



Graves' disease following SARS-CoV-2 vaccination

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To the Editor:

Vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) are rapidly being developed using several different platforms. Some of these are traditional approaches, such as inactivated whole-virus (CoronaVac, Covaxin, BBIBP-CorV). Newer platforms have been introduced for vaccine development at pandemic speed and induce more potent protective immune response than traditional vaccines, including protein subunit (NVX-CoV2373), viral vector (Ad5-nCoV, Ad26.COV2.S, ChAdOx1 nCoV-19/AZD1222, Gam-COVID-Vac/Sputnik V), and mRNA (BNT162b2, mRNA-1273) vaccines. Heterologous vaccination refers to the administration of booster and priming vaccines developed with different platforms. This strategy has been considered for some circumstances, such as vaccine shortages, vaccine-related adverse events, and increasing immunogenicity to combat emerging variants of concern. However, the vaccination may trigger autoimmune diseases, including autoimmune thyroid disease in some predisposed patients. There are increasing case reports on Graves' disease following SARS-Cov-2 vaccination [1–3] (Table 1). We herein report a patient who rapidly developed Graves' disease after the second dose of the ChAdOx1 nCoV-19 vaccine.

A 70-year-old man presented to his primary care physician with a 10-day history of exertional dyspnea, myalgia, and palpitation. He had been in his usual state of health until 2 days after received the second dose of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2. He did not report any side effects following the first dose of the vaccine. His activity tracker recorded that a resting heart rate rose from 70 to 100 beats per minute. He had

poor appetite and lost 3 kg. There was no personal history or family history of autoimmune and endocrine diseases. On examination, the blood pressure was 120/80 mmHg, the pulse rate 102 beats per minute, and the respiratory rate 18 breaths per minute. The weight was 53 kg, the height 165 cm, and the body-mass index 19.5 kg/m². The thyroid gland was not enlarged. His thyroid function tests (TFTs) were as follows (10th day after the second dose of vaccine): free T₃ > 20 pg/mL (1.88–3.18), free T₄ 3.19 ng/dL (0.7–1.48), and TSH < 0.0036 mIU/L (0.35–4.94). TSH receptor antibody was positive (3.23 IU/L, normal < 1.75). TFTs were normal 9 months prior to presentation. Serum high-sensitivity C-reactive protein level was 1.01 mg/L (normal < 3). He was diagnosed with Graves' disease and treated with methimazole 15 mg per day with a good response. At the 60th day after the second dose of vaccine, serum SARS-Cov-2 anti-RBD IgG level and surrogate neutralization test were 1093.4 BAU/mL and 99.4%, respectively.

Particular attention should be paid to new vaccines, especially when they induce a strong immune response. Vaccines have been suspected to play a role in triggering autoimmune diseases. To date, there is no proven causal association between SARS-CoV-2 vaccination and the development of autoimmune diseases. Most of these phenomena were published in the literature only as case reports. Appropriate clinical and immunological investigations should be systematically included in clinical trials. Clinical surveillance of potential autoimmune adverse effects should be considered in the monitoring protocol. It is important that this report should not be misinterpreted and discourage people from being vaccinated. In an emergency pandemic

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Table 1 A summary of case reports of Graves' disease following SARS-Cov-2 vaccines

	Age (years)	Sex	Preexisting AITD	History of COVID-19 infection	SARS-Cov-2 vaccine before GD	Onset of thyrotoxic symptoms ^a
1 [1]	40	F	No	Yes	BNT162b2 x1	2 days
2 [1]	28	F	No	No	BNT162b2 x1	3 days
3 [2]	71	F	Yes, GD	No	BNT162b2 x2	~1 month
4 [2]	46	M	No	No	BNT162b2 x1	15 days
5 [3]	30	F	Yes, GD	No	CoronaVac x2 ChAdOx1 nCoV-19 x1	4 days
6 (This case)	70	M	No	No	ChAdOx1 nCoV-19 x2	2 days

AITD autoimmune thyroid disease, COVID-19 coronavirus disease 2019, F female, GD Graves' disease, M male

^aAfter the last dose of vaccine

situation, the benefits of vaccination far outweigh the potential risks.

Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

Ethical approval Written consent was obtained from the patient. This case report was approved by the Human Research Ethics Committee, Faculty of Medicine Ramathibodi Hospital, Mahidol University.

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