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Possible Association between Prenatal COVID-19 mRNA Vaccine Exposure and Dilated Cardiomyopathy: A Case Report

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Abstract: ***Pediatric Dilated Cardiomyopathy (DCM) is a cardiac condition characterized by systolic dysfunction, accompanied by bi-ventricular and atrial dilatation and reduced myocardial contractility (Ashworth, 2019). Pediatric DCM may develop as a primary congenital condition or result from another underlying condition that stresses the heart. Common etiologies include inborn errors of metabolism, syndromic causes, myocarditis, and familial cardiomyopathy. Inflammation, toxicities, or inherited pathogenic variants may also play a central role in the development of DCM. However, most pediatric DCM cases (66%-69%) remain idiopathic (Malinow, 2024). These idiopathic cases are largely believed to stem from underlying genetic abnormalities. After mass vaccination with messenger RNA (mRNA) vaccines against coronavirus disease 2019 (COVID-19), myocarditis in male teenagers emerged as a possible rare side effect (Caforio, 2021). The possible relationship between Covid-19 mRNA vaccination during pregnancy and dilated cardiomyopathy was discussed in the case of a 2-year-old boy who was diagnosed with dilated cardiomyopathy 2 years after birth, whose mother received the Covid-19 mRNA vaccine twice in the last trimester of pregnancy. Our knowledge on this subject will become clearer with further examination of the reported cases. This case report is published to contribute to this subject.***

Keywords: mRNA COVID-19 vaccine, dilated cardiomyopathy, pregnant vaccination

1. Introduction

Vaccination plays a crucial role in protecting against COVID-19 infection. However, pregnant and lactating women are excluded from clinical trials of vaccines due to the unknown effects of the vaccine on the expectant mother, fetus, and infant. Pregnancy and the following lactation periods are long processes with unique physiological, psychological, and pathological characteristics, in which many practices are discussed for the mother and the baby. Based on the limited data available on the mechanisms of action of vaccine types, COVID-19 vaccines are unlikely to pose any risk to pregnant women and nursing mothers (Bicer, 2023). The first study in pregnant women began in February 2021 as a clinical trial in the US (NCT04754594). This is a Phase II/III, randomized, placebo-controlled, observer-blinded study in 700 healthy pregnant women who received vaccinations at 4 weeks. The study assessed the safety, tolerability, and immunogenicity of two doses of the Pfizer/Biotech vaccine administered 21 days apart versus a placebo. According to the CDC, from January 2020 to July 2021, approximately 102 thousand pregnant women with COVID-19 were in the United States.448 (0.44%) patients were admitted to an ICU, and 114 (0.11%) patients died. A CDC study found that vaccinated pregnant women have a substantially lower risk of SARS-CoV-2 infection compared to those who are not vaccinated, and Pfizer's vaccines were determined to be safe (https: //www.health. nd. gov/sites/www/files/documents/COVID-19).

Two cases of fetal supraventricular tachycardia following the administration of the Pfizer-BioNTech COVID-19 vaccine during pregnancy were reported in 2022 (Abdallah, 2022). They concluded that continued safety monitoring and further longitudinal follow-up are necessary to assess the fetal impact after maternal COVID-19 vaccination.

The health authorities should, therefore, recommend offering COVID-19 vaccines to pregnant and breastfeeding women, as the potential benefits of maternal vaccination outweigh the risks (Muyldermans, 2022).

2. Case Presentation and Laboratory Results

G. A. Ş., a baby boy was born on July 19, 2022, from a 27-year-old mother as the first baby after a healthy 38-week pregnancy. There is no consanguinity between the parents. There was no cardiac disease in their family. The mother has hypothyroidism, and the grandfather has hypothyroidism. His mother received two doses of the BNT162b2 mRNA vaccine (Pfizer–BioNTech) in the third trimester of her pregnancy.

He grew up generally without complaints until the end of February 2025, experiencing normal physical and psychosocial development. At the end of February 2025, he was admitted to intensive care with a diagnosis of aspiration pneumonia in the hospital, where he was due to milk aspiration. While he was being treated for aspiration pneumonia at the Ministry of Health City Hospital, advanced tests were performed because his heart failure was getting worse. He was monitored at the university hospital with low-dose aspirin and angiotensin inhibitors. In the examinations, dilated cardiomyopathy was diagnosed, and an angiotensin inhibitor, furosemide as a diuretic, and salicylate were started for abnormal coagulation prevention.

