

THYROID COMPLICATIONS POST COVID -19 INFECTION----- CASE REPORT AND LITERATURE REVIEW.

Surgery

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ABSTRACT

Subacute thyroiditis also called subacute granulomatous or de Quervain thyroiditis, is an uncommon condition, yet to be considered the most common cause of painful thyroiditis. It is usually a self-limiting inflammatory disorder with varying typical and atypical presentations. Though the exact cause of the disease is still enigmatic various viruses including reoviruses, mumps virus, hepatitis B and C viruses, cytomegalovirus, enterovirus, and coxsackie viruses A and B. However, the exact etiology of SAT is unknown.

Clinically, the condition is recognised because of its severe pain in the anterior aspect of the neck which is radiating to the angles of the jaw, ear lobules. The tender palpable thyroid gland functionally is either hyper, hypo or euthyroid state. As for the time being only few facts are available concerning COVID-19 and SAT. The clustering of our cases in the post covid period strongly suggest the causal relationship.

The SARS-CoV-2 has wreaked havoc globally and has claimed innumerable lives all over the world. The symptoms of this disease may range from mild influenza-like sickness to severe acute respiratory distress syndrome with high morbidity and mortality. With improved diagnostic techniques and better disease understanding, an increased number of cases are being reported with extra pulmonary manifestations of this disease ranging from renal and gastrointestinal, pancreatic, cardiac, hepatic, neurological, endocrinological and hematologic dysfunction.

KEYWORDS

COVID-19, Sub Acute Thyroiditis(SAT).

CASE REPORTS:-

In February 2021, two previously healthy (61, 55 year) presented with fever, anosmia, generalised aches and pains and were found to be RT/PCR for COVID-19 positive. Though both of them had an uneventful symptomatic recovery, a month later both of them landed with an ENT specialist with severe pain over the thyroid radiating to both the ear lobules they had tender left lobe in one case and both lobes in the second case respectively. On there atypical maging presentation raising suspicion of malignancy. For this they both underwent thyroid gland FNAC which showed an inflammatory process and no atypical cells Thyroid function suggestive of hyperthyroid state with undetectable TSH, T4 total 10.5 mcg/dL, 12.3mcg/dl, T4 free 1.6 ng/dL, 1.8ng/dl and T3 total 200 ng/dL, 190 ng/dl respectively. Anti-Tg and anti-TPO were negative in both.

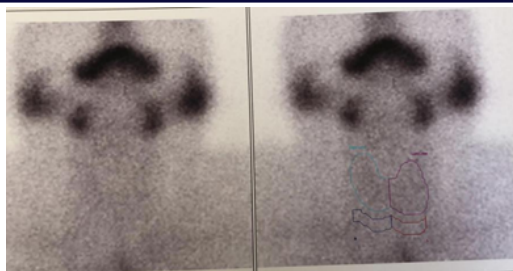
There lab test results showed elevated ESR 65 mm/hr, 70mm/hr and

CRP 62 mg/L, 58mg/l and normal platelet and leukocyte counts. Both the ladies received analgesics for there symptoms and became asymptomatic and became euthyroid state within 4-6 weeks.

Four more patients aged between 45-55 years had a similar history to share where they had fever and cough and on nasopharyngeal swab they were confirmed to have COVID -19 positive. They were all kept under home quarantine and within the following days they recovered fully. Almost a month and a half later these four patients had severe neck pain and had odynophagia the pain was radiating to the ear. None were known to have any co-morbidity and any previous history of thyroid dysfunction.

The Table no 1 shows the comparative clinical and laboratory features of sub acute thyroiditis cases post COVID-19 infection.

Parameters	Patients					
Age/Sex	61y/F	55y/F	50 y/F	49y/F	59y/F	60y/F
Time lapse between COVID-19 infection and Thyroiditis features	4 weeks	4 weeks	6 weeks	6 weeks	5 weeks	5 weeks
Clinical Features	severe ear pain irradiating to the left jaw and neck.	severe ear pain irradiating to the left jaw and neck.	severe neck pain and had odynophagia the pain was radiating to the ear, with fever and fatigue	severe neck pain and had odynophagia the pain was radiating to the ear with fever and cough	severe neck pain and had odynophagia the pain was radiating to the ear with palpitations, fever and cough.	severe neck pain and had odynophagia the pain was radiating to the ear with fever.
Thyroid Function Test	Thyrotoxic Anti Tg & Anti TPO Negative	Thyrotoxic Anti Tg & Anti TPO Negative	Thyrotoxic Anti Tg & Anti TPO Positive	Thyrotoxic Anti Tg & Anti TPO Negative	Thyrotoxic Anti Tg & Anti TPO Negative	Thyrotoxic Anti Tg & Anti TPO Negative
Ultrasound findings	1.Heterogenous thyroid gland 2.Bilateral patchy ill-defined	1.Heterogenous thyroid parenchyma 2. Relative diffuse decrease of	1.Heterogenous thyroid parenchyma 2. Relative diffuse decrease of	1.Heterogenous thyroid parenchyma 2.Decreased vascularity	1.Heterogenous thyroid parenchyma 2.Vascularity present.	1. Heterogenous thyroid parenchyma
Thyroid scan	Suggestive of Sub Acute Thyroiditis	Suggestive of Sub Acute Thyroiditis	Suggestive of Sub Acute Thyroiditis	Suggestive of Sub Acute Thyroiditis	Suggestive of Sub Acute Thyroiditis	Suggestive of Sub Acute Thyroiditis
Treatment	Anti inflammatory drugs and steroids	Anti inflammatory drugs and steroids	Anti inflammatory drugs and steroids	Anti inflammatory drugs and steroids	Anti inflammatory drugs and steroids	Anti inflammatory drugs and steroids
Post treatment Thyroid status	Euthyroid Within 4- 6 weeks	Euthyroid within 4-6 weeks	Hyperthyroid within 4-6 weeks	Euthyroid within 4-6 weeks	Euthyroid within 4-6 weeks	Euthyroid within 4-6 weeks



