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CASE REPORT

Reactive arthritis after COVID-19 vaccination

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ABSTRACT

The severe acute respiratory syndrome coronavirus 2-induced coronavirus disease 2019 (COVID-19) has had a global spread. Vaccines play an essential role in preventing the spread. However, almost all types of vaccines have been reported to be associated with adverse events. Reactive arthritis (ReA) after vaccination has been reported; however, ReA after COVID-19 vaccination has not been reported. We reported a 23-year-old woman who suffered from an acute ReA on her left knee joint after COVID-19 vaccination and discussed the etiology and preventive strategy. She presented with swollen, painful left knee joint for 18 d. She had been inoculated 0.5 ml CoronaVac vaccine on 0 d and the 14th day with deltoid intramuscular injection. Finally, she was diagnosed as ReA after CoronaVac vaccination and was administered a single intra-articular injection of 1 ml compound betamethasone. The swelling and pain nearly disappeared after 2 d. On 1month follow-up, her condition was normal. ReA after COVID-19 vaccination is rare. The benefits of vaccination far outweigh its potential risks and vaccination should be administered according to the current recommendations. Further attentions should be put to determine which individual is at higher risk for developing autoimmune diseases after COVID-19 vaccination. More versatile and safer vaccines should be explored.

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Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus-induced coronavirus disease 2019 (COVID-19) has had a global spread. A comprehensive strategy for precautions includes handwashing, social distancing, isolation and mask-wearing. Besides, vaccines play an essential role in preventing the spread. Several different types of vaccines including inactivated vaccines, protein vaccines, vectored vaccines, and nucleic acid vaccines have been developed. So far, there is no conclusion about which vaccine is the most efficient; however, safety is a top consideration. Almost all types of vaccines have been reported to be associated with adverse events (AEs). Most AEs are mild and serious conditions are rare.[1] AEs range from local reactions such as injection-site pain to systemic side effects, such as fever, headache, coughing, loss of appetite, vomiting, diarrhea, joint pain, and autoimmune conditions. Autoimmune inflammatory diseases (AIIDs) following vaccinations include reactive arthritis (ReA), systemic lupus erythematosus, diabetes mellitus, thrombocytopenia, vasculitis, dermatomyositis, Guillain–Barré syndrome, demyelinating disorders, etc.[2] ReA was first used in 1969 to describe a sterile arthritis usually developing 1–3 weeks after a genitourinary or gastrointestinal bacterial infection; however, viruses including SARS-CoV-2 have also been reported to trigger ReA.[3] The mechanisms of ReA are plausible. Homology between human and viral proteins is an established factor in viral- or vaccine-induced autoimmunity.[4] Positive HLA-B27 is known to be an important susceptible factor for the development of ReA. The majority of people can vaccinate without any risk of autoimmunity onset, and autoimmune reactions after vaccination constitute probably less than 0.01% worldwide.[2] Although rare, we should pay special attention to those susceptible individuals.[5] Here, we reported a 23-year-old woman who suffered from an acute ReA on her left knee after COVID-19 vaccination and discussed the etiology and preventive strategy. To our knowledge, this is the first report on the ReA after COVID-19 vaccination. Written informed consent was obtained from this patient.

Patient presentation

A 23-year-old woman presented to the orthopedic department with swollen, painful left knee joint for 18 d. She had been inoculated 0.5 ml CoronaVac vaccine on 0 d and the 14th day with deltoid intramuscular injection. Three days after the first shot, she had pain on her left knee. She thought this was a common AE of arthralgia after vaccination and did not care. Seven days later, the knee began to swell. She had similar symptom induced by common cold 2 years before and the test of joint fluid was exudative, sterile, and without microcrystals. ReA was diagnosed at that time and she was administered celecoxib orally and intraarticular corticosteroid injection. Thereafter, there was no recurrence. For this time, she took celecoxib and then swelling relieved slightly. The second shot was continued on the 14th day. Two days later, she experienced an aggravated swelling and pain on the ipsilateral knee and celecoxib lost effectiveness. On admission, she walked lamely and her left knee was with tenderness, swelling, and decreased range of movement. She had no morning stiffness, conjunctivitis, skin rash, genitourinary, or gastrointestinal symptoms. She had no similar family history and no history of drug allergy. Her vital signs were normal. Tests for complete

