INTRODUCTION

The World Health Organization declared coronavirus disease 2019 (COVID-19) as a global pandemic in March 2020. It is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection which primarily manifests with acute respiratory symptoms. It is well known to produce extrapulmonary symptoms, either at the initial presentation or as a later complication. De Quervain’s thyroiditis duet to post-COVID-19 sequelae is rarely reported.

Hereby, we report a case of subacute (de Quervain’s) thyroiditis triggered by recent SARS-CoV-2 infection. To the best of our knowledge, eight cases of subacute thyroiditis (SAT) following COVID-19 infection have been reported so far in world literature [1-5], none of them is from the Indian population. The purpose of presenting this case is to alert clinician about this new complication following COVID-19 as well as identify the thyrotoxic symptoms which may be missed during the current devastating pandemic.

CASE REPORT

Patient consent was taken for publishing purposes. A 29-year-old female medical practitioner with no comorbidities presented to the emergency room with persistent high-grade fever and worsening swelling of 10 days duration associated with pain which was radiating from the left side to right side of the neck. The pain was exacerbated by swallowing, bending, and turning the neck to the side. History of bilateral hand tremors, fatigue, and palpitation for 4 days was also elicited.

A detailed enquiry revealed that 6 weeks before the onset of symptoms, she had suffered several days of fever, cough, and other flu-like symptoms. Reverse transcriptase-polymerase chain reaction by nasopharyngeal swab was positive for SARS-CoV-2 during that time. In about a week of that time, she presented with persistent fever and neck pain following recent COVID-19 infection. A persistent fever and neck pain following recent COVID-19 infection should alert clinician toward the possibility of de Quervain’s thyroiditis following severe acute respiratory syndrome coronavirus 2.

She was started on oral indomethacin 25 mg and propranol 40 mg thrice daily. She had tremors, fatigue, and palpitation. A careful enquiry revealed that she had been diagnosed with coronavirus disease 2019 (COVID-19) infection 6 weeks ago and had recovered uneventfully with conservative management. Her laboratories showed leukocytosis, elevated erythrocyte sedimentation rate, and C-reactive protein. Thyroid function tests (TFTs) yielded low thyroid-stimulating hormone, and high T3 and free T4. Ultrasoundography neck was suggestive of thyroiditis. Thyroid scintigraphy demonstrated very low technetium uptake which confirmed SAT. Her symptoms ameliorated with nonsteroidal anti-inflammatory drug and beta-blockers and her TFTs improved during follow-up. We report this as emerging sequelae of COVID-19 infection. Persistent fever and neck pain following recent COVID-19 infection should alert clinician toward the possibility of de Quervain’s thyroiditis following severe acute respiratory syndrome coronavirus 2.

Keywords: Coronavirus disease 2019 infection, De Quervain’s thyroiditis, Severe acute respiratory syndrome coronavirus 2, Subacute thyroiditis, Tender goiter.
It was first defined by Friz De Quervain in 1904. He distinguished this disease pathologically from other forms of thyroiditis. De Quervain thyroiditis is also called subacute granulomatous thyroiditis, subacute non-suppurative thyroiditis, giant cell thyroiditis, pseudo-granulomatous thyroiditis, pseudo-tuberculous thyroiditis, or struma granulomatosa [7].

The incidence is 12.1 cases per 100,000/year affecting younger and middle adulthood age groups with female preponderance. Disease frequency decreases with increasing age [8,9]. Viruses such as mumps, measles, adenovirus, Epstein-Barr virus, Coxsackie virus, influenza, Echovirus, and Enterovirus are commonly associated virus causing SAT [9].

However, the incidence of novel COVID-19-induced SAT appears to be reporting more during the current pandemic situation. The reported case of SAT following COVID-19 infection is enumerated in Table 1.

