Subacute thyroiditis with liver dysfunction following coronavirus disease 2019 (COVID-19) vaccination: report of two cases and a literature review

Miyako Kishimoto1), 2), Takuya Ishikawa3) and Masato Odawara1), 2)

1) Clinical Research Center, Department of Medicine, International University of Health and Welfare, Tokyo 107-0052, Japan
2) Department of Internal Medicine, Sanno Hospital, Tokyo 107-0052, Japan

Abstract. Subacute thyroiditis is a transient inflammatory thyroid disease characterized by neck pain, fever, and typical symptoms associated with thyrotoxicosis. The incidence of subacute thyroiditis is higher in female than in male, and susceptibility is prominent in the 30–50-year age range. The variety of case reports on subacute thyroiditis associated with coronavirus disease 2019 (COVID-19) appears to be increasing, and subacute thyroiditis following COVID-19 vaccination has recently been reported. Herein, we report two cases of subacute thyroiditis that developed after receiving the COVID-19 mRNA vaccine, one of which exhibited remarkable liver dysfunction. The mechanism underlying the development of post-vaccination subacute thyroiditis remains unknown; however, one theory suggests that adjuvants contained in vaccines may play a role in triggering diverse autoimmune and inflammatory responses. Another possibility is the potential cross-reactivity between the coronavirus spike protein target produced by the mRNA vaccine and thyroid cell antigens. Common side effects of the COVID-19 vaccine include pain at the injection site, fever, fatigue, headache, muscle pain, chills, and nausea. These symptoms are usually resolved within a few days. Subacute thyroiditis may present symptoms similar to those of short-term vaccination side effects or exhibit non-specific symptoms, potentially leading to misdiagnosis or underdiagnosis. Therefore, clinicians should be aware of the possible development of subacute thyroiditis after COVID-19 vaccination.

Key words: Coronavirus disease 2019 (COVID-19), Vaccination, Subacute thyroiditis, Liver dysfunction

CORONAVIRUS DISEASE 2019 (COVID-19) is caused by a recently discovered coronavirus, namely, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was hitherto unknown before the outbreak began in Wuhan, China, in December 2019 [1]. The World Health Organization (WHO) declared COVID-19 a public health emergency on January 30, 2020, and subsequently graded it as a pandemic, affecting many countries worldwide. As of January 9, 2022, the WHO has reported nearly 289 million confirmed COVID-19 cases, with the death toll exceeding 5.4 million [2]. Safe and effective vaccines are promising COVID-19-prevention strategies and are critical for terminating the pandemic [3]. Common side effects of COVID-19 vaccines include pain at the injection site, fever, fatigue, headache, muscle pain, chills, and nausea [4]. These symptoms are usually resolved within a few days; however, if the symptoms, particularly fever and fatigue, last longer than expected, or additional symptoms develop, a broader differential diagnosis should be considered. Herein, we present two cases of subacute thyroiditis (SAT) after receiving the COVID-19 vaccine with the aim of alerting clinicians to the possible development of this disease as a post-vaccination side effect.