The patient was referred to AnkaPedia due to anemia detected during follow-up at a private hospital in Ankara and at Gazi

University Hospital, where the condition could not be diagnosed.

During the physical examination of the patient in AnkaPedia, it was found that her body weight was 18 kg (97th percentile) and her height was 103 cm (also at the 97th percentile).

An echocardiogram reveals the phenotype characteristic of left ventricular (LV) dilatation, accompanied by systolic dysfunction. Dilatation refers explicitly to the left ventricular end-diastolic diameter (LVEDD), whereas systolic dysfunction concerns the ejection fraction (EF) or fractional shortening.

Metabolic tests for mitochondriopathy were negative, while Coxsackie A and B IgM were positive, and IgG was negative. Cardiac MR shows dilated cardiomyopathy. Troponin was normal. The electrocardiogram did not show any fatal or pathologic arrhythmias.

Extensive genetic testing excluded known familial cardiomyopathy variants.

Hb: 9.4 g/dL; the ferritin level (20 ng/mL) was lower than the normal range. Lactoferrin was started. The patient, who was admitted to the Hacettepe University Children's Hospital Intensive Care Unit due to severe heart failure, became stable after 4 days and was transferred to the regular ward. The patient was monitored in the intensive care unit twice with a clinical Picture of cytokine release syndrome.

He is currently being monitored for a heart transplant.

Possible Mechanisms

The spike mRNA sequence is encapsulated in lipid nanoparticles (LNPs) for delivery in mRNA vaccines. The LNPs can elicit a variety of cytokines and chemokines, which can trigger a proinflammatory response that impacts the myocardium.

As autoimmune responses can drive myocarditis, molecular mimicry between spike protein and antigens associated with myocarditis in terms of protein sequence and structure could lead to myopericarditis by triggering cross-reactivity and genetic factors, such as specific HLA genes, may contribute to the risk of developing myocarditis upon mRNA vaccination as seen with viral infection associated myocarditis may also possible pathogenetic explanations (Buoninfante, 2024).

Some possibilities can be considered in our patient's development of dilated cardiomyopathy.

1) Our patient is at the 97th percentile of the developmental curve and does not exhibit any prominent clinical findings that suggest congenital myocardial disease.
2) It may have developed after a severe infection. However, only IgG antibodies to Cosacxkie eliminate the possibility of an acute infection. This condition may have developed as a result of a long and slowly progressive myocarditis and may have been aggravated by aspiration pneumonia.
3) There is also a strong possibility that myocardiopathy developed after birth with a slow clinical course and then decompensated with aspiration pneumonia due to mRNA vaccination.
4) The septic picture and cytokine storm picture that developed due to influenza A, which he had experienced twice, may be due to an underlying but undetectable immune deficiency, or it may have caused both myocardiopathy and cytokine release as a direct result of influenza itself.

3. Discussion

Cardiomyopathy is categorized into primary and secondary types, resulting in distinct phenotypes, including dilated, hypertrophic, and restrictive patterns. Dilated cardiomyopathy (DCM) is a mixed bag of heart diseases with the unique features of cardiac dilatation and subnormal to poor myocardial contractility. Dilated cardiomyopathy in the pediatric age group is generally characterized by unobstructed, dilated, and contracting left ventricular chamber defects and is associated with heart failure. Other causes include genetic juvenile-onset cardiomyopathy, drug-induced cardiomyopathy, stress-induced cardiomyopathy, hemochromatosis, endocrine disorders (such as thyroid disease and pheochromocytoma), autoimmune diseases, and nutritional deficiencies (including selenium and thiamine). It is characterized by thinning of the left ventricle, a dilated left ventricle or biventricular dilatation, left ventricular systolic dysfunction, left ventricular diastolic dysfunction, global hypokinesia, and cardiomegaly, all of which are visible on a chest X-ray. Decreased cardiac output leads to fatigue, cachexia, narrow pulse pressure, a dicrotic pulse or hypokinetic pulse, dyspnea, cool extremities, decreased blood supply to the brain (resulting in cognitive dysfunction), and reduced blood supply to the kidneys (leading to renal failure). Left ventricular diastolic dysfunction can lead to symptoms such as dyspnea, orthopnea, and paroxysmal nocturnal dyspnea. Cardiomyopathy can also occur with or without left ventricular dysfunction, as in left ventricular non-compaction cardiomyopathy (LVNC), a rare heart disease caused by two likely pathogenic nonsense mutations: DSG2-p. S363X and TBX20-p. D278X.

