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Subacute Thyroiditis Due to COVID-19 Vaccine

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Abstract

In this report, we present a case of a 90-year-old female who exhibited a sudden onset of confusion and severe generalized weakness after receiving her second dose of mRNA SARS-CoV-19 vaccination 19 days prior to her admission in 2021. Her thyroid-stimulating hormone (TSH) levels were low, while her thyroxine (T4), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels were elevated. Triiodothyronine (T3) level was not measured. Ultrasonography of the thyroid revealed multiple nodules with heterogeneous tissue, and a nuclear medicine thyroid uptake scan showed very low uptake. These findings indicated limited thyroid destruction in the form of subacute thyroiditis, likely triggered by the mRNA SARS-CoV-2 vaccine. This case illustrates an acute complication due to a novel vaccine. There are three key takeaways for physicians. First, there should be a discussion of the benefits and risks of Covid-19 vaccine. Second, patients who present with encephalopathy should have their thyroid function checked. Third, clinicians must be aware of the signs and symptoms of potentially life-threatening hyperthyroidism. Additional studies are needed to identify those patients at highest risk for Covid-19 vaccine complications.

Keywords: Subacute thyroiditis, COVID 19 vaccination

1. Introduction

The COVID-19 pandemic has been devastating with almost 1 billion confirmed cases and 7 million confirmed deaths across the world.¹ Without the development of over a hundred COVID-19 vaccines, these figures would likely be significantly higher, as vaccination has proven to be an effective strategy in reducing deaths linked to the virus.² Despite their efficacy, COVID-19 vaccines remain relatively new and side effects are still being studied. Common side effects of mRNA COVID-19 vaccines include pain, redness or swelling at the site of vaccine shot, fever, fatigue, headache, and other complications such as pericarditis and diabetes with ketoacidosis.^{3–6}

Subacute thyroiditis, usually a self-limiting inflammatory illness that is caused by viral infections or postviral inflammatory reactions, has also been reported as a possible side effect to the COVID-19 vaccine.^{7–13} Although most of these thyroid

complications are transient and self-resolving, the thyroid affects every organ system. The subclinical hyperthyroid or hypothyroid state is associated with increased cardiovascular morbidity and mortality, which is why the diagnosis must not be missed.¹⁴ Some studies show that hypothyroidism can even be permanent after subacute thyroiditis.¹⁵ Clinicians need to be cognizant of signs and symptoms of potentially life-threatening subacute thyroiditis with hyperthyroidism.

2. Case presentation

A 90-year-old female presented to a community hospital with generalized weakness and altered mental status for a one-day duration prior to admission. She received a second dose of mRNA Pfizer-BioNTech COVID-19 vaccine 19 days prior to her presentation to the hospital in 2021. Her first dose was administered 5 months prior, in early 2021. Review of systems was positive for nocturnal

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tachycardia and 20-pound weight loss. She denied excessive sweating, heat intolerance, or neck pain. Her past medical history was significant for Parkinson's disease, atrial flutter, hypertension, depression and mild hyponatremia. The patient had no history of thyroid disorders, contrast studies prior to admission and no prior use of amiodarone. Vitals were notable for heart rate of 101 beats per minute, blood pressure of 152/102 mm Hg. She appeared anxious and disoriented. No thyromegaly, neck tenderness or neck pain was noted. Cardiac exam notable for irregular rate and rhythm.

Laboratory data revealed normocytic anemia with hemoglobin 8.8 g/dL (normal range, 12–15 g/dL) and hyponatremia with sodium 132 mmol/L (normal range 135–145 mmol/L) (Table 1). Thyroid function tests revealed suppressed thyroid stimulating hormone (TSH) 0.03 mIU/mL, (normal range, 0.50–4.50 mIU/mL), free thyroxine (free T4) was 3.8 ng/dl (normal range, 0.9–1.7 ng/dl). Triiodothyronine (T3) level were not measured at the time of admission. Thyroid peroxidase antibody, thyroglobulin antibody, and thyroid stimulating immunoglobulin were all within normal limits. C-reactive protein was elevated at 68.9 mg/L (normal range, less than 5 mg/L) and erythrocyte sedimentation rate was also elevated at 127 mm/h (normal range, less than 30 mm/h) (Table 1). SARS-CoV-2 test was negative.