Case 1

A 54-year-old Japanese female presented to the outpatient clinic of our department with fever, anterior neck pain, general fatigue, and shortness of breath. The patient received COVID-19 vaccination shots (BNT162b2/COMIRNATY®; Pfizer, NY, USA) on July 22 and August 5, 2021. On August 6, the patient presented with a low-grade fever of 37.0°C; however, on August 8, her fever increased to a maximum of 38.5°C, and she began to experience odynophagia, general fatigue, and shortness of breath. Antipyretic agents ameliorated her symptoms; however, they were not sufficient. A COVID-19 polymerase chain reaction (PCR) test performed on September 3 was negative, and oropharyngeal and
otologic examinations were normal. Because her symptoms persisted, the patient made her initial visit to our clinic on September 6. The patient’s blood pressure was 128/89 mmHg, and her pulse was regular (97 beats/min). The patient initially complained of bilateral thyroid tenderness which later became more prominent on the right side with a more swollen appearance compared to the left. The patient had no family history of thyroid disease or upper respiratory tract infection. Laboratory examinations revealed a suppressed thyroid stimulating hormone (TSH) level of <0.01 mIU/L (reference range: 0.61–4.23) as well as elevated free triiodothyronine (FT-3) and free thyroxine (F-T4) levels of 6.85 pg/mL (reference range: 2–4.5) and 2.34 ng/dL (reference range: 0.7–1.8), respectively. Anti-thyroid stimulating hormone receptor antibodies (TRAb) were negative; however, anti-thyroglobulin (anti-Tg) antibody was positive (79.4 IU/mL: reference range: <19.3) and anti-thyroid peroxidase (anti-TPO) antibody was also positive (10.4 IU/mL: reference range: <3.3). The thyroglobulin level was elevated to 267 ng/mL (reference range: <35.1). The patient’s C-reactive protein (CRP) level was also high at 4.64 mg/dL (reference range: <0.14). Thyroid ultrasonography revealed an enlarged right lobe and bilateral focal hypoechoic areas with decreased blood flow (Fig. 1). Due to anti-Tg and anti-TPO positivity findings, the patient could have already been presenting with Hashimoto’s thyroiditis (HT). Therefore, the possibility of acute exacerbation of HT could not be excluded. However, based on her clinical findings, we diagnosed her with newly onset SAT, and treatment with prednisolone 20 mg/day was initiated. On the day of treatment initiation, the patient’s symptoms dramatically improved. Corticosteroid therapy was gradually tapered, and after 4 weeks, both F-T3 and F-T4 levels decreased to the normal range. In the evaluation in December, the levels of anti-Tg antibody, anti-TPO antibody, and thyroglobulin were 28.4 IU/mL, 30.5 IU/mL, and 53.5 ng/mL, respectively, and her thyroid function remained euthyroid. As regards liver function, on September 6, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were within the normal range; however, the γ-glutamyl transpeptidase (γ-GTP) level was slightly elevated to 66 U/L (reference range: <32). Abdominal ultrasound examination revealed mild fatty liver. One week after the cessation of prednisolone administration, her γ-GTP level decreased to 54 U/L.

Case 2

A 46-year-old Japanese male was diagnosed with hypercholesterolemia and had been treated with rosuvastatin (2.5 mg/day) for over 5 years. The patient received the first COVID-19 vaccination shot (mRNA-1273; Moderna) on July 30, 2021. On August 10, the patient presented with a high fever of 38.7°C. The next day, August 11, the patient visited the otolaryngology outpatient clinic complaining of a persistent fever, odynophagia, and bilateral anterior neck pain. Laboratory examinations at the clinic revealed a suppressed TSH level of <0.01 mIU/L. FT-3 and F-T4 levels were elevated (14.6 pg/mL and 3.46 ng/dL, respectively). The CRP level was high (8.78 mg/dL). The patient’s thyroid exhibited diffuse enlargement, and tenderness was remarkable in both lobes. The PCR test for COVID-19 was negative. Based on these clinical findings, the otorhinolaryngologist diagnosed him with SAT, and prednisolone 20 mg/day was initiated on August 14. With a referral letter from the otorhinolaryngologist, he visited our clinic on August 20. The patient’s thyroglobulin level was elevated to 64.3 ng/mL; however, TRAb, anti-Tg, and anti-TPO were all negative. Thyroid ultrasonography revealed diffuse enlargement of the bilateral thyroid and heterogeneous echotexture (Fig. 2). These results were consistent with the clinical diagnosis of SAT. The patient’s symptoms disappeared soon after

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**Fig. 1** Thyroid ultrasonography of the right (A) and left (B) lobes of Case 1
The right lobe appears enlarged, and both lobes revealed heterogeneous echotexture and focal hypoechoic areas.
initiation of corticosteroid therapy. Blood examination on August 20 revealed remarkable liver dysfunction, such as AST, 291 U/L; ALT, 291 U/L; and γ-GTP, 656 U/L. In May, his γ-GTP level was 172 U/L, which was moderately higher than the normal range; however, his AST and ALT levels were within the normal range (Table 1). The patient was a social drinker, and alcohol consumption did not change for a long time. No additional medication or supplement tablets had recently been administered to the patient. Abdominal ultrasound examination revealed fatty liver and gallbladder polyps and these findings were consistent with those of the abdominal ultrasound examination performed in May. Specific antibodies for infected viral hepatitis, such as hepatitis A, hepatitis B, hepatitis C, Epstein–Barr virus, and cytomegalovirus, ruled out recent infection with these viruses. Specific immunological parameters characteristic of autoimmune liver diseases, such as anti-nuclear antibody, antimitochondrial M2 antibody, immunoglobulin G and M (IgG and IgM) were all negative or within a normal range. Therefore, viral hepatitis or autoimmune liver disease were unlikely to be the cause of the abrupt liver dysfunction. Corticosteroid therapy was gradually tapered and discontinued on September 11. As the patient’s thyrotoxicosis improved, his liver dysfunction also improved (Table 1). In the evaluation in November, his thyroid function was euthyroid.

