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Case Report

Thyroid storm with acute heart failure and cardiogenic shock in a relapse of pre-existing Graves' disease after the first administration of Medigen COVID-19 protein subunit vaccine

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Abstract:
Most people in the world including Taiwan received different coronavirus disease-2019 (COVID-19) vaccines for herd immunity to control the COVID-19 pandemic. Many published studies have reported vaccine-associated adverse events including thyroid disorders. Herein, we reported a relapse case of pre-existing Graves' disease that rapidly progressed to thyroid storm, acute heart failure, and cardiogenic shock after the first dose of Medigen COVID-19 vaccine. Thyroid storm is a rare life-threatening thyrotoxicosis and requires multidisciplinary approach and management. The exacerbation of thyroid diseases may be considered a complication of COVID-19 vaccination.

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Keywords: COVID-19 Medigen vaccine, Graves' disease, Thyroid storm, Heart failure

1. Case Report

A 40-year-old man has been diagnosed with Graves' disease since 2007 (at the age of 26). He was treated with antithyroid medications for approximately 5 years until 2012 at a local health department. Regular follow-up thyroid function test showed a euthyroid state. During the COVID-19 pandemic, he received the first dose of Medigen COVID-19 protein subunit vaccine (MVC-COV1901) on August 27, 2021. Subsequently, he experienced intermittent palpitation, progressive shortness of breath, abdominal distension, and leg edema. On August 31, 2021 (4 days after vaccination), he visited the gastrointestinal outpatient department (OPD) of our hospital for help. Chest X-ray (CXR) at the OPD showed no cardiomegaly (Fig. 1A). Abdominal sonography showed massive ascites. On presentation, he was very dyspneic and tachycardic and was transferred urgently to the emergency department. Emergency triage showed blood pressure (BP) of 126/100 mmHg, heart rate of 193 beats per minute (bpm), alert consciousness, and dyspnea, and he looked acutely ill. Electrocardiography (ECG) showed atrial fibrillation with a rapid ventricular response (Fig. 2A). Unfortunately, the patient had severe shortness of breath, unstable hemodynamics, and cardiogenic shock (BP, 47/34 mmHg; heart rate, 77 bpm) after receiving adenosine intravenously followed by 20 mg of propranolol orally. Cardiopulmonary resuscitation, endotracheal intubation, and vasopressor administration were initiated. The follow-up CXR showed cardiomegaly with acute pulmonary edema after 4 h of the initial one (Fig. 1B). A cardiologist was consulted, and a bedside cardiac echo illustrated

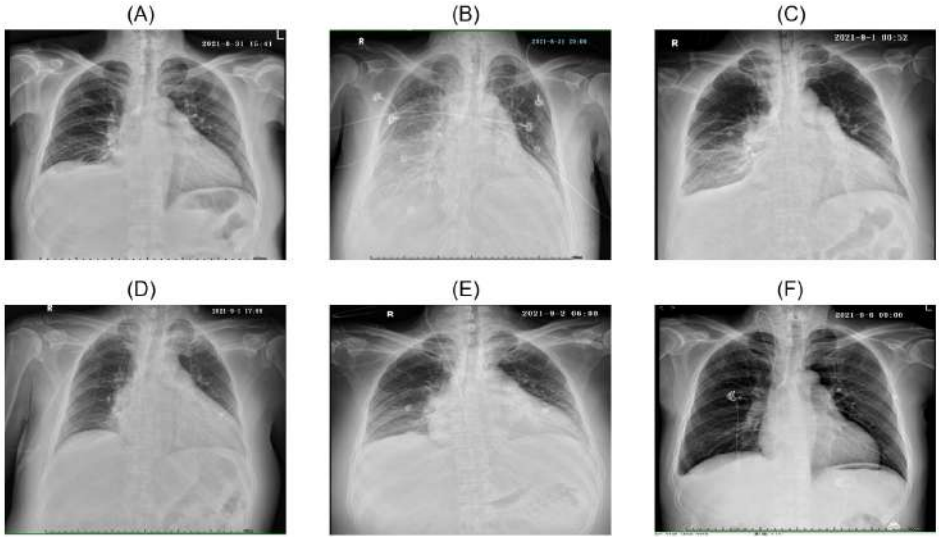

Figure 1. (A) Initial CXR. (B) CXR after 4 hours of initial one (Rapidly progressed to acute pulmonary edema). (C) CXR after 7 hours of initial one (Improving acute pulmonary edema, prominent right sided pleural effusion). (D) CXR after thoracentesis. (E) CXR after 2 days of admission. (F) CXR after 6 days of admission.

