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Case study of hypertriglyceridemia from COVID-19 Pfizer-BioNTech vaccination in a patient with familial hypercholesteremia

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Abstract. – The Pfizer-BioNTech coronavirus disease 2019 (COVID-19) vaccine is the first novel nucleoside-modified messenger ribonucleic acid (modRNA) vaccine to receive Emergency Use Authorization from the Food and Drug Administration in the United States. It is indicated to be used in patients ≥12 years-of-age as of May 25th, 2021, including populations with high atherosclerotic cardiovascular disease (ASCVD) burden. However, little is known about the potential impact this vaccine may have on serum lipoprotein levels in patients with familial hypercholesteremia (FH), who are predisposed to high ASCVD burden due to elevated low-density lipoprotein cholesterol (LDL-C). We present an interesting case where a patient with heterozygous FH (HeFH) and elevated triglycerides (TG)-controlled for years on medication and apheresis-experienced significantly elevated TG, one day after receiving his second Pfizer-BioNTech COVID-19 vaccine dose. It is not known whether this adverse event may be seen in other FH patients and may be worth assessing in such patients to determine the possibility of a rare adverse reaction from a COVID-19 vaccine.

Key Words:
COVID-19, Dyslipidemia, LDL apheresis, Triglycerides, Vaccine.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic is caused by multiple genetic variants of coronavirus-2 (SARS-CoV-2), which is a positive-sense single-stranded ribonucleic acid (RNA) virus[1]. The United States has been disproportionately affected by this virus, as over 33 million of the over 165 million global cases and almost 600,000 of the almost 3.5 million deaths as of May 2021, are in the United States alone[2]. An accelerated vaccine development process resulted in 3 commercially available novel vaccines in record time, with the Pfizer-BioNTech COVID-19 vaccine being the first to receive Emergency Use Authorization on December 11, 2020, from the United States Food and Drug Administration[3,4]. Since then, over 285 million vaccines have been administered to Americans, with almost 130 million and 40% of Americans fully vaccinated as of May 25th, 2021[5].

Some of the widely known side effects of the novel Pfizer-BioNTech vaccine in the general population include pain, swelling, and erythema at the injection site. Other common side effects include fatigue, headaches, fevers, chills, joint pain, nausea, and vomiting[3]. However, little data have been reported regarding the potential impact on cardiometabolic health in patients at high atherosclerotic cardiovascular disease (ASCVD) event risk. One such high-risk group includes patients with familial hypercholesterolemia (FH), which is an autosomal codominant genetic disorder associated with very high levels of low-density lipoprotein cholesterol (LDL-C) due to defective hepatic uptake via LDL receptors, which leads to premature ASCVD[6-8]. Little data are available about the potential impacts that the novel Pfizer-BioNTech vaccine has on serum lipoprotein levels in patients with FH. We present an adult man with heterozygous FH (HeFH) with a history of elevated TG controlled with medication and LDL apheresis who experienced very high levels of TG one day after receiving his second COVID-19 vaccination.

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Case Presentation

This is a 60-year-old man seen in our preventive cardiology clinic for weekly LDL apheresis treatments for HeFH, which was diagnosed with a Dutch Lipid Clinic Network score of 11. He has a history of hypertension, hypothyroidism, ischemic cardiomyopathy, heart failure with reduced ejection fraction, 5 myocardial infarctions (MI), status post coronary artery bypass graft and 20 coronary artery stents. He has been compliant with his weekly apheresis treatments and medications, which include rosuvastatin 40 milligrams daily (mg/d), ezetimibe 10 mg/d, fenofibrate 145 mg/d, icosapent ethyl (IPE) 2 grams twice daily, alirocumab 150 mg biweekly, prasugrel 10 mg/d, metoprolol 200 mg/d, amlodipine 10 mg/d, Isosorbide dinitrate was taken 20 mg three times/d, ranolazine 1000 mg twice/d, and Levothyroxine was taken at 350 micrograms/d. Just prior to each apheresis treatment, he has been receiving hydrocortisone 50 mg intravenously (equivalent to ~12.5 mg of oral prednisone) due to prior intolerance since when starting these treatments. The patient has maintained a Mediterranean style diet and regularly exercises. Family history includes his father, paternal aunt, and paternal grandfather who all had MIs at or before the age of 50. His most recent body mass index was 27.1 kg/m^2, and physical exam was nonrevealing. No tendon xanthomata nor arcus cornealis were recently appreciated.