### Discussion

SAT is a transient inflammatory thyroid disease characterized by neck pain, fever, and typical symptoms associated with thyrotoxicosis [5-7]. Although its etiology remains unclear, direct and indirect evidence, including a preceding upper respiratory tract infection, support viral infection, such as that from the coxsackie virus, adenovirus, or influenza virus, as an origin of this disease [5-7]. Regarding genetic factors, an association between this disease and HLA-Bw35 has been reported [8]. The incidence of SAT is higher in female than in male, and susceptibility is prominent in the 30–50-year age range. SAT can resolve naturally; however, β-blockers, non-steroidal anti-inflammatory drugs, or corticosteroids are usually administered if necessary. In both of our cases, prednisolone was tapered successfully, and no relapse was recognized thereafter. As for Case 1, acute exacerbation of HT could be considered a
differential diagnosis. Acute exacerbation of HT, also known as painful HT, is a rare variant of HT. The close similarities of clinical features, such as the symptoms of thyrotoxicosis, accompanied with fever and neck pain during the initial phase for both acute exacerbation of HT and SAT make it particularly difficult to accurately diagnose these diseases [9-11]. To differentiate between these two diseases, a biopsy is necessary. The typical pathological findings of acute exacerbation of HT are lymphocyte infiltration, germinal centers, Hurthle cells, and variable degrees of fibrosis, while those of SAT are noncaseating granulomas, neutrophils, and giant cells [10-12]. Because biopsy of the thyroid in Case 1 has not been carried out, the possibility of acute exacerbation of HT cannot be excluded completely; however, based on the frequency of these two diseases and ultrasound features, we diagnosed case 1 with SAT. An overall age-and sex-adjusted incidence of SAT is said to be 4.9 cases per 100,000/year [13, 14], whereas only 20 cases of acute exacerbation of HT were said to have been reported in the recent years [13]. As for ultrasonography findings, in the case of SAT, intra-lesion blood flow is consistently reduced, while it is variable and often elevated in acute exacerbation of HT [9-11, 13, 15]. Thus, the ultrasonography findings were compatible with a diagnosis of SAT in Case 1. Both SAT and acute exacerbation of HT can be treated with glucocorticoid. However, in contrast to SAT, acute exacerbation of HT is only temporarily responsive to glucocorticoid treatment, and a significant number of reported patients experienced repeated relapses which eventually required a thyroidectomy [9, 10, 12]. Therefore, the successful clinical course with glucocorticoid treatment in Case 1 also supported the diagnosis of SAT.

As regards the liver dysfunction in Case 1, thyrotoxicosis might have contributed to a certain extent; however, because of the sole abnormality of γ-GTP, fatty liver was considered the main cause of liver dysfunction in this patient. In Case 2, liver dysfunction was considerably more severe than in Case 1. Based on the negative results of other differential diagnoses and the subsequent reversal of the patient’s liver dysfunction following thyroid improvement, we considered his liver dysfunction might be partially explained by thyrotoxicosis with SAT. Several mechanisms contribute to liver dysfunction in a state of thyrotoxicosis. These include: 1) direct liver toxicity caused by prolonged exposure to excessive thyroid hormone production, 2) hepatocyte anoxia as a result of the hypermetabolic state, 3) metabolic dysfunction due to liver glycogen and protein decomposition, 4) autoimmune-related liver injury, 5) drugs such as antithyroid medications induced liver injury, and 6) hepatic congestion and hepatic necrosis from thyrotoxic heart failure [16-21]. However, because liver dysfunction in Case 2 was too severe to be explained solely by thyrotoxicosis, we speculated that the vaccine might have affected his liver function. Some hepatotoxicity cases caused by vaccines, such as anti-rabies vaccination, influenza virus, hepatitis A, and B vaccines have been reported [22-29]. Although, actual incidence of liver dysfunction in cases with COVID-19 vaccine-induced SAT is unclear, according to the “COVID-19 mRNA Pfizer/BioNTech vaccine analysis print” published in December 2021, among over 430,500 of “total reactions for drug”, a total of 208 cases had “hepatic disorders” and three cases had drug-induced liver injury [30]. A 61-year-old female who developed liver dysfunction nine days after receiving a second dose of Pfizer COVID-19 vaccine was also reported [31].