dilatation of all heart chambers (internal diameter of the left atrium, 60 mm; internal diameter of the left ventricle, 56 mm; internal diameter of the right atrium, 52 mm; and basal diameter of the right ventricle, 42 mm), and global hypokinesia with severe left ventricular systolic dysfunction (ejection fraction, 25%) (Fig. 3). After the initial treatment, the follow-up EKG showed atrial fibrillation with a moderate ventricular response (Fig. 2B). Laboratory data showed high D-dimer and high bilirubin levels (Table. 1). He was admitted to the cardiac care unit under cardiologist service. He received diuretics, dopamine, norepinephrine, and intensive care. The follow-up CXR performed 6 h after the first one showed improving acute pulmonary edema and more prominent right-sided pleural effusion (Fig. 1C). Therapeutic thoracentesis was performed, in which 880 mL of clear transudative pleural fluid was obtained. Follow-up CXR showed improving pleural effusion (Fig. 1D). The endotracheal tube was successfully removed within 24 h of ER arrival. An endocrinologist was consulted on day 2 of admission. Physical examination after the removal of the endotracheal tube revealed a thin man with alert consciousness, orientation, smooth respiration, and marked proptosis; body height, 175 cm; body weight, 70 kg; heart rate, 100–146 bpm; BP, 110–123/65–86 mmHg; and body temperature, 36°C. On neck examination, he had a grade 3 diffuse goiter with thrill and bruit. Both hands were moist and warm with mild tremors. Chest examination revealed coarse breath sounds with irregular heartbeat and systolic murmur. His abdomen was distended. Both legs had pitting edema. The total calculated Wartofsky score was 80 [gastrointestinal (20), cardiovascular (heart rate 25 + atrial fibrillation 10), heart failure (pulmonary edema 15), precipitating factor +10]. The impression was thyroid storm. He received a high dose of propylthiouracil, parenteral administration of steroids, and intensive care. He was transferred to the ordinary ward on day 3 of admission. Thyroid sonography showed heterogenous background with enlarged lobes, which was compatible with autoimmune thyroid disease (Fig. 4). Serial follow-up laboratory data, thyroid function (Table 2), and CXR findings improved rapidly (Fig. 1D–F). His clinical condition (Fig. 5) got better under a multidisciplinary approach (cardiologist, endocrinologist, and chest physician) and intensive care management. He was discharged on day 10 of admission. His thyroid function improved significantly at OPD follow-up. We notified this case to Taiwan Communication Disease Control Center as Medigen COVID-19 vaccination-induced severe life-threatening thyroid storm that rapidly progressed to acute heart failure and cardiogenic shock.

Table 1. Laboratory data at admission.

Variable	Result	Reference Range	Variable	Result	Reference Range
WBC, 10^3/uL	6.9	4.0 - 10.0	Calcium, mg/dL	8.0	8.6-10.0
Neutrophil, %	61.7	40.0 - 75.0	Sodium, mmol/L	134	136-145
Hemoglobin, g/dL	13.5	12.3 - 18.3	Potassium, mmol/L	3.9	3.5-5.1
Platelet, 10^3/uL	161	130-400	Magnesium, mg/dL	1.77	1.60-2.60
ALT, U/L	40	10-50	Creatinine mg/dL	0.47	0.70-1.20
BUN, mg/dL	18.9	6.0-20.0	eGFR, ml/min/1.73m^2	210	>60
AST, U/L	367	10-50	CK-MB, ng/mL	1.1	<3.6
Total bilirubin, mg/dL	2.14	<1.4	NT-pro BNP, pg/mL	2497	<125
Direct bilirubin, mg/dL	2.00	<0.4	Troponin I, pg/mL	281.9	<60.4
CRP, mg/dL	0.22	<0.5	Albumin, g/dL	3.2	3.5-5.2
D-Dimer, mg/L FEU	4.19	<0.55	CPK, U/L	253	39-308

