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# Journal of Clinical and Translational Endocrinology: Case Reports

journal homepage: [www.elsevier.com/locate/jctecasereports.com](http://www.elsevier.com/locate/jctecasereports.com)

## A case report of new onset graves' disease induced by SARS-CoV-2 infection or vaccine?

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### ARTICLE INFO

#### Keywords:

Graves' disease  
Hyperthyroidism  
COVID-19  
Vaccine

### ABSTRACT

The virus responsible for the COVID-19 pandemic continues to pose unmatched challenges in the world. It can cause systemic inflammation, which can lead to multiorgan involvement and subsequent damage. The relationship that possibly exists between the COVID-19 infection, the newly developed vaccines, and thyroid disease are still under extensive investigation. We are reporting the first case of new-onset graves' disease in a young, healthy man after COVID-19 infection and receiving a COVID-19 vaccine dose.

### 1. Introduction

As the world continues to fight against the Coronavirus disease (COVID-19) pandemic, there have been more than 4 million deaths to date reported worldwide by the World Health Organization (WHO) [1]. The COVID-19 disease is caused by the severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) and can directly or indirectly affect the endocrine system on multiple levels by affecting the hypothalamus-pituitary axis (HPA) [2]. Arising research suggests that there may be a direct effect of SARS-CoV-2 on thyroid function, leading to new onset of thyroid disease [3] or exacerbation of a pre-existing one [4]. Due to the deadly consequences of the infection, several vaccines against the SARS-CoV-2 were developed and received emergent use authorization by health agencies worldwide after an expedited evaluation of safety [5] and effectiveness [6]. However, these new vaccines must be continuously and closely monitored for possible adverse events [6]. Several cases of Graves' disease (GD) in individuals who had either COVID-19 infection or received the Pfizer-BioNTech COVID-19 vaccine were recently reported [7]. In this report, we describe for the first time a case of GD that developed after SARS-CoV-2 infection preceded by an administration of one dose of a COVID-19 vaccine.

### 2. Case presentation

We report a case of a 32-year-old male patient without significant medical history who developed a dry cough, low-grade fever, generalized body aches, and fatigue ten days after receiving the first dose of the BNT162B2 SARS-CoV-2 (Pfizer-BioNTech) vaccine. Infection with SARS-CoV-2 was suspected and later confirmed via SARS-CoV-2 detecting nasopharyngeal polymerase chain reaction (PCR) test and was treated symptomatically on an outpatient basis. Acute flu-like symptoms lasted for five days. However, the patient presented to the emergency department one week after flu-like symptoms resolution, with palpitations, insomnia, tremor, irritability, diaphoresis, and dyspnea at rest. The patient denied any vision changes, exophthalmos, increased defecation, erectile dysfunction, reduced libido, weight, or skin changes. Family history was negative for any autoimmune thyroid disease or thyroid cancer. Neck examination was normal without tenderness, nodules, thyromegaly or cervical lymphadenopathy. Skin and eye examination were unremarkable with no erythema, thickening, pretibial myxedema, or proptosis. The patient was noted to have elevated blood pressure (BP) of 170/101 mmHg and a heart rate (HR) of 130 beats per minute. Electrocardiogram (ECG) revealed sinus

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<https://doi.org/10.1016/j.jecr.2021.100104>

Received 19 August 2021; Received in revised form 12 December 2021; Accepted 13 December 2021

Available online 17 December 2021

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tachycardia with premature ventricular contractions (PVCs). Thyroid function tests (TFTs) showed low thyroid-stimulating hormone (TSH), and an elevated serum free thyroxine hormone (T4) level, and total triiodothyronine hormone (T3) level. Serology tests were positive for thyroid-stimulating immunoglobulin (TSI), thyroid peroxidase antibodies (*anti-TPO*), and anti-thyroglobulin (*anti-TG*) (Table A). Thyroid ultrasonogram revealed heterogeneous thyroid with underlying micronodules suggestive of thyroiditis. Radioactive iodine uptake (RAIU) test revealed 72% homogeneous uptake. The diagnosis of GD was confirmed by his clinical presentation, the thyroid function test results, the positive TSI, and the RAIU results. The patient was initially started on Methimazole 20 mg once daily, Propranolol 20 mg three times daily, and a 7-day course of Prednisone 20 mg once daily. However, the patient continued to have palpitations, insomnia, and irritability with elevated BP and HR. Subsequently, Methimazole and Propranolol were increased to 40 mg once daily and 40 mg three times daily. After six weeks of treatment, the patient's symptoms improved progressively, and T3 and T4 levels normalized within two months of his diagnosis of COVID-19 infection (Table A).