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blood count, blood chemistry, hepatitis, syphilis, HIV, antistreptolysin O, mycoplasma, antinuclear antibody, rheumatoid factor, anti-CCP antibody, and HLA-B27 were negative. Erythrocyte sedimentation rate was 32 mm/h (reference, <20 mm/h) and C-reactive protein was 15.0 mg/L (reference, <8 mg/L). The total T lymphocytes was within normal range, and total B lymphocyte was 21.17% (reference, 5–18%). The concentration of Immunoglobulin G was 18.56 g/L (reference, 7.23–16.85 g/L). Magnetic resonance imaging showed moderate knee effusion. Arthrocentesis of her left knee was performed on the 18th day after vaccination and revealed yellow, cloudy synovial fluid. The fluid analysis was exudate. The count of leukocytes was 20–25/HP, among which neutrophils account for 90%, lymphocytes 4%, and monocytes 6%. The gram stain and bacterial cultures were negative; no crystals were seen. The viral arthritis, gouty arthritis, septic arthritis, rheumatoid arthritis, and other seronegative spondyloarthritis were excluded. According to the diagnostic criteria for ReA,[6] she was diagnosed as ReA after CoronaVac vaccination and the AE was reported to local epidemic prevention department. She was administered a single intra-articular injection of 1 ml compound betamethasone. The swelling and pain nearly disappeared after 2 days. On 1-month follow-up, her condition was normal. The anti-SARS-CoV-2 antibodies were positive.

Discussion

ReA after vaccination, being one of AIIDs, has been reported and the etiologies are multiple with a combination of familial, genetic, hormonal, environmental, or other risk factors for overstimulation of the immune system.[7] For this patient, some elements are typical for ReA including youth, a delay of 1 week between the vaccination and the beginning of the rheumatological picture, a monoarticular inflammatory disease predominantly in the lower limbs, and the good effect treating with intra-articular corticosteroid injection. Some are however atypical: the female gender and the negative HLA-B27. Vaccines with inactivated viral products or attenuated living microorganisms may operate as autoimmune disease-triggering agents. Adjuvants within vaccines may also cause specific autoimmune AEs which are named as "Autoimmune/inflammatory Syndrome Induced by Adjuvant (ASIA)".[8] Two main mechanisms have been offered to explain the development of autoimmunity: one is antigen-specific, such as the molecular mimicry, the other is nonspecific known as "bystander activation".[9] Molecular mimicry refers to a significant similarity between certain pathogenic elements contained in the vaccine and specific human proteins. This similarity may lead to immune cross-reactivity, wherein the reaction may harm the similar human proteins, essentially causing autoimmune disease. The latter is characterized by autoreactive B and T cells that undergo activation in an antigen-independent manner. For this patient, her elevated immunoglobulin G antibody level was correlated with the immune response for generating the neutralizing antibodies after vaccination.

Continuing assessment of post-license vaccine safety is important for the detection of rare and longer-term side effects.[10] This is particularly important in a pandemic situation, such as the COVID-19 pandemic, as rapid clinical development of several vaccines is likely to take place and large numbers of people are likely to be vaccinated within a short time.[11] CoronaVac, an inactivated COVID-19 vaccine developed by Sinovac Biotech, is China's second self-developed COVID-19 vaccine that has got conditional market approval on February 6. It is safe and effective, and the reported AEs are mild and self-limited.[12] ReA after CoronaVac vaccination was first reported here. Although rare, we are cautious, especially for individuals who are prone to develop autoimmune diseases. Four groups of individuals who might be susceptible to develop vaccination-induced ASIA were defined:[5] patients with prior postvaccination autoimmune phenomena, patients with a medical history of autoimmunity, patients with a history of allergic reactions, and individuals who are prone to develop autoimmunity. For these individuals, if vaccination is of utmost importance, it might be given, but the patients should be followed closely and treated if necessary. Additionally, vaccinations should preferably be given when the disease is in a quiet phase; it is also preferred to vaccinate before planned immunosuppression if feasible.[13] Current vaccine development is largely "empirical vaccinology", the "one-size-fits-all" approach, which ignores the complexity and diversity of the human immune system and host genome. In the future, however, personalized vaccinology is the goal of new vaccine development which means to provide the right vaccine for the right patient at the right time and with the right dose.[14] Finally, more versatile and safer vaccines should be explored. Different vaccine platforms have their own advantages and challenges. Recent studies demonstrate that mRNA vaccines surpass others in patients with AIIDs. The mRNA vaccines can be used to turn down an unwanted immune response and have shown promise in autoimmunity.[15,16] Additionally, mRNA is a noninfectious, nonintegrating vector. The possibility of contamination or insertional mutagenesis is not even theoretically present. Even so, real data on COVID-19 vaccines in patients with AIIDs tend to zero. It is imperative to develop better, safer vaccines.

In summary, ReA after COVID-19 vaccination is rare. Although vaccine administration has been associated with autoimmune manifestations in certain genetically predisposed individuals, the benefits of vaccination far outweigh its potential risks and vaccination should be administered according to the current recommendations. Further attention should be put to determine which individual is at higher risk for developing autoimmune diseases after COVID-19 vaccination. More versatile and safer vaccines should be explored.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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