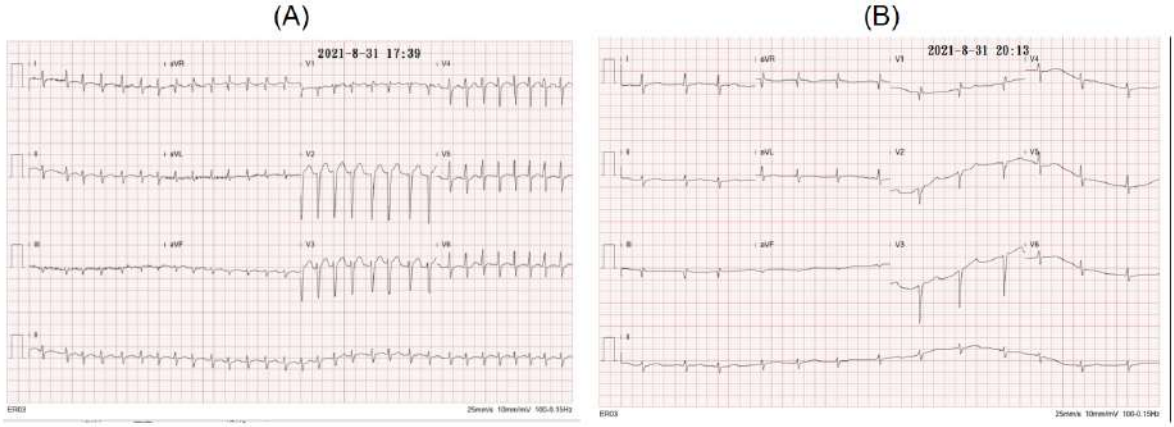

Figure 2. (A) Initial EKG. (B) EKG after CPCR.

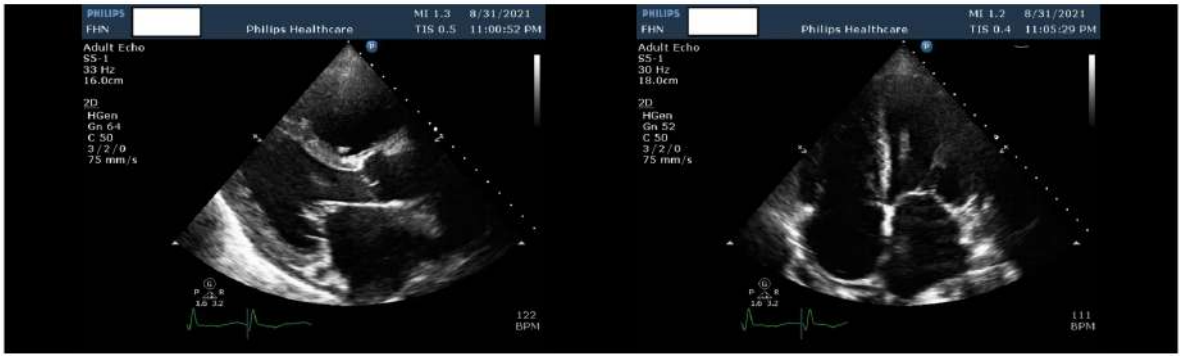

Figure 3. Echocardiography illustrated dilatation of all heart chambers, and global hypokinesia with severe left ventricular systolic dysfunction (ejection fraction 25%).

2. Discussion

COVID-19, which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first emerged in Wuhan, Hubei Province, China, in November 2019, and then rapidly and widely spread to many countries [1,2]. The World Health Organization declared the COVID-19 pandemic on March 11, 2020 [1,2]. Vaccination-induced herd immunity has an important role in pandemic control [3]. Several types of vaccines producing immunity via different mechanisms, such as mRNA, adenovirus vector, and inactivated virus, have been provided in different countries [2–5]. The MVC COVID-19 vaccine designated as MVC-COV1901 and known as the Medigen COVID-19 vaccine is a protein subunit COVID-19 vaccine developed by Medigen Vaccine Biologics Corporation in Taiwan,

