Subacute Thyroiditis Following Third Dose of Pfizer-BioNTech COVID-19 (mRNA) Vaccine in a Patient with Clear Cell Renal Cell Carcinoma: A Case Report

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Received: 4 September 2023

Accepted: 14 December 2023

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DOI 10.5001/omj.2026.10

Abstract

Over 160 cases of subacute thyroiditis (SAT) following COVID-19 vaccination or infection have been reported in the literature thus far. Roughly one-half were attributed to either the first or second dose of the COVID-19 vaccine. We report a rare case of SAT in in a 47-year-old male patient with a history of clear cell renal cell carcinoma (ccRCC) and advanced chronic kidney disease (CKD) among other comorbidities, excluding thyroid disease. After he received the third dose of the Pfizer mRNA vaccine, a deranged thyroid profile was accidentally discovered. His SAT remained asymptomatic and normalized in about six months without treatment. SAT post-COVID vaccination is a self-limiting and rare condition that should be considered in the differential diagnosis of silent thyroiditis.

Keywords: Subacute Thyroiditis; mRNA Vaccines; COVID-19; Pfizer-BioNTech COVID-19 Vaccine; ASIA Syndrome; Oman

Introduction

Many cases of subacute thyroiditis (SAT) have been reported following COVID-19 infections. Rare cases of SAT are also being reported following COVID-19 vaccination.[1] We present a case of 'silent' SAT following the administration of the third dose of the mRNA Pfizer BioNTech vaccine in a patient with a history of clear cell renal cell carcinoma (ccRCC), chronic kidney disease (CKD), and hypertension (HTN).

Case Report

The patient, 47-year-old man, was diagnosed in April 2021 with ccRCC of the left kidney, along with a left renal vein thrombus extending into the inferior vena cava. He underwent left radical nephrectomy, adrenalectomy, and cavectomy. His preoperative COVID-19 test was negative, and no documented COVID-19 infection occurred thereafter. Postoperatively, he was not exposed to chemotherapy, anti-angiogenesis, or immunotherapy drugs, but was subjected to surveillance every three months by the oncology team.

Seven months after the surgery, he was referred to the nephrology team for persistent preoperative CKD and uncontrolled HTN. He had a history of longstanding HTN, and poorly controlled diabetes mellitus (DM). His preoperative HbA1c was 8.6%, which improved to 6.5% postoperatively. He had proteinuric CKD stage IV (urinary PCR 500mg/mmol, eGFR 23.7 ml/min) presumed to be secondary to diabetic nephropathy. The patient was a cigarette

smoker for two decades and occasionally consumed beer. He was morbidly obese with a body mass index (BMI) of 43kg/m^2. He had obesity-related severe obstructive sleep apnea (OSA) (apnea-hypopnea index: 41.9) and was not compliant with continuous positive airway pressure (CPAP) ventilation. He suffered from cor-pulmonale and heart failure with reduced ejection fraction which postoperatively improved from 38% to 69%. There was no medical history suggestive of prior thyroidal illness.

His home medications were nifedipine 90 mg once daily, labetalol 200 mg twice daily, hydralazine 50 mg thrice daily, furosemide 40mg once daily, darbepoetin alpha injection 30 mcg every three weeks, aspirin 100 mg once daily, and one Neurobion® Forte tablet (vitamin B1, B6, and B12 combination) daily.

Despite elevated automated office blood pressure (AOBP) readings in our clinic (average of 155/66 mmHg), the patient seemed to be in good general condition. He did, however, have mild bilateral leg edema as well as significant acanthosis nigricans in both legs. Thyroid gland palpation revealed a non-tender, normal sized gland with no signs of hyperthyroidism such as tachycardia or fine tremors. His thyroid stimulating hormone (TSH) was found to be normal in November 2021 [Table 1]. The patient received appropriate care for his CKD and his blood pressure (BP) medications were adjusted accordingly. A 24-hour urine protein excretion test in August 2021 showed 4.6g per day corresponding to a protein-to-creatinine ratio of 500 mg/mmol.

The patient was vaccinated thrice against COVID-19 with Pfizer BioNTech BNT162B2 (June, August, December 2021) and did not report any medical concerns following them. However, two weeks after the third dose, a thyroid function test fortuitously revealed elevated serum free T4 (fT4) with suppressed serum TSH [Table 1].

Table 1: Date-wise summary of the patient's laboratory results.

Date	TSH (N:0.34–5.60 mIU/L)	Free T4 (N: 7.9–14.4 pmol/L)	TRAb (N: <1.8 IU/L)	Anti-TPO Antibodies (N: <34 IU/mL)	Anti-TGAb (N: <115 IU/mL)	Hemoglobin (N:11.5–15.5 g/dL)	Hematocrit (N: 0.35–0.45 L/L)	Ferritin (N: 24–336 mcg/L)
09/11/2021	–	–	–	–	–	11.7	0.37	–
10/11/2021	3.19 (N)	–	–	–	–	–	–	117.0
21/12/2021	*Third dose of Pfizer BioNTech BNT162B2 vaccine*							
04/01/2022	–	–	–	–	–	11.0	0.36	–
05/01/2022	0.29 (L)	19.27 (H)	–	–	–	–	–	131.6
24/02/2022	0.02 (L)	19.10 (H)	–	–	–	–	–	–
26/03/2022	0.03 (L)	21.89 (H)	–	–	–	–	–	–
30/05/2022	–	–	< 0.20 (N)	7.46 (N)	16.18 (N)	–	–	–
10/07/2022	1.30 (N)	16.85 (H)	–	–	–	–	–	–

L: low; N: normal range; H: high; T4: thyroxine; TSH: thyroid stimulating hormone; TRAb: thyrotropin receptor antibodies; TPO: thyroid peroxidase; TGAb: thyroglobulin antibodies.

