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SARS-CoV-2 vaccination related hyperthyroidism of Graves' disease

The ongoing global pandemic outbreak due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has necessitated the development of long-term strategies to reduce the healthcare burden. Therefore, from a public health perspective, vaccination against SARS-CoV-2 seems to be the main strategy for achieving the final herd immunity. However, for years, vaccine hesitancy has remained an issue in various viral outbreaks.¹ The success of vaccination programs is usually threatened by vaccine-related side effects, especially for the concern of autoimmune or inflammatory disorders.² In certain circumstances, autoimmune/inflammatory events might be triggered in patients with silent autoimmune disorders.² Therefore,

vaccine-related autoimmune effects should be cautiously monitored. Herein, we report three cases of SARS-CoV-2 vaccination-related hyperthyroidism.

A 39-year-old apparently healthy woman with known euthyroid autoimmune thyroid disease for several years received vaccination (Moderna, Spikevax) on July 13, 2021. Two weeks after vaccination, she experienced palpitation with hand tremor. She visited our endocrine outpatient clinic, and hyperthyroidism was confirmed 46 days after vaccination. She was prescribed carbimazole 10 mg once daily. Another 59-year-old woman who had no personal history of autoimmune thyroid disease, but whose sister had hyperthyroidism, received vaccination (AstraZeneca,

Table 1 Demographic characteristics of patients with SARS-CoV-2 vaccination-related hyperthyroidism.

	Case 1	Case 2	Case3
Gender	Female	Female	Female
Age (years)	39	59	44
Vaccine	Moderna (Spikevax)	AstraZeneca (Vaxzevria)	AstraZeneca (Vaxzevria)
Vaccination date	2021/7/13	2021/7/20	2021/5/21
Diagnostic date	2021/8/27	2021/8/27	2021/6/21
Free T4 (ng/dL) (R: 0.70–1.48)	1.54	2.28	2.74
TSH (mIU/L) (R: 0.35–4.94)	<0.0038	<0.0038	<0.0038
Family or Personal AIT history	Yes	Yes	No
Anti-thyroglobulin Ab (IU/mL) (R: <14.4)	<3.0	1494.78	2904.39
Anti-TPO Ab (IU/mL) (R: < 5.61)	64.58	<3.0	206.64
TRAb (%) (R: < 10.0)	42.4	68.7	80.9
Days between vaccination and diagnosis	46	39	31
Latest thyroid function before vaccination			
Date	2021/2/9	2019/4/24	N/A
Free T4 (ng/dL)	1.03	1	N/A
TSH (mIU/L)	0.99	1.79	N/A
Latest thyroid function after vaccination			
Date	2021/11/10	2021/11/30	2022/1/3
Free T4 (ng/dL)	1.29	1.06	0.83
TSH (mIU/L)	<0.0038	0.0091	<0.0038

Abbreviations: Ab: antibody; N/A: not available; R: reference range; TPO: thyroid peroxidase; TRAb: TSH receptor antibody.

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Vaxzevria) on July 20, 2021. Approximately 2 weeks later, she experienced dyspnea and dizziness with palpitation. Hyperthyroidism was confirmed 39 days after vaccination; she was prescribed carbimazole 10 mg twice daily. Another 44-year-old woman without any personal or family history of autoimmune thyroid disease received vaccination (AstraZeneca, Vaxzevria) on May 21, 2021. Four days later, tremor developed, followed by heat intolerance and weight loss. Hyperthyroidism was confirmed 31 days after vaccination, and she was prescribed carbimazole 10 mg twice daily (Table 1). Autoimmune thyroid disease is prevalent in Taiwan, with an estimated prevalence of approximately 15% in general population. However, most patients maintain a life-long euthyroid state.³ The dynamic and preserved balance between cellular apoptosis and cellular proliferation in patients with autoimmune thyroid disease might be impaired by vaccination.³ Two cases of hyperthyroidism following SARS-CoV-2 vaccination have been recently reported,⁴ and similar manifestations of other autoimmune entities might occur after vaccination. The underlying mechanism of hyperthyroidism development in such cases remains unclear. The above cases underline the importance of establishing a registered reporting system for thyroid function follow-up after SARS-CoV-2 vaccination in patients with euthyroid autoimmune thyroid disease.

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Declaration of competing interest

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References

1. Dubé E, Laberge C, Guay M, Bramadat P, Roy R, Bettinger J. Vaccine hesitancy: an overview. *Hum Vaccines Immunother* 2013;9:1763–73.
2. Bragazzi NL, Hejly A, Watad A, Adawi M, Amital H, Shoenfeld Y. ASIA syndrome and autoimmune endocrine disorders. *Best Pract Res Clin Endocrinol Metabol* 2020;34:101412.
3. Wang CY, Zhong WB, Chang TC, Tsai YF. Circulating soluble Fas ligand correlates with disease activity in Graves' hyperthyroidism. *Metabolism* 2002;51:769–73.
4. Vera-Lastra O, Ordinola Navarro A, Cruz Domiguez MP, Medina G, Sánchez Valadez TI, Jara LJ. Two cases of Graves' disease following SARS-CoV-2 vaccination: an autoimmune/inflammatory syndrome induced by adjuvants. *Thyroid* 2021;31:1436–9.

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