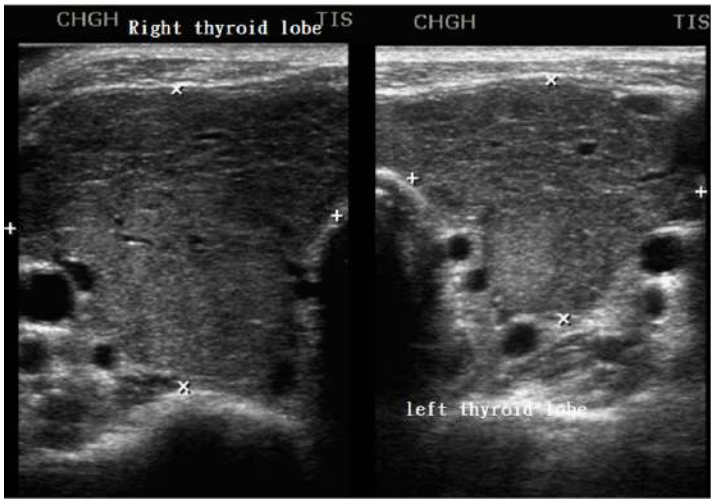

Figure 4. Thyroid sonography showing heterogenous background with enlarged size.

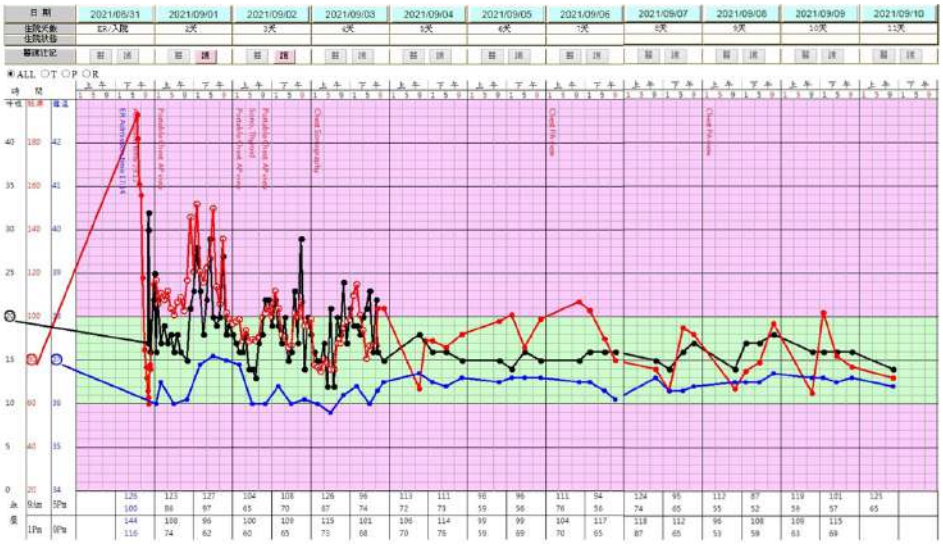

Figure 5. Clinical condition and vital signs while admission.

Table 2. Serial thyroid function during hospitalization

	2021/8/31	2021/9/2	2021/9/6	2021/9/8	2021/9/15	Reference Range
TSH, uIU/mL	<0.005					0.27 - 4.20
Free T4 ng/dL	>7.77	3.90	1.42	1.41	1.50	0.93 - 1.7
T3, ng/mL	1.93	1.08				0.8-2.00
T4, ug/dL	15.20	11.40				5.10-14.10
TSH receptor Ab, IU/L		>40				≤1.75
Anti-Thyroid Peroxidase Ab, IU/mL		>600				≤34
Anti-Thyroglobulin Ab, IU/mL		794.0				≤115

Dynavax Technologies in the USA, and the US National Institutes of Health. On July 19, 2021, the MVC COVID-19 vaccine obtained Emergency Use Authorization (EUA) approval from the Taiwanese government after fulfilling the EUA requirements set by the Taiwanese authority [6]. Most of the Taiwanese have received Medigen vaccines since August 23, 2021 [6]. Our patient received this

Medigen vaccine on August 27, 2021. In the literature, only a few cases of Graves' disease after mRNA SARS-CoV-2 vaccination were reported [2–4]. To our knowledge, this is the first case of protein subunit COVID-19 vaccine-induced relapse of pre-existing Graves' disease that rapidly progressed to thyroid storm, acute congestive heart failure, and cardiogenic shock. Future studies are needed to determine COVID-19 vaccine-related endocrine disorders and thyroid diseases.

Conflicts of Interest:
The authors declare no conflict of interest.

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