General Case Report

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Reactivation of minimal change disease after Pfizer vaccine against COVID-19

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Abstract: This case follows a 54-year-old woman with a medical history of hypertension who experienced reactivation of minimal change disease (MCD) after receiving the Pfizer vaccine against COVID-19. She had her first episode of MCD 15 days after receiving the influenza vaccine in 2018. She remained in remission for over 3 years following treatment with steroids. She experienced foamy urine and leg edema after receiving the first dose of the Pfizer vaccine, but she did not consult medical professionals until she received the second dose. She wanted to be fully vaccinated because she worked in healthcare. Her initial diagnosis of MCD in 2018 was made following a kidney biopsy. The diagnosis of reactivation following COVID-19 vaccine was made with labs and presenting symptoms. At presentation, her urine protein was 9,977 mg/day. She was treated with prednisone 50 mg/day following her relapse with improvement in her urine protein to 85 mg/g within 4 weeks of starting treatment. She is currently undergoing treatment with prednisone with improvement in her presenting symptoms, which included foaming of urine and edema of legs. This case demonstrates the importance of vigilance in patients with a history of MCD when receiving the COVID-19 vaccine, particularly if they have a history of such reactions to other vaccines. Patients should discuss the benefits and risks of receiving the vaccine with their medical professionals and stay cognizant about the possibility of reactivation after receiving the COVID-19 vaccine.

Keywords: COVID; minimal change disease; MCD; vaccine.

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Minimal change disease (MCD) is a common cause of nephrotic syndrome in children and a rare cause in adults. The classic histology noted with MCD is diffuse fusion of epithelial foot processes on electron microscopy. The effacement resolves with resolution of proteinuria. The etiology of MCD is not known, but various theories have been suggested. The most common theory is that systemic T cell dysfunction leads to the production of a glomerular permeability factor. This factor affects the glomerular capillary wall, which can lead to proteinuria and fusion of the foot processes. An observation that supports the previously mentioned theory is the association of relapse in children with glucocorticoid-sensitive MCD with a decrease in regulatory cells. Glucocorticoids and cyclophosphamide have been shown to be effective in the treatment of MCD by mediating the cell responses. There may be a role of B cells in the etiology of MCD given the positive effect of rituximab which works by depleting the CD20 B cells [1]. Antibodies against nephrin were found 18 out of 62 patients with MCD, which further supports an antibody-mediated etiology [2].

Secondary forms of MCD can be caused by allergic reactions, the use of drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs), malignancies such as lymphomas and leukemias, and infections including syphilis, hepatitis C, and tuberculosis [3]. The development of MCD has also been reported after influenza, hepatitis B, pneumococcal, measles, and tetanus–diphtheria–poliomyelitis vaccines [4]. There have been various cases of reactivation of MCD after the administration of the influenza vaccine [5, 6]. The exact pathogenesis of MCD following influenza vaccination is not known; however, it is plausible for immune complexes to form or deposit in the subepithelial space because of the interaction between the influenza vaccine antigen and native antibodies, leading to this pathological process [6]. Given that the phenomenon of reactivation of MCD has been described after various vaccines, it is not surprising that the vaccine against COVID-19 can also lead to reactivation of MCD. A recent literature review showed that most cases of MCD occurred within 10 days after receiving the first dose in those vaccines that require two doses [7]. It was also found that mRNA

vaccines, especially that of Pfizer, tend to cause this disease more frequently than other vaccines [7].

The target of therapy for patients with MCD is to significantly reduce proteinuria and thereby induce remission. This is primarily achieved through the use of immunosuppressive agents, most commonly glucocorticoids. A complete remission is a reduction in proteinuria to <300 mg/day, stable serum creatinine, and serum albumin >3.5 g/dL [8]. In addition to treatment with steroids, symptomatic treatment can also be achieved with osteopathic manipulative treatment (OMT). In the case of MCD, edema can be a debilitating symptom and can be addressed with lymphatic OMT. Some techniques that can be utilized are a pedal pump, a thoracic pump, thoracic inlet release, and an extremity pump [9]. Osteopathic examination typically reveals tenderness at T10–T11. Chapman's reflexes would be present superior and lateral to the umbilicus anteriorly and at T12 and L1 posteriorly. In one case of IgA nephropathy, OMT led to symptomatic improvement and even avoidance of treatment with cyclophosphamide [10].