Ultrasound of the thyroid gland showed a very heterogenous gland throughout, no large thyroid nodules were noted. No hypervascularity noted on color flow study (Fig. 1A). Nuclear medicine I-123 thyroid uptake scan showed low thyroid uptake: the 2-h uptake was 1.02 % (normal 5–15 %) and the 24-h uptake was not above 0 (normal 15–35 %) (Fig. 1B). Thyroid biopsy was not indicated. Biochemical,

hormonal, and imaging studies confirmed the diagnosis of thyrotoxicosis, likely due to subacute thyroiditis associated with the mRNA Pfizer-BioNTech COVID-19 vaccine administration.

Patient was resumed on her home dose of metoprolol of 25 mg twice daily and prednisone 30 mg daily was started. Patient's tachycardia improved and she was discharged. When patient returned for a follow-up visit two weeks later, she clinically improved back to baseline. Hyperthyroidism improved as well: free thyroxine improved to 1.1 ng/dL (normal 0.9–1.7 ng/dL), TSH improved to 2.98 mIU/mL, (normal range, 0.50–4.50 mIU/mL) (Table 2). Prednisone was tapered and stopped.

3. Discussion

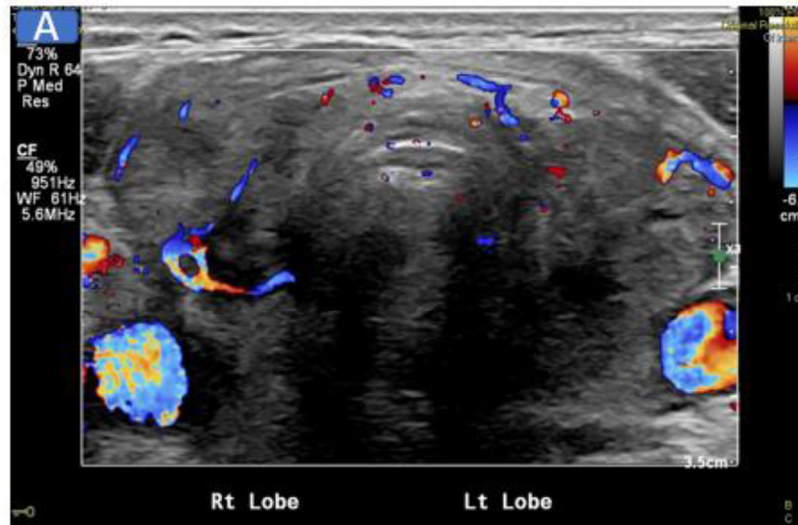
In this case report, we present a patient who was found to have subacute thyroiditis with atrial fibrillation with rapid ventricular rate after COVID-19 mRNA vaccination. Thus, awareness of this vaccine's side effects is warranted given the potential for serious medical emergencies such as thyrotoxicosis.

There are three key takeaways for physicians. First, there should be a discussion of the benefits and risks of the Covid-19 mRNA vaccine. Second, patients who present with encephalopathy should have their thyroid function checked. Third, clinicians must be aware of the signs and symptoms of potentially life-threatening hyperthyroidism.

The exact effects of Covid-19 vaccine on thyroid function are unknown. Subacute thyroiditis triggered by the vaccine have been reported.^{9,11–13,16} Jafarzadeh et al. reviewed 83 cases of thyroid abnormalities caused by various COVID-19 vaccines, with the highest incidence (60.2 %) in subacute thyroiditis

Table 1. Patient lab values at admission and follow up.