Although the true prevalence of thyroid dysfunction in COVID-19 patients is unknown, the number of case reports and reviews on COVID-19-associated SAT seems to be increasing as the awareness of this disease as a COVID-19 complication continues to grow [32-61]. The pathophysiology of COVID-19-associated SAT is thought to be either direct infection, similar to other viral conditions, or a post-viral inflammatory reaction targeting the thyroid of genetically susceptible individuals. In particular, interactions with angiotensin-converting enzyme 2 (ACE2) receptors have been suggested [44, 48, 62-64]. ACE2 receptors are considered essential in enabling SARS-CoV-2 to infect human host cells and are more prevalent in thyroid cells than in lung cells [41, 65]. The abundance of ACE2 receptors in the thyroid potentially explains the mechanism underlying direct viral injury to the thyroid in SAT [47, 54]. In addition, interactions via the activation of inflammatory mediators and indirect immune-mediated damage have also been proposed [41, 45].

Various drugs and vaccines for COVID-19 are undergoing rapid development and some of these are already in clinical use. There are several types of vaccines for COVID-19 including mRNA-based vaccines, DNA-based vaccines, viral vector-based vaccines, live attenuated vaccines, inactivated virus vaccines, and recombinant protein vaccines [66-73]. Large phase-3 trials for mRNA vaccines, BNT162b2 and mRNA-1273, demonstrated that both vaccines were >94% effective against symptomatic COVID-19 [71, 74]. The adverse events of mRNA vaccines during the first month of the vaccination program in the United States have been monitored using the Vaccine Adverse Event Reporting System (VARES) [75], a spontaneous reporting system, and V-safe, an active surveillance system [76]. During the surveillance period, the symptoms most frequently reported in the VARES were headache (22.4%),
As for ordinally SAT, the average age of onset was matched vaccinated persons to unvaccinated persons, the analysis reported in Israel, which compared individually matched vaccinated persons to unvaccinated persons, the BNT162b2 mRNA vaccine was most strongly associated with an elevated risk of myocarditis, lymphadenopathy, appendicitis, and herpes zoster infection [78].

SAT following COVID-19 vaccination has recently been reported [79-96]. Details in these 23 cases and the two present cases are summarized in Table 2. Among them, thirteen, five, and six cases received the mRNA-based, viral vector-based, and inactivated virus vaccines, respectively (one case unknown). Because the total number of people who received individual vaccines is unidentified, the incidence of vaccine-induced SAT is unclear, thus we are not able to conclude that mRNA vaccine is most likely to develop vaccine-induced SAT. Among these 25 cases, 15 cases developed SAT after the 1st dose and 10 cases developed SAT after the 2nd dose.

The reason why some developed it after the 1st dose and others did after the 2nd dose is not clear but genetically predisposed factors in individuals could be a possibility. The average age of these cases was 44.7 years (range, 26–75 years) and female-male ratio was 5.3:1 (n = 21/4). As for ordinally SAT, the average age of onset was mid-40’s and the female-male ratio was 3.5–7:1 [5, 14].

Among 34 published cases who developed SAT during/after COVID-19 [32-43, 49-57], the average age was 39.2 years (range, 18–69 years) and female-male ratio was 3.3:1 (n = 26/8). Therefore, there were no significant differences among ordinal SAT, SAT during/after COVID-19, and SAT after COVID-19 vaccination in terms of ages and sex ratio. The duration from vaccination to the onset of SAT varied, ranging from 12 hours to 3 weeks. This duration was shorter in comparison to the onset duration of ordinal SAT (usually two to eight weeks after viral infection) [80].