A score of 7 in the Naranjo Adverse Drug Reaction Probability Scale suggested that the Pfizer-BioNTech COVID-19 vaccine was the most probable cause of SAT.[2] The endocrinology team made a provisional diagnosis of silent thyroiditis associated with recent exposure to an mRNA vaccine and a matching thyroid profile. A thyroid gland ultrasound revealed a normal-looking thyroid gland with a solitary small spongiform nodule in the right lobe, measuring approximately 11 × 10 × 7 mm, and two small spongiform nodules in the left lobe, with the largest measuring approximately 10 × 9 × 8 mm. There was no evidence of enlarged cervical lymph nodes. No treatment was given as the patient was asymptomatic, and the inflammation of the thyroid gland was expected to be transient. He was advised to avoid exposure to iodinated contrast materials and iodine-rich foods.

On a follow up visit five weeks after receiving the third dose of the vaccine, the patient was free from thyroid disease-related symptoms including pain, goiter, and lymph node enlargement. A follow-up thyroid profile continued to exhibit suppressed TSH and elevated fT4.

On March 31, 2022, a 99-Tc thyroid scan revealed severely low thyroid uptake of 0.1% (Normal: 1%–4%). Tests for thyrotropin receptor antibodies (TRAb), thyroid peroxidase antibodies (TPOAb), and thyroglobulin antibodies (TGAb) yielded negative results [Table 1].

Six months later, our patient continued to be asymptomatic for thyroid dysfunction. He reported no exposure to intravenous iodinated contrast or ingestion of any iodine-rich foods. Repeat thyroid profiling continued to display suppressed TSH and elevated fT4 [Table 1].

In July 2022, during a follow-up visit with the oncology team, another thyroid profile test revealed normal TSH levels. However, his fT4 remained elevated, though lower than earlier. No treatment was given for his subclinical hyperthyroidism throughout the six-month follow-up period.

Discussion

SAT is an inflammatory thyroid disease that may follow an acute symptomatic or asymptomatic viral illness, predominantly an upper respiratory tract infection (URTI). The absence of pain (as in our patient) does not rule out the diagnosis.[3,4] COVID-related thyroid gland involvement may accompany severe COVID-19 infections with multi-organ spreading (most frequently associated with lung involvement) or manifest as an asymptomatic infection, with SAT being the sole manifestation or the initial presentation.[5]

The first cases of SAT associated COVID-19 vaccinations were reported after administration of CoronaVac®, a virus-vector (non-mRNA) vaccine.[6,7] Our patient was administered an mRNA vaccine, which can induce immune responses by activating specific toll-like receptors (TLRs).[8] A systematic review has suggested that a prior history of autoimmune thyroiditis might also be a risk factor.[9]

The largest literature review of SAT cases following COVID-19 vaccines (on 80 patients) concluded that vaccine-related SAT was typically less symptomatic than other types of SAT, with incidents occurring variably following either the first or second dose of the vaccine within an average of two weeks.[10]

Different pathogenic mechanisms have been hypothesized to explain the development of SAT following COVID-19 vaccinations. One suggests that viral upper respiratory tract infections may trigger SAT in genetically predisposed individuals with specific HLA haplotypes, such as HLA-B*35, HLA-B67, and HLA-Drw8. (TThis hypothesis is a likely explanation for the development of SAT in our patient although this test was not conducted on our patient.) .The proposed mechanism involves the infiltration of the virus into the follicular cells of the thyroid gland, leading to cytotoxic T-cell activation, follicular destruction, and subsequent thyroid dysfunction.[9,11,12]

Another hypothesis centers around the overactivation of the immune system, combined with molecular mimicry between thyroid tissue (specifically thyroid peroxidase peptide sequences) and vaccine components, particularly the spike protein.[5,6] A third hypothesis based on the autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA syndrome) suggests that adjuvants in the vaccine may trigger an autoimmune thyroid response, leading to an abnormal increase in thyroid hormone levels, particularly in patients at higher risk for coagulation anomalies.[5,6,13] The current case appears to be more in line with the first hypothesis.

In general, COVID-19 vaccine-related adverse effects have observed to be fewer in cancer patients than in those without cancer. Notably, the SOAP-O2 study found lower incidences of local (52% vs. 36%) and systemic (32% vs. 25%) symptoms following the Pfizer/BioNTech vaccine in cancer patients.[14] Among the possible reasons may be higher pain threshold in cancer patients, and overlap between symptoms related to chemotherapy and those related to their chronic illnesses, potentially leading to underreporting and delayed diagnosis.[15]

Another possibility is the lower rates of immunogenicity in cancer patients. This may explain why only three cases of post-COVID-19 vaccination-induced SAT in cancer patients has been reported in three cases, all related to mRNA vaccines. One of these patients had concurrent papillary thyroid cancer and received the Pfizer vaccine, the second

patient had colorectal cancer and received the Moderna vaccine, and the third patient had multiple myeloma and received the Pfizer vaccine.[10,16,17]

Conclusion

To our knowledge, this is the first reported case of SAT following the administration of the third dose of the SARS-CoV-2 Pfizer BioNTech BNT162b2 vaccine. Furthermore, it represents the first case of SAT following mRNA vaccine administration in a patient diagnosed with ccRCC. Lastly, this marks the fourth reported case of SAT post COVID-19 vaccination in the cancer population at large. We present this case to contribute to the growing body of evidence in medical literature indicating that in rare cases, SAT can develop after COVID-19 mRNA vaccination.

Disclosure

The authors declare no conflicts of interest. Written informed consent was obtained from the patient.

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