

Hypertensive crisis following mRNA COVID-19 vaccination in adolescents: two case reports

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In response to the global coronavirus disease 2019 (COVID-19) pandemic, vaccines were developed and approved quickly. However, numerous cardiovascular adverse events have been reported. We present two adolescent cases who developed a hypertensive crisis following NT162b2 mRNA COVID-19 vaccination. Patient 1 was an 18-year-old male and his systolic blood pressure was 230 mmHg one day after the second vaccine. He was obese. No secondary cause of hypertension other than the vaccine was identified. Patient 2 was an 18-year-old male who complained with palpitation after the first vaccine. His blood pressure was 178/109 mmHg. He had autosomal dominant polycystic kidney disease. Both were treated with continuous infusion of labetalol followed by losartan, and blood pressure was controlled. Patient 2 received second vaccination and his blood pressure did not rise. It is warranted to measure blood pressure in adolescents at high risk of hypertension after NT162b2 mRNA COVID-19 vaccination.

Keywords: Adolescent; Blood pressure; COVID-19 vaccines; Hypertension; Messenger RNA

Introduction

Coronavirus disease 2019 (COVID-19) is a major public health issue worldwide. Vaccines are considered the best strategy to prevent the spread of the virus and reduce its severity. More than 80% of people were vaccinated in Korea. Vaccination was also approved for adolescents and children. However, the record speed of the development and approval of these vaccines, as well as high vaccination rates have raised concerns regarding their safety. We present two adolescent cases that developed a hypertensive crisis following NT162b2 (Pfizer-BioNTech) mRNA COVID-19 vaccination.

Cases report

Case 1

Patient 1 was an 18-year-old male who complained of fever discovered a day after the second NT162b2 mRNA COVID-19 vaccine. His systolic blood pressure measured at a local hospital was 230 mmHg. Four days later, the patient visited our hospital with persistent hypertension. His initial blood pressure was 190/125 mmHg, but he was asymptomatic. He denied the relevant past medical history. He remembered that his systolic blood pressure was 130 mmHg a year prior. He did not complain of any symptoms after the first vaccine. His father had hypertension. His height and weight were 185 cm and 100 kg, respectively (body mass index, 29.2 kg/m²). Renal and thyroid function test results were all within the normal ranges. Plasma

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renin activity and aldosterone levels were 0.18 ng/mL/hr (reference range, 0.17–5.38 ng/mL/hr) and 6.4 ng/dL (reference range, 2.5–39.2 ng/dL), respectively. The aspartate aminotransferase and alanine aminotransferase levels were 48 IU/L and 80 IU/L, respectively. The creatine kinase-MB, troponin I, brain natriuretic peptide levels were all within the normal ranges. Urinalysis and urinary metanephrines results were normal. Doppler ultrasonography revealed no evidence of renal artery stenosis but showed diffusely increased hepatic parenchymal echogenicity, consistent with nonalcoholic steatohepatitis. His blood pressure subsequently normalized after initiation of labetalol continuous infusion therapy at a rate of 0.5 mg/min and then switched to 100 mg daily oral losartan. Echocardiography revealed no left ventricular hypertrophy but showed mild diastolic abnormality due to obesity. Fundus examination results were normal. After 5 months, his blood pressure was maintained at 135/81 mmHg with 100 mg of daily losartan.

Case 2

Patient 2 was an 18-year-old male who complained of palpitation and dyspnea 3 hours after the first NT162b2 mRNA COVID-19 vaccine. His vital signs included a blood pressure of 178/109 mmHg, a heart rate of 75 beats/min, and a respiratory rate of 20 breaths/min. His mother and grandmother had autosomal dominant polycystic kidney disease (ADPKD). At the age of 4 years, he had a splenic rupture in a car accident and bilaterally enlarged kidneys were confirmed. However, he was not followed up. He remembered that his systolic blood pressure was 140 mmHg at a routine school checkup 3 years ago. His height and weight were 185 cm and 78 kg, respectively. Blood and urine tests, including evaluation of hormone levels, were all normal. Plasma renin activity and aldosterone levels were 0.19 ng/mL/hr and 10.3 ng/dL, respectively. Kidney ultrasonography revealed enlarged kidneys with numerous variable-sized cysts, which were compatible with ADPKD. Echocardiography revealed a small amount of pericardial effusion, consistent with mild acute pericarditis, which improved a week later. No left ventricular hypertrophy was observed. A labetalol continuous infusion at a rate of 0.5 mg/min was started and the blood pressure decreased. The patient was switched to losartan therapy. Fundoscopy and brain magnetic resonance imaging revealed no abnormalities. Four months later, the patient received a second NT162b2 mRNA vaccination without a hypertensive episode. His blood pressure was 137/85 mmHg with 100 mg of losartan daily in the outpatient clinic after 5 months.