The mechanism underlying the development of post-vaccination SAT remains unknown; however, there is a theory that adjuvants contained in vaccines may play a role in triggering diverse autoimmune and inflammatory responses [97, 98]. Adjuvants are substances commonly found in vaccines to enhance their effects. Although it is usually safe and effective, adjuvant administration in genetically susceptible individuals may lead to serious side effects, namely, “autoimmune/inflammatory syndrome induced by adjuvants” (ASIA), by disrupting the host’s immunological balance through molecular mimicry, triggering polyclonal activation of B lymphocytes or other similar etiopathogenetic mechanisms [80, 99].

Several post-vaccination autoimmune and subacute thyroiditis cases have been reported, reflecting the clinical manifestation of ASIA; however, data on ASIA following COVID-19 vaccination are limited [80, 97].

mRNA vaccines, such as BNT162b2 and mRNA-1273, are lipid nanoparticle-encapsulated mRNA-based vaccines, which encode the prefusion-stabilized full-length spike protein of SARS-CoV-2 [71, 74, 100]. The developers of mRNA vaccines, Pfizer/BioNTech and Moderna do not explicitly state the use of adjuvant with their vaccines, however, Pfizer/BioNTech do mention that the RNA acts as an adjuvant because RNA can induce immune responses by activating specific toll-like receptors (TLRs), mainly TLRs 3, 7, and 8 [73, 101]. In addition, the lipid nanoparticles they use with their vaccines to help protect against degradation as well as employ chemical modification to improve RNA stability is suggested to be conferring adjuvant properties [73]. Another possibility is the potential cross-reactivity between the coronavirus spike protein target produced by the mRNA vaccine and thyroid cell antigens [82, 85, 102]. As previously mentioned, the thyroid expresses the ACE2 receptor at a high concentration. Therefore, the SARS-CoV-2 spike protein presumably enters the thyroid cells via the ACE2 receptor and potentially mediates immunization-induced damage [64, 65, 84]. Inactivated vaccines, such as CoronaVac, uses the native rendered replication deficient from heat or chemical treatment [73]. The vaccine contains aluminum hydroxide as an adjuvant, and SAT as a phenomenon of post-vaccination ASIA syndrome has been reported [80]. In addition, because inactive vaccines contain various proteins belonging to the pathogen virus and similar antigenic parts, and considering the increased affinity of the SARS-CoV-2 towards the thyroid, we may speculate that this inactive vaccine itself may also affect the thyroid tissue [93]. A viral vector-based vaccine encapsulates the genome of a different weakly pathogenic virus with additional DNA that encodes the target viral antigen [73]. ChAdOx1-s or Ad5-nCoV is classified as a viral vector-based vaccine. The innate immune environment activated by signaling and inflammation caused by the adenovirus may possibly be related to the development of vaccine induced SAT in a certain population with genetic susceptibility [103].

Not only SAT but cases of other thyroid diseases developing or worsening after COVID-19 vaccination have been reported. One of these diseases is Graves’ disease, the most common cause of hyperthyroidism [104]. Although factors underlying Graves’ disease are not clear, it appears that genetic, epigenetic, and environmental determinants are potential factors for the disease [104]. Some cases of Graves’ disease after mRNA-based
### Table 2  Cases of subacute thyroiditis after COVID-19 vaccination