The study of familial forms of LVNC is helpful for risk prediction and genetic counseling of relatives. Right ventricular chamber failure can be identified on the electrocardiogram as sinus tachycardia and non-specific ST/T changes. The complications include arrhythmia (atrial fibrillation) and thromboembolism (left ventricular mural thrombosis). It is of utmost importance in the field of heart transplantation as the definitive treatment of the disease. Heart transplantation is now an acceptable treatment option for patients with dilated cardiomyopathy. This brief review highlights various methods for detecting and diagnosing dilated cardiomyopathy, as well as the available treatment modalities (Mallavarapu, 2022).

The course of COVID-19 vaccine-associated myocarditis in pediatric patients appears to be mild and differs from that of non-vaccine-associated myocarditis. Due to the presence of numerous residual symptoms and diagnostic abnormalities at follow-up, further studies are necessary to elucidate the long-term implications (Raulfs, 2024).

Of 15 children who were hospitalized with myocarditis after receipt of the BNT162b2 messenger RNA COVID-19 vaccine for 1 to 5 days, boys were most often affected after the second vaccine dose. Three patients had ventricular systolic dysfunction, and 12 patients had late gadolinium enhancement on cardiac magnetic resonance imaging. There was no mortality, and all but one patient had typical echocardiogram results on follow-up 1 to 13 days after discharge (Dionne, 2021).

Most cases of suspected COVID-19 vaccine myocarditis in individuals under 21 years old have a mild clinical course with rapid symptom resolution (Truong, 2021).

It has been noted that pharmacovigilance surveillance and observational studies have shown an increased risk of myocarditis in predominantly younger males following the administration of the two COVID-19 mRNA vaccines, as well as after vaccination with the adjuvanted protein-based vaccine Nuvaxovid and the adenovirus vector-based vaccine JCVI-Covid-19.

However, some studies have not found any complications in the vaccine administered to pregnant women. In a population-based cohort study in Ontario, Canada, COVID-19 vaccination during pregnancy, compared with vaccination after pregnancy and with no vaccination, was not significantly associated with increased risk of adverse peripartum outcomes. Study interpretation should consider that the vaccinations received during pregnancy were primarily mRNA vaccines administered in the second and third trimesters (Rolfs, 2022; Kalafat, 2022).

This case of a 2-year-old boy developing dilated cardiomyopathy following prenatal exposure to the BNT162b2 mRNA vaccine highlights a potential, albeit unproven, association warranting further scrutiny. While alternative triggers, such as infection or immune responses, cannot be ruled out, the temporal link to maternal vaccination raises questions about the long-term effects on the fetus. Establishing registries to track such cases could clarify whether this is an isolated incident or part of a broader pattern, informing future vaccination guidelines for pregnant women.

As a final comment, dilated cardiomyopathy (DCM) in children is often idiopathic, with potential triggers including genetic factors, infections, or toxicities. This case report examines a 2-year-old boy diagnosed with DCM, born to a mother who received two doses of the BNT162b2 mRNA COVID-19 vaccine during her third trimester. Following normal development until age 2, the child presented with heart failure after aspiration pneumonia, leading to a DCM diagnosis. While myocarditis has been noted as a rare side effect of mRNA vaccines in adolescents, this case raises questions about prenatal exposure and long-term cardiac outcomes. Further investigation and monitoring of such cases are essential to clarify this potential association.

In light of this extensive literature, it would be prudent to closely monitor the babies of women who received an mRNA COVID-19 vaccine during pregnancy, establish a registry system, and track them for potential long-term complications.

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