Discussion

A hypertensive crisis is an acute episode of severe elevation in blood pressure with the potential for end-organ damage [1]. It is a clinical diagnosis and there are no specific cutoffs in pediatric patients [1]. Hypertensive crisis in pediatric patients is mainly due to secondary causes and medications are one of them [1]. Meylan et al. [2] reported nine adult cases of hypertensive crisis following mRNA COVID-19 vaccination. Eight patients received NT162b2 vaccine and one did mRNA-1273 (Moderna) vaccine [2]. Eight patients had a medical history of hypertension [2]. A hypertensive crisis was documented within minutes of vaccination [2]. It was even reported that an elderly female without a past history of hypertension passed away of intracranial hemorrhage due to hypertensive crisis (blood pressure 210/110 mmHg) after mRNA-1273 COVID-19 vaccination [3]. According to VigiBase, the global database of individual case safety reports, there were more cardiovascular adverse events following immunization with mRNA COVID-19 than other vaccines [4]. Compared to influenza vaccination, mRNA COVID-19 vaccines showed a higher risk for hypertensive crisis (adjusted reporting odds ratio, 12.7; 95% confidence interval, 2.47–65.5) [4].

We hypothesized that NT162b2 mRNA COVID-19 vaccination provoked a hypertensive crisis in our cases. Patient 1 had obesity and patient 2 had ADPKD as a risk factor for high blood pressure. However, considering the usual blood pressure they remembered, there was a factor that raised blood pressure rapidly. We examined in detail the causes. They were vaccinated just before their blood pressure was measured high and no other suspects were found. There was also no end-organ damage suggesting chronic exposure to high blood pressure. The most reliable mechanism by which mRNA COVID-19 vaccination raises blood pressure is the interaction between the spike protein and angiotensin-converting enzyme 2 (ACE2). A spike protein is a glycoprotein on the surface of the COVID-19 virion. It enables entry of the virion into cells through binding to ACE2 [5]. The NT162b2 vaccine consists of mRNAs that encode a spike protein to utilize the spike protein as its antigen [5]. The NT162b2 vaccine increases the endogenous synthesis of the spike protein. A spike protein binds to ACE2 to enter the cell and downregulates ACE2-involving pathways concomitantly [6]. The functions of ACE2 are the synthesis of inactive angiotensin-(1–9) from angiotensin I and the catabolism of angiotensin II to produce angiotensin-(1–7) which reduces vasoconstriction, and water retention [7]. Eventually, downregulation of ACE2

Table 1. Patients characteristics

Characteristic	Patient 1	Patient 2
Age (yr)	18	18
Sex	Male	Male
Blood pressure at diagnosis (mmHg)	Systolic blood pressure 230	178/109
Time of diagnosis	1 day after vaccination	3 hr after vaccination
Vaccine	NT162b2	NT162b2
Dose	Second	First
Risk factors for hypertension	Obesity, family history of hypertension (father)	Autosomal dominant polycystic kidney disease

contributes to an increase in the vasoconstrictor angiotensin II and a decrease in the vasodilator angiotensin-(1–7). Angiotensin II negatively regulates renin release. Hypertension in ADPKD or obesity is associated with high plasma renin activity [8,9], whereas both our patients had low normal plasma renin activity levels. Meanwhile, the rapid elevation of blood pressure after vaccination is not explained by this hypothesis. Some cases of hypertensive crisis following mRNA vaccines occurred within minutes of the vaccination [2], which is too short for cellular uptake and translation of mRNA to a spike protein [10].

There are some limitations to our hypothesis. We did not measure the blood pressure before vaccination and did not measure the plasma levels of angiotensin II. If the level of angiotensin II is measured in patients with elevated blood pressure after vaccination, our hypothesis can be verified.

We describe two adolescent cases that had a risk factor for high blood pressure, obesity and ADPKD, and then suffered from a hypertension crisis after NT162b2 (Pfizer-BioNTech) mRNA COVID-19 vaccination (Table 1). Monitoring blood pressure in adolescents at high risk of hypertension after mRNA COVID-19 vaccination is warranted.

Ethical statements

This study was approved by the Institutional Review Board of Hallym University Sacred Heart Hospital (IRB No. 2022-01-025). We were given exemption from getting informed consent by the institutional review board because the study was a retrospective study and personal identifiers were completely removed.

Conflicts of interest

Myung Hyun Cho and Hae Il Cheong are editorial board members of the journal but were not involved in the peer reviewer selection, evaluation, or decision process of this article. No

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