Fig. 1: Tc99 thyroid scan shows no uptake of the radiotracer

Table 1: List of SAT cases following COVID-19 infection reported in the literature to date

<table>
<thead>
<tr>
<th>References</th>
<th>Current case</th>
<th>Age and sex</th>
<th>Past h/o thyroid disease</th>
<th>Type of COVID-19 test</th>
<th>Time of onset between COVID-19 infection and SAT features</th>
<th>Presenting SAT symptoms</th>
<th>TFT and thyroid antibodies</th>
<th>Ultrasound thyroid with color Doppler with features of goiter, hypoechoic areas, and absent or low vascularity</th>
<th>Tc 99m thyroid Scintigraphy</th>
<th>Treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>29 years, female</td>
<td>Nil</td>
<td>Swab</td>
<td>45 days</td>
<td>Neck pain, fever, palpititation, tremor, anxiety tender, thyromegaly</td>
<td>TSH – 0.007 FT4 – 7.77 tT3 – 5.05</td>
<td>Present</td>
<td>No uptake</td>
<td>NSAID beta-blocker</td>
<td>Normal</td>
</tr>
<tr>
<td>[1]</td>
<td></td>
<td>18 years, female</td>
<td>Nil</td>
<td>Swab</td>
<td>17 days</td>
<td>Neck pain, fever, typical symptoms of SAT</td>
<td>TSH – 0.01 FT4 – 29.3 tT3 – 8.0</td>
<td>Present</td>
<td>–</td>
<td>Steroid</td>
<td>Normal</td>
</tr>
<tr>
<td>[2]</td>
<td></td>
<td>38 years, female</td>
<td>Nil</td>
<td>Swab</td>
<td>16 days</td>
<td>Neck pain, fever, typical symptoms of SAT</td>
<td>TSH – 0.01 FT4 – 27.2 tT3 – 8.9</td>
<td>Present</td>
<td>–</td>
<td>Steroid</td>
<td>Normal</td>
</tr>
<tr>
<td>[2]</td>
<td></td>
<td>29 years, female</td>
<td>Nil</td>
<td>Swab</td>
<td>30 days</td>
<td>Neck pain, typical symptoms of SAT</td>
<td>TSH – 0.01 FT4 – 27.2 tT3 – 8.9</td>
<td>Present</td>
<td>–</td>
<td>NSAID, Steroid, beta-blocker</td>
<td>Subclinical</td>
</tr>
<tr>
<td>[2]</td>
<td></td>
<td>46 years, female</td>
<td>Nil</td>
<td>Swab</td>
<td>36 days</td>
<td>Neck pain, typical symptoms of SAT</td>
<td>TSH – 0.01 FT4 – 29.3 tT3 – 8.0</td>
<td>Present</td>
<td>–</td>
<td>NSAID</td>
<td>Subclinical</td>
</tr>
<tr>
<td>[2]</td>
<td></td>
<td>43 years, female</td>
<td>Nil</td>
<td>Swab</td>
<td>20 days</td>
<td>Neck pain, typical symptoms of SAT</td>
<td>TSH – 0.01 FT4 – 30.6 tT3 – 3.39</td>
<td>Present</td>
<td>–</td>
<td>NSAID</td>
<td>Subclinical</td>
</tr>
<tr>
<td>[2]</td>
<td></td>
<td>41 years, female</td>
<td>Nil</td>
<td>Swab</td>
<td>40 days</td>
<td>Neck pain, typical symptoms of SAT</td>
<td>TSH – 0.01 FT4 – 29.3 tT3 – 8.0</td>
<td>Present</td>
<td>–</td>
<td>NSAID</td>
<td>Subclinical</td>
</tr>
<tr>
<td>[3]</td>
<td></td>
<td>37 years, male</td>
<td>Nil</td>
<td>Antibody</td>
<td>14 days</td>
<td>Neck pain, typical symptoms of SAT</td>
<td>TSH – 0.01 FT4 – 29.3 tT3 – 8.0</td>
<td>Present</td>
<td>–</td>
<td>NSAID</td>
<td>Subclinical</td>
</tr>
</tbody>
</table>

TFT: Thyroid function test, SAT: Subacute thyroiditis, COVID-19: Coronavirus disease 2019, TSH: Thyroid-stimulating hormone, NSAID: Nonsteroidal anti-inflammatory drug
Relationship between thyroid and COVID-19 infection

Due to the increased expression of angiotensin-converting enzyme 2 and transmembrane protease serine 2 levels in the thyroid gland than in the lungs, these act as the key routes for virus entry into host cells in susceptible patients. Abnormal immunological response and cytokine storm due to COVID-19 may also provoke thyroiditis [10].