| No. | Age (years) | Sex | Vaccine name | Company | Vaccine type | Onset of symptoms | CRP (<5.0 mg/L) | ESR (<20 mm/h) | TSH | F-T4 | F-T3 | TRAbs | TGAb | TPOAb | Glucocorticoid usage | Clinical outcome | Reference |
|-----|-------------|-----|--------------|---------|--------------|-------------------|----------------|----------------|-----|------|------|--------|------|-------|----------------------|----------------|----------|
| 1   | 67          | M   | CoronaVac®  | Sinovac | Inactivated  | 17–18 days after 2nd dose | 53.9           | 67             | ↓↓ | ↑   | ↑   | Negative | Negative | Negative | —                   | In the 4th week of treatment, still use methylprednisolone 16 mg/day | 8 weeks after onset, euthyroid | 79       |
| 2   | 35          | F   | CoronaVac®  | Sinovac | Inactivated  | 4 days after 2nd dose | 100.5          | 53             | →  | →   | ↑   | Negative | Negative | Negative | methylprednisolone 16 mg/day | In the 10th week of treatment, still use methylprednisolone 8 mg/day | 80       |
| 3   | 34          | F   | CoronaVac®  | Sinovac | Inactivated  | 4 days after 1st dose | 6.0            | 19             | ↓↓ | ↓   | ↑   | Negative | Negative | Negative | methylprednisolone 16 mg/day | 8 weeks after onset, euthyroid | 80       |
| 4   | 37          | F   | CoronaVac®  | Sinovac | Inactivated  | 7 days after 2nd dose | 2.4            | 25             | →  | →   | ↑   | Negative | Negative | Negative | —                   | At the 8th week control visit, euthyroid | 80       |
| 5   | 26          | F   | Vaxzevria®  | AstraZeneca | Viral vector  | 2 days after 1st dose | 29.4           | NA             | →  | →   | ↑   | Negative | Negative | Negative | prednisolone 50 mg/dL | 6 weeks follow-up, euthyroid | 81       |
| 6   | 49          | F   | Spikevax®   | Moderna | mRNA        | 1 week after 1st dose | 21.9           | NA             | →  | →   | →   | Negative | Negative | Negative | prednisolone 20 mg/dL | euthyroid | 81       |
| 7   | 55          | F   | ChAdOx1-S   | AstraZeneca | Viral vector  | 3 weeks after 1st dose | 87             | 51             | ↓   | ↑   | ↑   | NA      | Negative | Negative | —                   | After 6 weeks, severe hypothyroidism | 82       |
| 8   | 57          | F   | BNT162b2    | Pfizer-BioNTech | mRNA  | 1 day after 2nd dose | NA             | NA             | ↓↓ | ↑   | ↑   | NA      | Negative | Negative | prednisolone (dosage NA) | NA | 83       |
| 9   | 75          | M   | Vaxzevria®  | AstraZeneca | Viral vector  | 14 days after 1st dose | NA             | NA             | ↓↓ | ↑   | ↑   | Negative | Negative | Negative | —                   | 4 weeks later, euthyroid | 84       |
| 10  | 42          | F   | BNT162b2    | Pfizer-BioNTech | mRNA  | 5 days after 1st dose | NA             | 62             | ↓   | →   | ↑   | Negative | Negative | Negative | prednisolone 40 mg/dL | 25 days after onset, thyrotoxicosis | 85       |
| 11  | 34          | F   | COVAXIN®    | Bharat Biotech | Inactivated  | 5 days after 1st dose | 9.8            | 60             | ↓   | ↑   | ↑   | NA      | NA      | NA      | prednisolone 15 mg/day | 7 weeks after initiation of treatment, euthyroid | 86       |
| 12  | 51          | F   | BNT162b2    | Pfizer-BioNTech | mRNA  | 4 days after 1st dose | 135            | 103            | ↓   | ↑   | →   | Negative | Negative | Negative | methylprednisolone 16 mg/day | 8 weeks after initial assessment, euthyroid | 87       |
| 13  | 39          | F   | ChAdOx1-S   | AstraZeneca | Viral vector  | 3 weeks after 1st dose | 1.0            | 17.0           | ↓   | ↑   | →   | Negative | Positive | Positive | —                   | 8 weeks later, euthyroid | 87       |
Table 2