Test	Laboratory value at admission	Laboratory value on follow-up (16 days later)	Normal range
White Blood Cell count	5.53	7.44	4.50–11.00 K/cu mm
Hemoglobin	8.8	11.3	12.0–15.0 g/dL
Hematocrit	28.5	36.7	36.0–46.0 %
Mean corpuscular Volume	94.1	93.9	80.0–100.0 fL
Mean Corpuscular Hemoglobin	29.0	28.9	26.0–34.0 pg
Platelet count	367	394	150–350 K/cu mm
Sodium	132	132	135–148 mmol/L
Potassium	4.3	4.0	3.5–5.1 mmol/L
Chloride	95	98	98–110 mmol/L
Urea Nitrogen	18	30	7–30 mg/dL
Glucose	120	137	71–99 mg/dL
Calcium	10.1	9.3	8.4–10.5 mg/dL
Anion Gap	14	10	7–16 mmol/L
Blood Urea Nitrogen/Creatinine Ratio	36	75	
Carbon Dioxide	25	24	21–31 mmol/dL
Creatinine	0.5	0.4	0.5–1.2 mg/dL
Estimated Glomerular Filtration Rate	86	107	>60 mL/min/1.73 sqm



Color flow image on initial presentation demonstrating lack of hypervascularity

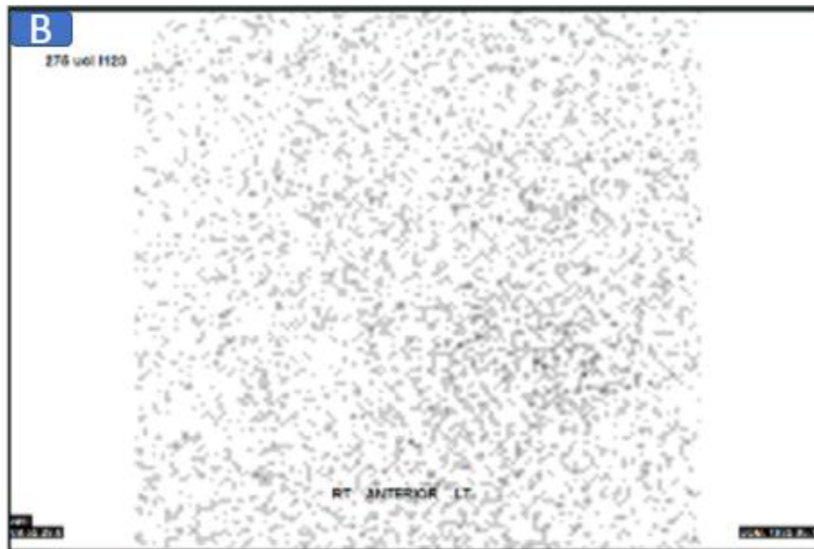


Fig. 1. A: Color flow image on thyroid ultrasound demonstrating lack of hypervascularity. B: Thyroid uptake scan: The 2-hour uptake was 1.02% (normal 5–15%) and the 24 hour uptake was not above 0 (normal 15–35%). Imaging of the thyroid gland demonstrated no visible thyroid activity.

Table 2. Patient thyroid function markers at admission and followup.

Test	Laboratory value on admission	Laboratory value on outpatient follow up (24 days later)	Laboratory value on outpatient follow up (5 months later)	Normal Range
Thyroid Stimulating Hormone	0.03	17.20	2.98	0.50–4.50 mcIU/ml
Free Thyroxine	3.8	1.0	1.1	0.9–1.7 ng/dL
Thyroid Stimulating Immunoglobulin	<89			<140 % baseline
Thyroid peroxidase antibodies	19.1			≤34.0 IU/mL
Thyroglobulin antibodies	<0.9			≤3.9 IU/mL
Erythrocyte Sedimentation Rate	127			≤ 30 mm/h
C-Reactive Protein	68.9			≤5.0 mg/L

cases and with most cases (68.7 %) occurring after mRNA-based vaccines (Moderna, Pfizer/BioNTech).¹⁷ In this context, subacute thyroiditis responds well to appropriate therapy with complete resolution observed in 2–20 weeks.¹⁸

