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CASE REPORT

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Multiple COVID reinfections in a vaccinated psoriatic patient receiving adalimumab

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ABSTRACT

Currently, psoriasis patients are advised to follow their standard therapeutic regimen, and are advised to be vaccinated against Covid-19. However, the data about the antibody responses, induced by the various kinds of SARS-CoV-2 vaccines in psoriasis patients who require systemic immunosuppressive treatment is scant. In this case report, we describe antibody responses induced by COVID-19 vaccine, in a 26-year-old male patient with psoriasis being treated with anti-TNF biotherapy, adalimumab biosimilar every two weeks. The patient was vaccinated against COVID-19, according to the national protocol. He experienced three episodes of symptomatic COVID-19. His first and second exposures did not result in antibody production. After the third episode of COVID-19, The SARS-CoV-2 anti-spike antibody (IgG) was more than 100 Ru/mL (ELISA; ≥8 Ru/mL is considered positive), and SARS-CoV-2 neutralizing antibody (total) was more than 40 micg/mL (ELISA; ≥2.5 micg/mL is considered positive). This is the first case with weak antibody response to vaccination and multiple episodes of COVID infection in a psoriatic patient with adalimumab biosimilar. However, we cannot assume causality due to the treatment.

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KEYWORDS
COVID-19; vaccine; psoriasis; adalimumab

Introduction

In the face of the COVID-19 pandemic, psoriasis patients are recommended to follow their therapeutic regimen, protective procedures and social distancing. They are also advised to be vaccinated as soon as possible. However, antibody responses induced by the various kinds of SARS-CoV-2 vaccines in psoriatic patients are not well characterized (1,2).

Psoriasis is an immune mediated disease in which TNF-α plays an important role. Anti-TNF-α agents are considered to be highly effective for psoriatic patients. However, anti-TNF-α agents, such as adalimumab, may also reduce the IgG humoral response and CD27 memory B cell levels (3). In this report, we describe the anti-S IgG and neutralizing antibody responses – induced by the aluminum-hydroxide-adjuvanted, inactivated whole virus vaccine of COVID-19, Sinopharm (developed by China) – in a 26-year-old male patient with psoriasis being treated with anti-TNF biotherapy.

Case presentation

Our patient was negative for HLA-CW6, HLA-B27, and antinuclear antibody. The patient received adalimumab (biosimilar Cinnora) 50 mg/mL (0.8 mL), 40 mg subcutaneously every 2 weeks, for the last 26 months. He had received methotrexate as the initial therapy, but he was non-responsive to the treatment. Methotrexate was discontinued after administrating adalimumab biosimilar. He experienced three episodes of symptomatic PCR-positive COVID-19 disease. Immunoglobolin G (IgG) had been checked after each episode. The results showed non-protective ranges until the third episode of the infection.

The patient was vaccinated with Sinopharm vaccine, according to the recommended protocol, on 22 August 2020. This was followed by a second dose on 23 September 2020. The patient received adalimumab 1 week before the first dose and the second dose of the vaccine. The first episode of PCR-positive COVID-19 was on 14 November 2020. Immediately, we assessed the blood sample for a quantitative serologic test (Pishtazteb® SARS-CoV-2 TrimericS IgG assay; Tehran, Iran), to determine the IgG levels against the trimeric form of theSARS-CoV-2 spike protein. This evaluation was performed 106 days after the first vaccine injection. There were no anti-S IgG antibodies, indicating the lack of a positive response to the first dose of the vaccine (1).

The patient experienced the second episode of PCR-positive COVID-19 on 6 March 2021 and IgG antibody was evaluated which was still negative. The third PCR-positive COVID-19 episode was on 9 February 2022. The SARS-CoV-2 anti-spike antibody (IgG) was more than 100 Ru/mL (ELISA; ≥8 Ru/mL is considered positive), and SARS-CoV-2 neutralizing antibody (total) was more than 40 micg/mL (ELISA; ≥2.5 micg/mL is considered positive) on 23 February 2022.