| No. | Age (years) | Sex | Vaccine name and company | Vaccine type | Onset of symptoms (after vaccine) | CRP (<5.0 mg/L) | ESR (<20 mm/h) | TSH | F-T4 | F-T3 | TRAbs | TGAb | TPOAb | Glucocorticoid usage | Clinical outcome |
|-----|-------------|-----|--------------------------|--------------|----------------------------------|----------------|---------------|-----|------|------|--------|------|--------|----------------------|-----------------|
| 14  | middle age  | F   | BNT162b2, Pfizer-BioNTech | mRNA         | 2 weeks after 2nd dose           | NA             | NA            | ↓↓ | ↓↓   | ↑    | ↓↓     | NA    | NA      | —                    | Euthyroid       |
| 15  | NA          | F   | mRNA-1273, Moderna        | mRNA         | 6 days after 1st dose            | NA             | NA            | NA | NA   | NA   | NA      | NA    | NA      | —                    | NA              |
| 16  | 42          | F   | BNT162b2, Pfizer-BioNTech | mRNA         | 5–6 days after 2nd dose          | NA             | NA            | NA | NA   | NA   | NA      | NA    | NA      | —                    | NA              |
| 17  | 40          | F   | BNT162b2, Pfizer-BioNTech | mRNA         | 12 hours after 2nd dose          | NA             | NA            | NA | NA   | NA   | NA      | NA    | NA      | —                    | NA              |
| 18  | 35          | F   | CoronaVac, Sinovac Biologics | Inactivated | 14 days after 1st dose           | NA             | NA            | NA | NA   | NA   | NA      | NA    | NA      | —                    | Euthyroid       |
| 19  | 32          | F   | BNT162b2, Pfizer-BioNTech | mRNA         | 4 days after 2nd dose            | NA             | NA            | NA | NA   | NA   | NA      | NA    | NA      | —                    | Euthyroid       |
| 20  | 38          | F   | SARS-CoV-2 vaccine (name NA) | mRNA         | 7 days after 1st dose            | NA             | NA            | NA | NA   | NA   | NA      | NA    | NA      | —                    | NA              |
| 21  | 48          | F   | COMIRNATY® (name NA)      | mRNA         | 11 days after 1st dose           | NA             | NA            | NA | NA   | NA   | NA      | NA    | NA      | —                    | NA              |
| 22  | 53          | F   | CoronaVac, Sinovac Biologics | Viral vector | 15 days after 1st shot           | NA             | NA            | NA | NA   | NA   | NA      | NA    | NA      | —                    | NA              |
| 23  | 54          | F   | COMIRNATY® (name NA)      | mRNA         | 3 days after 2nd dose            | NA             | NA            | NA | NA   | NA   | NA      | NA    | NA      | —                    | NA              |
| 24  | 46          | F   | BNT162b2, Pfizer-BioNTech | mRNA         | 8 days after 1st shot            | NA             | NA            | NA | NA   | NA   | NA      | NA    | NA      | —                    | NA              |
| 25  | 46          | F   | mRNA-1273, Moderna        | mRNA         | 9 days after 1st shot            | NA             | NA            | NA | NA   | NA   | NA      | NA    | NA      | —                    | NA              |

Abbreviations: M, male; F, female; CPR, C reactive protein; ESR, erythrocyte sedimentation rate; TSH, thyroid-stimulating hormone; F-T4, free thyroxine; F-T3, free triiodothyronine; TPOAbs, thyroid peroxidase antibodies; TgAbs, thyroid autoantibodies; TRAbs, TSH receptor antibodies; TgAbs, anti-thyroglobulin antibody; TPOAbs, anti-thyroid peroxidase antibody; NA, not available.

TSH: → within normal range, ↓ 0.01–0.2 mIU/L, ↓↓ <0.01 mIU/L
F-T3 and F-T4: → within normal range, ↓ decreased, ↑ increased.
vaccination have been reported, and vaccine induced autoimmune hypersensitivity was suggested as a cause [95, 97, 105]. Additionally, a case of silent thyroiditis 10 days after receiving the 1st dose of mRNA-based vaccine was reported [95]. Eight weeks later, the patient presented with overt hypothyroidism and treatment with levothyroxine was initiated. Another case was a 13-year-old female who had been diagnosed with HT prior to vaccination [106]. After the 1st dose of mRNA vaccination, her anti-TPO levels increased and six weeks after the second vaccination, the anti-TPO levels further increased. TSH level also increased, and she required more supplementation of the thyroid hormone.

More discussion will be needed regarding the necessity and the timing of repeated or booster doses in cases of COVID-19 vaccine-induced SAT. However, because SAT is relatively mild and appears to be self-limiting, it is suggested that clinicians carefully monitor their patients after receiving the COVID-19 vaccination rather than forgoing the follow-up dose [80, 88, 107].

In conclusion, we reported two cases of subacute thyroiditis, one of which exhibited remarkable liver dysfunction, after receiving COVID-19 mRNA vaccines. SAT may present symptoms similar to those of short-term vaccination side effects or exhibit non-specific symptoms, potentially leading to misdiagnosis or under-diagnosis. We hope the present case report raises awareness of the possible development of SAT after exposure to the COVID-19 vaccine.

Disclosure

The authors declare that they have no conflict of interests.

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Ethics Approval

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and the Helsinki Declaration of 1975, as revised in 2000 and 2008. This case report was approved by the Ethics Committee of International University of Health and Welfare.

Informed Consent

We obtained written informed consent from the patients for the publication of this case report.

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