Case description

This case follows a 54-year-old woman with a medical history of hypertension who had reactivation of MCD after receiving the Pfizer vaccine. The patient provided informed verbal consent for her case to be presented. She was initially diagnosed with MCD in June 2018, approximately 15 days after receiving the influenza vaccine. The initial presenting symptoms included foaming of the urine and severe edema of the legs. The diagnosis was made following a kidney biopsy. After a course of prednisone therapy, she remained in remission for 4 months. However, she relapsed in October 2018 and was deemed to be in remission after being treated with prednisone the second time. She was tapered off the prednisone over the next 3 months, after a 6 months taper was originally planned. However, the patient experienced moon facies and blistering skin as adverse effects of taking steroids, so she requested a shorter taper period. She was diagnosed with chronic kidney disease (CKD stage 2) after the first episode of MCD. She did not receive the influenza vaccine or any other vaccine during the time she was in remission because she was concerned about a relapse. She chose to receive the Pfizer vaccine against COVID-19 because she works in healthcare (Figure 1).

The presenting symptoms after reactivation included lower-extremity edema and foaming of urine. She experienced foaming of urine 1 week after the first dose of the Pfizer vaccine in January 2021. She continued to have foaming of urine, but she chose to receive the second dose of the Pfizer vaccine 3 weeks following the first dose. She did not consult her doctors after she experienced symptoms following the first dose and chose to receive the second dose because she wished to be fully vaccinated. Within a week after receiving the second dose, she experienced worsening edema in her legs. Edemas a result, she was unable to walk, which prompted her to call her nephrologist, who ordered labs immediately (Figure 1). Eleven weeks had elapsed since she received her second dose of the vaccine and prior to her presenting to her nephrologist. Her serum creatinine upon presentation was 0.55 mg/dL, and her urine protein was 9,977 mg/day. The diagnosis of relapse was made based on her labs and presenting symptoms. She was treated with prednisone 50 mg/day, with improvement in her urine protein to 85 mg/g within 4 weeks. The dose of prednisone remained 50 mg/day during the 4 week period with a plan to taper the dose afterwards. She was encouraged to start treatment with rituximab, but the patient declined when she had to travel to her home country to care for her elderly mother. She is currently on a prolonged prednisone taper with plans to start treatment with rituximab if she relapses. Symptomatic treatment can also be provided with the use of OMT techniques such as a pedal pump, a thoracic pump, a thoracic inlet release, and an extremity pump.

Discussion

This case describes a 54-year-old woman that presented with reactivation of MCD in the setting of a recent COVID-19 vaccine administration. The possibility that the relapse

Figure 1: Timeline illustrating the course of a patient with MCD, including relapses.

could be secondary to stopping the steroid taper earlier than planned after the first episode of MCD cannot be ruled out. However, the fact that the initial episode of MCD occurred following the influenza vaccine and the fact that she was in remission for more than 3 years prior to having her COVID-19 vaccination points to the vaccine as the major factor for the relapse.

The pathophysiology of MCD secondary to having her COVID-19 vaccines is hypothesized to be related to molecular mimicry. The *t* cells produced after vaccine administration attack the podocytes, leading to injury [8]. Development of MCD has also been reported after influenza, hepatitis B, pneumococcal, measles, and tetanus–diphtheria–poliomyelitis vaccines [4]. So far, there have been eight reported cases of reactivation of MCD worldwide following vaccination against COVID-19 with the Pfizer, AstraZeneca, and Moderna vaccines. The vaccines from Pfizer and Moderna are both mRNA-based vaccines, whereas AstraZeneca's vaccine is a DNA-based vaccine. Among the above cases, five were reported following the Pfizer vaccine, two occurred after the AstraZeneca vaccine, and one followed the Moderna vaccine [11].

Although further studies of the relationship between MCD and the COVID-19 vaccine are warranted, awareness of this phenomenon may be beneficial in early diagnosis and treatment. At this time, more cases of reactivation of MCD have been reported following the Pfizer vaccine when compared to the Moderna vaccine, even though they are both mRNA vaccines. Further data are required to determine whether one vaccine is more likely to lead to reactivation of MCD than others. In addition, it is important to monitor the disease course of patients who experience reactivation of MCD after receiving a COVID-19 vaccine in order to weigh the risks vs benefits of any type of COVID-19 vaccine in patients with a history of MCD, especially in the setting of the pandemic and evolving data.

Conclusions

Patients with a history of activation or relapse of MCD after prior vaccines should be cautious when considering receiving the COVID-19 vaccine. If patients choose to receive the COVID-19 vaccine after weighing the risks and benefits, they should be informed to stay vigilant about the presenting symptoms of MCD and be encouraged to receive treatment as soon as possible. Treatment could include a combination of glucocorticoids and symptomatic treatment with OMT.

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Competing interests: None reported.

Informed consent: Informed consent was obtained from the patient prior to the writing this case report.

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