Discussion

There are few data about vaccine response in patients with psoriasis receiving anti-TNF-α therapy. Near-normal andimpaired immune responses to vaccines can occur in patients taking

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immunomodulatory drugs (1,2,4). Anti-TNF-α agents have been shown to reduce the antibody response to the hepatitis A and B vaccines (1,2).There are few and conflicting data regarding the vaccines' immunogenicity in patients receiving immunosuppressive agents. Pestana et al. demonstrated a seroconversion rate of 15.2% among kidney transplant recipients, which was clinically insignificant (5), while Karacin et al. reported that more than half of cancer chemotherapy patients had seroconversion (6). One study showed that patients with chronic inflammatory diseases receiving anti-TNF-α agents had lower levels of neutralizing antibodies (NAbs) to SARS-CoV-2 mRNA vaccines but not lower anti-S IgG titers compared to immunocompetent controls (7). In another study vaccination with an mRNA SARS-CoV-2 vaccine resulted in lower levels of anti-S and NAbs in patients with rheumatoid arthritis who had received an anti-TNF- α agents and/or leflunomide compared to control subjects (8). Also, weaker anti-S IgG or weaker anti-receptor binding domain total immunoglobulin responses to SARS-CoV-2 vaccines occurred in Crohn patients treated with anti-TNF-α compared to those on vedolizumab or control patients (9,10). Even at low doses, combined methotrexate-adalimumab can be associated with a weak immune response to the mRNA1273 vaccine in elderly patients with rheumatoid arthritis (11). Interestingly, 56.3% of arthritis rheumatoid diseases patients developed detectable NAbs post-vaccination without statistically significant difference in neutralizing activities between patients with rheumatoid arthritis and healthy controls (12). In return, another cohort, evaluating patients with different immune-mediated diseases demonstrated a significant number of patients with low SARS-CoV2 specific antibody titers (13).

Seree-Aphinan et al. found that a subset of patients with immune-mediated skin conditions respond poorly to the vaccine despite having a low-level immunosuppression. Patients using azathioprine, cyclosporin, mycophenolate mofetil, or prednisolone $\geq$ 10 mg/day had a lower level of serum anti-SARS-CoV-2 IgG antibody and serum NAbs than those received methotrexate $\leq$ 10 mg/week, prednisolone $<$ 10 mg/day, or biologics like Secukinumab, Ixekizumab, Omalizumab. Patients with Methotrexate $\leq$ 10 mg/week, prednisolone $<$10 mg/day or the biologics had a similar immunogenicity profile to those without immunosuppressive therapies (14).

Seroconversion status associates with different underlying pathophysiological states. Seronegative COVID19 patients have hyperactive T cells and NK cells, high levels of IFN alpha, gamma and lambda ligands, markers of systemic complement activation, neutropenia, lymphopenia and thrombocytopenia. In seropositive patients, all of these processes are weakened. Increases in B cell subsets, emergency hematopoiesis, increased markers of platelet activation, and hypoalbuminemia are observed instead (15).

The possibility of seroconversion from repeated COVID-19 infection in our patient should be considered as well. Large studies have revealed seroconversion rates from 91 to 99%. Over 80% of patients have IgM and IgG seroconversion between 8- and 10-days post onset of syndrome (POS). Additionally, a positive IgG titers are found in most mild and moderate patients after 2–3 weeks. Several studies, suggest that seroconversion of both IgM and IgG happens at around 12 days POS with broad variation, but does not correlate with severity. NAbs are frequently correlated with long-term immunity in several viral infections. Most infected patients develop variable NAbs titers between days 14 and 20 POS. NAbs have a positive correlation with age, male sex and severity of the disease (16).

Our patient did not produce anti-S IgG after two vaccinations suggesting that the previous anti TNF-a therapy (immunomodulatory therapy) and/or the timing of administration (very close to administration of the vaccine) may have had an impact on the response to vaccination.

Treatment with adalimumab biosimilar was associated with a weak immune response to the Sinopharm vaccine in a young patient with psoriasis. The difference in response pattern to vaccination between patients with different immune-mediated diseases could be due to the interaction between hosts' comorbidities and their therapeutic regimen, in addition to the individual factors (14).

The immunogenicity of the various kinds of SARS-CoV-2 vaccines in psoriatic patients receiving different immunosuppressive agents and at different dosages necessitates more studies to provide an appropriate guideline.

Informed consent

Authors have obtained written informed consent to publish the details from the patient.

Disclosure statement

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