The natural history of SAT involves four phases, starting with a hyperthyroid phase and then followed by a transient asymptomatic euthyroid phase, a hypothyroid phase, and a final phase euthyroid phase on recovery. Each phase lasts for approximately 4–6 months [11].

The disease classically presents as anterior lower neck pain which radiates to upper neck, throat, jaw or ears and exacerbated by moving the head, swallowing, or coughing. Associated flu-like symptoms such as fever, malaise, fatigue, and myalgia may be present. Diffuse tender thyromegalgy with clinical features of hyperthyroidism such as tachycardia, tremor, weight loss, palpitation, and anxiety during the initial stage is common at presentation [12].

Diagnosis is mainly based on classical clinical history and physical and laboratory findings. TFTs should be done initially in all patients with suspected SAT followed by ESR and CRP level. Serum anti-thyroid peroxidase, anti-thyroglobulin antibodies, and TSH receptor antibodies are usually absent or present at low titer. Serum thyroglobulin levels may be elevated due to follicular destruction [12].

Radioactive uptake or technetium (99mTc) pertechnetate thyroid scan during the hyperthyroid phase helps to confirm the diagnosis. It is due to destruction of thyroid follicles with iodine trap defect. USG thyroid may help to assess the size, nature, echogenicity, and vascularity of the thyroid gland [12].

Characteristics features of Graves’ disease such as exophthalmos, pretibial myxedema, thrill, or bruit over thyroid gland are absent. A low radioactive iodine uptake study, high ESR and CRP. Decreased vascular flow patterns in color Doppler USG during the hyperthyroid phase of SAT also aid to distinguish it from Graves’ disease, which has increased flow [12]. USG-guided fine-needle aspiration cytology is rarely needed in doubtful cases with unilateral thyroid involvement, which helps to distinguish thyroid abscess, hemorrhage, or thyroid lymphoma from SAT [12].

Septic workup is usually needed in patients with fever, and a thorough cardiology evaluation may be warranted if tachycardia is present.

Treatment should aim at alleviating anterior neck pain and ameliorating thyrotoxic symptoms. Mild-to-moderate pain is usually managed with nonsteroidal anti-inflammatory drugs and salicylates. Severe pain can be managed with steroids, which provides a dramatic response within 24–48 h. Hyperthyroid symptoms are best treated with beta-blockers such as propranolol or atenolol till the free T4 level returns to normal [13].

Hyperthyroid phase lasts for shorter periods, and with milder symptoms, and hence, treatment is not often required. However, patients with moderate-to-severe symptoms can be managed with thyroxine till the TSH level returns to normal. In a rare patient with recurrent relapse and distressing local symptoms despite sufficient treatment, thyroidectomy may be indicated [13].

Regular TFT monitoring should be done every 2–8 weeks to understand the natural history of the disease and yearly thereafter [13]. Even though we could not directly isolate the COVID-19 virus in thyroid tissue, current epidemiological and serological reports of our patient substantiate viral infection 4 weeks before the onset of SAT.

CONCLUSION

The clinician should have a strong suspicion of SAT in any patient presenting with persistent neck pain and odynophagia despite the remission of COVID-19 symptoms. Such individuals should be screened by TFTs, ESR, CRP, and thyroid imaging (USG or scintigraphy). Early identification and anti-inflammatory treatment often result in good outcomes.

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REFERENCES