Radio active iodine uptake study showing Sub acute thyroiditis.

These Patients ultimately were referred to an endocrinologist who after getting their radioactive iodine uptake study labelled them as sub acute thyroiditis.

DISCUSSION AND CONCLUSION:-

Subacute thyroiditis most commonly affects females compared to males with a ratio of 4:1 and occurs at age range of 40-50 years [4,5]. The condition is recognized as self-limited inflammatory disorder of the thyroid gland that can manifest both during the active viral infection as well as with in two to eight weeks of recent viral infection [4]. The most commonly implicated viruses are coxsackie virus, mumps, measles, rubella, adenovirus, influenza, parvovirus B19, and many others. The novel coronavirus has lately been recognized with growing awareness of the complications [6,7].

In a usual clinical course, half of the patients experience transient symptoms of thyrotoxicosis followed by euthyroidism, hypothyroidism, and normal thyroid function within three months.

In patients with subacute thyroiditis thyroid dysfunction is usually triphasic: thyrotoxicosis develops in the majority of patients, followed by hypothyroidism (uncommon) and mostly achieving a euthyroid state within 3-5 weeks. The pathogenesis of subacute thyroiditis has not been absolutely cleared up, but it is accepted that this disease is due to viral infection or to a postviral inflammatory reaction in genetically predisposed persons [8,9,10]. There are no data that patients with autoimmune thyroid disease are most sensitive to viral infection (including SARS-CoV-2), nor that they run the risk of developing more severe COVID-19.

Brancatella et al. reported thyroiditis in an eighteen year old female after fifteen days of infection, symptoms resolved in a week and thyroid functions turned to baseline in forty days. Thyrotoxicosis and COVID-19 infection share symptoms including sore throat, fatigue, chills, anorexia, fever and weight loss. This common symptomatology can be easily confused for COVID-19 symptoms [9]. Therefore, a strong clinical suspicion is required to rule out both diseases simultaneously.

In a recently published study by Muller I et al., the prevalence of thyrotoxicosis being suggestive of subacute thyroiditis was investigated [11]. Patients treated in high intensity of care units (HICU) in 2020 due to COVID-19 (HICU-20, n = 93) were compared with SARS-CoV-2 negative patients admitted to the same HICU in 2019 (HICU-19, n = 101). Data of patients with known thyroid disease were not included. 15% of HICU-20 and only 1% of HICU-19 patients had thyrotoxicosis. In HICU-20 patients the serum TSH levels were lower than in HICU-19 patients (1.04 mIU/L vs. 1.43 mIU/L, $p = 0.018$), while serum fT_4 levels showed no difference between the groups. There was no significant difference between the fT_3 levels, the main non-thyroidal illness syndrome (NTIS) indicator, which were low in both groups. The authors conclude that a significant number of patients admitted to the HICU with COVID-19 have thyrotoxicosis and low TSH concentrations. These alterations demonstrate that SARS-CoV-2 can induce subacute thyroiditis and NTIS. To test this hypothesis, thyroid imaging was done nearly two months following discharge of some patients with former thyroid dysfunction.

The pathogenesis and mechanisms involved are still a medical enigma. However various studies point towards inflammatory process caused by the virus since the thyroid follicular cells also share the angiotensin converting enzyme 2 theory as it is confirmed that ACE 2 is the functional receptor for SARS-COV [12].

Our patient had the clinical manifestations and laboratory findings of thyrotoxicosis, with imaging supportive of subacute thyroiditis. The time frame of appearance and evolution of symptoms fits with the known disease course of subacute thyroiditis – a gradual onset over 1–2 weeks, with fluctuating intensity for 3–6 weeks. COVID-19 diagnosis was noted by outpatient rtPCR testing prior to illness and later confirmed by serologic testing. Other infectious causes and triggers of subacute thyroiditis were ruled out. The prompt response to anti-inflammatory and steroid therapy further strengthens our suspicion of COVID-19 as the cause.

With the rapidly expanding knowledge of the late sequelae of COVID-19 infection, we report a case series of 6 patients of subacute thyroiditis occurring due to infection by SARS-CoV-2. Further research is needed to elicit this potential link, the mechanisms of thyroid injury as well as the long-term outcomes.

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