The patient received his first Pfizer-BioNTech vaccine shot on 3/10/21 and the second dose on 3/31/2021. His lipid panel on 4/1/2021 revealed in mg/dL: TG of 1308; TC of 285; direct LDL-C of 102; HDL-C of 35 (Table I). He received LDL apheresis but was unable to complete his session, as the apparatus had poor flow due to his very elevated triglycerides, which was verified by a Kaneka Medical America LLC representative. He received apheresis 7 days later without any complications with his pre-treatment lipid panel revealing (in mg/dL): TG of 196; TC of 188; LDL-C of 106; HDL-C of 43. He denied eating anything out of the ordinary, including fatty foods prior to his failed session or missing any of his regular medication. Prior to this episode, his average triglyceride levels, which were checked about every 3 months for the past 8 years, were 277 mg/dL and 114 mg/dL immediately pre- and post-apheresis, respectively (Table I). Of note, the patient did have very elevated TG of 1,093 mg/dL on 4/30/2020, which returned to baseline in the 200s mg/dL after starting on IPE 2 g twice daily within 1-2 weeks. This was attributed to eating uncommon food provided by friends containing beef and other sources of saturated fat.

Discussion

This case demonstrates a patient with HeFH and elevated TG quite well-controlled on medication and LDL apheresis who had very elevated serum TG >1300 mg/dL a day after receiving his second Pfizer-BioNTech vaccine shot. Seven days later at his next apheresis session, serum TG levels normalized from 196 mg/dl pre-apheresis to 88 mg/dL post-apheresis on April 8th, 2021. This also demonstrates the importance of FH screening. We were able to expeditiously identify derangements in the patient's serum TG levels potentially from the novel Pfizer-BioNTech COVID-19 vaccine and treated him 1 week later with LDL apheresis.

It is speculated that patients with FH should be regarded as a high-risk group, and in turn, should be prioritized for COVID-19 vaccination[6,9]. The Pfizer-BioNTech vaccine is indicated for patients who are ≥12 years-of-age as of May 10th 2021[10]. However, it is contraindicated in patients with a

Table I. Serum lipid levels prior to and after LDL apheresis.

Date	Average values for the past 8 years: Pre-apheresis†	Average values for the past 8 years: Post-apheresis†	4/1/21	4/8/21
Triglycerides (mg/dL)	277	114	1308	196
Total Cholesterol (mg/dL)	184	77	285	188
Low Density Lipoprotein (mg/dL)	90	16	102‡	106
High Density Lipoprotein (mg/dL)	53	51	35	43

†Pre-apheresis and Post-apheresis labs were obtained the same day of apheresis. ‡LDL-C that was directly measured, as TG was greater than 400 mg/dL

history of severe allergic reactions to the vaccine ingredients or had severe allergic reactions to a prior Pfizer-BioNTech vaccine dose[3,10]. To the best of our knowledge, no guidelines from societies explicitly recommend or discourage COVID-19 vaccination in patients with FH or those with hypertriglyceridemia.

The novel Pfizer-BioNTech COVID-19 vaccine uses the nucleoside-modified messenger RNA (modRNA) to generate an immune response to the SARS-CoV-2 spike protein. A solution of lipids is used to facilitate the delivery of modRNA in order to fuse with the cell membrane, which includes cholesterol, 2 [(polyethylene glycol)-2000]-N,N-di-(tetradecyl)acetamide, 1,2-Distearoyl-sn-glycero-3-phosphocholine, and (4-hydroxybutyl)azanediyl) bis(hexane-6,1-diyl)bis(2-hexyldecanoate)[10]. However, we are not aware of any evidence that these lipids elevate triglycerides.

Patients with COVID-19 infections typically have lower TC, LDL-C, and HDL-C than their baseline. In those who survive COVID-19 infections, these levels typically return to baseline 9 days after infection. In patients who die from COVID-19 infections, these levels continue to decline without recovery[1]. However, there is no known association between COVID-19 vaccination and elevated TG, to the best of our knowledge.

This case report raises many interesting questions. More research is needed to investigate the potential impact that Pfizer-BioNTech COVID-19 vaccination and the 2 other COVID-19 vaccines may have on serum lipid levels in the general population and patients with dyslipidemia, and specifically FH. To the best of our knowledge, there are no data investigating the impact of LDL apheresis on the Pfizer-BioNTech COVID-19 vaccine efficacy. LDL apheresis using dextran sulfate cellulose selectively filters atherogenic apoB100-containing molecules, such as LDL-C and very low-density lipoprotein cholesterol[11]. However, more research is needed to investigate if the lipids used in the Pfizer-BioNTech COVID-19 vaccine or other COVID-19 vaccines alter LDL apheresis, trigger high TG, and/or affects COVID-19 vaccine efficacy.

Conclusions

This case highlights the importance of investigating if novel COVID-19 vaccines greatly increase TG, putting patients at risk for pancreatitis and ASCVD events. If so, the mechanism should be investigated. In addition, patients and their families should be screened for FH, so that providers can expeditiously address any rare complications from novel COVID-19 treatments in order to minimize ASCVD risk.

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