland which resolves on its own. This illness is defined by a clinical course of hyperthyroidism, followed by hypothyroidism and return of thyroid functions to baseline in the majority of cases.⁶ Subacute thyroiditis may be the cause of thyrotoxicosis in 15-20% of patients and hypothyroidism in 10% of patients. Subacute thyroiditis, unlike other types of thyroiditis, most likely results from viral infection. It also has a possible association with pregnancy. Several HLA alleles increase the risk of acquiring the disease and its recurrence (HLA-B*35, HLA-B*18:01, -DRB1*01, and HLA-C*04:01). The thyroid enlarges in reaction to the infection, which can affect hormone synthesis. Inflammation and a range of symptoms occur as a result of this. The diagnosis of subacute thyroiditis is based primarily on clinical suspicion and is further supported by laboratory investigations and imaging.⁷ Important laboratory evaluations include: Decreased titre of circulating thyroglobulin and thyroid peroxidase antibodies, increased levels of T3, T4, and thyroglobulin, decreased TSH, increased CRP, and increased erythrocyte sedimentation rate (ESR). In this case, ESR, T4, and T3 were raised, and TSH was suppressed. Ultrasonographic findings during the acute phase show bilateral hypoechoic regions with decreased to non-existent vascularisation and a radionuclide thyroid scan reveals minimal to absent tracer uptake.⁸ The present case showed a thickened paravertebral stripe and mild fluid in the retropharyngeal space, more so opposite to C2 inferior endplate till C5, with subtle marginal enhancement.

Over the last few years, some case reports and case series have emerged showing that the COVID-19 virus may serve as a potential trigger for subacute thyroiditis, either during or after infection. The minimum and maximum intervals from the onset of COVID-19 symptoms to the onset of subacute thyroiditis symptoms are 5 days to 90 days.⁹ The present patient had symptoms, 15 days after the diagnosis. The first case report showing the association between subacute thyroiditis and COVID-19 infection was published in July 2020, in which a painful thyroid was noticed on palpation, and further examination revealed an elevated heart rate. On laboratory examination, the levels of T3 and T4 were increased. Inflammatory markers and WBC count were elevated. Ultrasound of the neck revealed areas that were diffusely hypoechoic in both lobes of the thyroid gland. The patient was started on prednisolone. The pain in the neck region and pyrexia became minimal in 2 days, and the rest of the symptoms resolved within a period of 6 to 7 days. The functional capability of the thyroid and acute markers of inflammation was normalised in 40 days.¹⁰

The accurate mechanism by which the novel coronavirus causes dysfunction of the thyroid gland is unknown. SARS-CoV-2 produces an exuberant inflammatory response in the host resulting in the introduction of programmed cell death via many viral protein receptors.¹⁰ Other than the lungs, angiotensin-converting enzyme 2 (ACE2) receptors are found in a variety of organs, including the thyroid.¹⁰ SARS-CoV-2 patients have deranged levels of thyroid hormones and loss of normal function of the thyroid gland due to follicular destruction, secondary hypothalamic-pituitary dysfunction, and central hypocortisolism in SARS-CoV-2 patients.¹⁰

Microscopically, subacute thyroiditis has been classified into three phases. The early phase is characterised by the presence of neutrophils and destroyed the normal architecture of follicles, in which colloid is depleted. In the middle phase, there is the formation of non-caseating granulomas surrounding the follicles and containing engulfed colloids. Whereas the late phase is characterised by dense fibrosis. In the present case, microscopic examination showed architectural distortion by multiple granulomas centred in the follicles and multinucleated giant cells around the colloid. Morphological differential diagnosis includes Riedel's thyroiditis, tuberculosis, and thyroiditis due to Teflon injection. The risk of progression of de Quervain's thyroiditis to carcinoma is 0.4%.¹⁰

Two recent studies with a very limited sub-acute thyroiditis population were conducted to address the incidence and characteristics of sub-acute thyroiditis during the pandemic.^{11,12} Pirola *et al.* compared 10 sub-acute thyroiditis patients in a seven-month period of the pandemic with the previous periods and found no difference in the incidence of sub-acute thyroiditis.¹¹ Brancatella *et al.* compared 46 newly-diagnosed sub-acute thyroiditis patients in 2020 with previous periods and found that newly-diagnosed sub-acute thyroiditis cases were comparable between years.¹²

Subacute thyroiditis and resultant thyrotoxicosis should be suspected in patients with COVID-19 infection who have symptoms and signs suggestive of the disease.

PATIENT'S CONSENT:

Patient's consent was taken telephonically.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

IM: Data collection, analysis, interpretation, and case report preparation.

ZA: Design, supervision, analysis, and interpretation of the data. Both authors approved the final version of the manuscript to be published.

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