The mechanism is Covid-19 vaccine causing subacute thyroiditis is not clear. It is thought to be immune-mediated, leading to the destruction of the thyroid gland.^{7,11,12,17,18} There appears to be an extensive immune cross-reactivity between anti-SAR-CoV2 protein antibodies and human tissue, including thyroid antigens, or by direct mitochondrial damage as the spike protein binds to the endothelial cells and causes thyroid destruction.^{11,17} This immune-mediated process and molecular mimicry not only influence the severity of the disease but can explain the involvement of multiple systems during the COVID-19 infection and the onset of auto-immune processes in those susceptible groups of people.^{7,12,17}

There has also been reporting of recurrence of subacute thyroiditis following revaccination.¹³ In this reported case, the patient was 36 years old and developed subacute thyroiditis 10 days following her first dose of the SARS-CoV-2 mRNA vaccine, Comirnaty (Pfizer/BioNTech). Physical exam was notable for thyroid region tenderness, mild tremor but no neck pain. The patient's condition improved, but then recurred 10 days following the second dose of the vaccine.¹³

In comparison, our case report was a 90-years old female who rather than presenting with anterior neck tenderness and fever, predominantly suffered generalized weakness and encephalopathy. She received her SARS-CoV-2 mRNA vaccine (Pfizer) 19 days before her presentation to the emergency room. Our patient had no report of recurrence, and her free T4 normalized on outpatient retesting 13 days following her discharge.

Previous case studies describe patients that are young to middle-aged, in contrast to our patient who is elderly. In one case series, subacute thyroiditis is described in 3 patients, all between the ages of 35–41 years, with predominately hyperthyroid symptoms, including tachycardia.¹⁶ The common clinical features were that in addition to being middle-aged, they also had no underlying history of thyroid disorder, developed thyrotoxicosis 4–27 days from their first dose of the Pfizer or Moderna vaccine, and had resolution of their symptoms following basic management including ibuprofen, propranolol and a prednisone taper.¹⁶ Similarly, our case report describes the patient as initially having decreased radioactive iodine uptake, consistent with subacute thyroiditis. Our patient also responded to

a two-week prednisone course followed by a taper. Based on the review of previous case reports, there appears to be no difference in the presentation of subacute thyroiditis^{9,16} when given either of the mRNA-based vaccines, Moderna and Pfizer.

In conclusion, there should be a heightened suspicion for COVID-19 vaccine induced subacute thyroiditis. Additional studies are needed to understand the mechanism of COVID-19 vaccines cause subacute thyroiditis.

4. Learning points

- Vigilance for uncommon side effects of COVID-19 vaccines: subacute thyroiditis, a self-limiting inflammatory condition affecting the thyroid, can be triggered by the vaccine. Clinicians should consider potential vaccine-related complications when assessing patients with unexplained symptoms after vaccination.
- The typical presentation of subacute thyroiditis is anterior neck mass/discomfort with possible fever and tachycardia, but presentation may also be more atypical in the form of fatigue and mental status change without any discomfort or fever, especially in the elderly.
- This case demonstrates that elderly patients can also develop vaccine-related thyroid complications. Healthcare professionals should be prepared to recognize thyroid-related symptoms across diverse patient populations.

Ethics approval statement

No approval from the Institutional Review Board was required.

Disclaimers

This article has not been submitted for publication at other journals nor presented at any conferences or meetings at this time.

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None.

Patient consent statement

Written informed consent for publication of their details was obtained from the patient's family.

Conflicts of interest

M.Z. reports consulting for EMD Serono and DexCom, Inc.

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