### 3. Discussion

While T3 and T4 hormones are essential for regulating normal growth and development and the general metabolism of the adult human body, excessive T3 and T4 production, also known as hyperthyroidism, can lead to hypermetabolic state [8]. Manifestations are usually gradual, ranging from mild to severe symptoms, such as unintended weight loss, heat intolerance, muscle weakness, insomnia, tachycardia, diaphoresis, irritability, restlessness, and fatigue. Moreover, patients with hyperthyroidism may exhibit brittle nails, hair changes, hyperreflexia, increased appetite, frequent bowel movements with irregular menstrual cycles in females, and erectile dysfunction in males [7]. GD is an autoimmune condition that causes hyperthyroidism, thyroid gland enlargement, and possibly eye and skin manifestations [9]. GD may present with eyelid lag and proptosis referred to as Graves' ophthalmopathy. Rarely, patients with GD may develop pretibial myxedema with redness and thickened skin lesions. GD might also lead to congestive heart failure and osteoporosis [7,9].

Once a diagnosis of hyperthyroidism is established via a suppressed serum TSH and high serum T3 and T4 levels [9], determining the etiology is necessary to guide the treatment. Aside from the very specific clinical features of GD, elevated TSI [10], uniform and homogenous RAIU [11], and a diffusely increased thyroid blood flow on ultrasound [12] can be used to distinguish GD from other causes of hyperthyroidism. The therapeutic approaches include controlling the hyperthyroid symptoms with a beta-blocker [13] and decreasing the thyroid hormones production with either thioamides, radioiodine ablation, or surgical excision [14]. Although not well demonstrated, glucocorticoids can decrease the conversion of T4 to the active form T3 and subsequently might decrease symptoms severity in GD [15]. In our case report, the patient had a typical clinical tableau in favor of hyperthyroidism, and GD was diagnosed via serology and imaging studies. He improved clinically only after using higher doses of beta-blocker and thioamide therapy for several weeks. The patient did not require any radioiodine ablation or surgical procedure.

It is difficult to determine whether the trigger for GD in this previously healthy male patient was the COVID-19 infection or an adverse event of the first dose of the BNT162B2 SARS-CoV-2 (Pfizer-BioNTech)

vaccine or whether it was a mere coincidence. A recently published review detailed five cases of female patients that developed GD or had flare-ups of controlled GD after COVID-19 infection showing that the SARS-CoV-2 can possibly trigger autoimmune hyperthyroidism [7]. Another recent report described a deterioration of thyroid function in a female patient with a pre-existing GD [16]. Many other autoimmune conditions induced by the virus were reported this past year, including autoimmune hemolytic anemia, Guillain-Barré syndrome, and autoimmune thrombocytopenic purpura [7]. Few cases of subacute thyroiditis were also reported after COVID-19 infection [17–19]. Moreover, a recently published article described two cases of female patients who developed GD within 2–3 days after receiving the first dose of the Pfizer-BioNTech COVID-19 vaccine [20]. The authors attributed the cause in these two patients to the phenomenon of autoimmune/inflammatory syndrome induced by adjuvants (ASIA) [20]. This syndrome was first described in 2011 as an entity that incorporates diverse autoimmune conditions triggered by various adjuvants [21]. It was postulated that exposure to some vaccine adjuvants could lead to a cascade of immunological responses leading to autoantibodies production [21,22]. The ASIA was also described in other studies where the patients developed autoimmune thyroiditis after the administration of a human papillomavirus (HPV) vaccine and an influenza vaccine [23]. Interestingly, the clinical manifestations of thyroid disease appeared within 60 days after vaccination in these reports [23]. Whereas, in our case, GD symptoms occurred 22 days after the administration of the first dose of the BNT162B2 SARS-CoV-2 (Pfizer-BioNTech) vaccine.

### 4. Conclusion

To the best of our knowledge, this is the first case report of a new-onset of GD in a young male adult following an administration of a COVID-19 vaccine and recovery from a mildly symptomatic COVID-19 infection. Whether the development of the GD in this patient was triggered by the COVID-19 infection, a side effect of the vaccine, both the infection and the vaccine, or purely coincidental is subject to further studies and analysis.

### Funding statement

The authors received no financial support or funding for the publication of this article.

### Patient consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-chief of this journal on request.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Acknowledgments

None.

## Appendices.

**Table A**  
Laboratory results

Measure	6/12/20	3/29/21	5/29/21	Normal Range
TSH uIU/mL	1.370	<0.005	0.008	0.282–4.000
Free T4 ng/dL	1.35	5.41	1.37	0.84–1.62
Total T3 ng/dL	123	397	137	69–154
TSI %		200		<125
Anti-TPO [IU]/mL		119		<35
Anti-TG [IU]/mL		53		<40
Thyroglobulin ng/mL		3.4		<55

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