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CASE REPORT

Adult-Onset Still's Disease following Covid-19 Vaccine - A Case Report

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Abstract

The spread of COVID-19 infection has led to rapid vaccine development. It has been shown that vaccination may lead to complications like adult-onset Still's disease. We report a case of a 47-year-old Latvian male who presented with a sore throat, persistent leukocytosis, a high spiking fever, and weakness within two days after receiving the first dose of the Moderna COVID-19 vaccine in April 2021. The patient was initially treated with empirical antibiotics; however, the symptoms did not improve, so glucocorticoids were added, which resulted in the improvement of the patient's condition. The extensive work-up ruled out infection and other inflammatory conditions that mimic AOSD as well as malignancies. The diagnosis of AOSD was established based on anamnesis, radiological and laboratory testing. At the time of the report, several AOSD cases had been reported after COVID-19 vaccine administration. Physicians should consider this condition in patients who have prolonged fever after COVID-19 vaccination, and a diagnosis should be made for proper early management to avoid future complications.

Keywords

Adult-onset still's disease, Covid-19 vaccine, mRNA covid-19 vaccine

Introduction

The spread of COVID-19 infection has led to rapid vaccine development, and at present, more than half of the world's population has received at least one dose of the vaccine. In the literature, several immune-mediated diseases following the COVID-19 vaccination have been reported. A rare but recently reported complication following vaccination is adult-onset Still's disease (AOSD). AOSD is an inflammatory disease characterised by quotidian fever, arthritis, and transient, evanescent, salmon-coloured, and macular or maculopapular skin rashes [1].

Case Description

We report a rare case of AOSD following mRNA COVID-19 vaccine. A 47-year-old Latvian male with no previous medical history developed a sore throat, fever, and weakness two days after the first dose of the vaccine, administered. He experienced a fever every day after the onset of symptoms. Management of the fever included nonspecific antipyretic medication. Even though the patient was feeling unwell, it was recommended that he receive the second dose of the vaccine. During the 2 weeks after the second vaccine, he developed a high-grade fever accompanied by chills and was hospitalised. Initial laboratory testing was notable for a leukocytosis of 24,88 × 10^9/L with neutrophils of 23.3 × 10^9/L, elevated C-reactive protein (CRP) of 129.5 mg/L, erythrocyte sedimentation rate (ESR), ferritin, and imagine studies showing splenomegaly. At the regional hospital, the patient was treated empirically with broad-spectrum antibiotics. His symptoms persisted despite antibacterial therapy, and it was decided to transfer him to the university hospital.

On admission to the university hospital, a physical examination showed no significant abnormalities, except for febrile fever. Initial laboratory testing was notable for leukocytosis, elevated CRP, ESR, and liver enzymes. Various investigations were performed. The

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patient had enlarged neck lymph nodes; thereupon, a biopsy of the lymph node was obtained. On histological examination, no malignancies were found. After three weeks at the hospital, the patient was presented with nausea, vertigo, and difficulty getting up from a lying position. The patient had unilateral facial weakness, an inability to wrinkle the left side of the forehead, and trouble closing the eye on the affected side. Lumbar puncture and laboratory testing were performed, and diagnostics showed serous meningitis. The testing for neuroborreliosis was negative. The patient received antibacterial treatment with ceftriaxone, and acyclovir. The neurologist confirmed that the patient had acute facial neuritis on the left side of the face.

While in the hospital, patient received antibacterial therapy and antipyretic drugs, which did not have the desired effect; therefore, it was decided to add glucocorticoids to the therapy. Glucocorticoid therapy had a positive effect, and the patient was discharged from hospital.

After six weeks of gradually decreasing methylprednisolone, persistent febrile fever, malaise, joint pain, and night sweats developed. The patient gradually increased the dose of methylprednisolone, which improved the general condition, but the fever persisted. After a few months, a patient was admitted to the hospital for the second time with a febrile fever for several weeks. Patients also had night sweats and bone pain; therefore, bone scintigraphy was performed. Scintigraphy revealed arthritic changes in both shoulders, hips, and sacroiliac joints. On the 4th day of admission, the patient developed a maculopapular rash over the neck, face, trunk, and both hands and on the hairy part of the head. The rash persisted for the next few days, without pain or itchiness. Examinations were carried out, and serological examinations for autoimmune diseases and infections were negative. Initial laboratory testing was notable for leukocytosis and elevated acute phase proteins. The AOSD diagnosis was established based on anamnesis with prolonged fever, arthritis, a typical rash, and radiological and laboratory testing results. The recommended therapy was methylprednisolone with a plan to decrease the dosage to the lowest effective level and the addition of methotrexate (MTX). After two weeks of hospitalization, the patient was discharged to continue treatment in outpatient care.

During the next few weeks, the dosage of methylprednisolone increased, which led to patient weight gain. The patient also developed steroid-induced impairment of glucose tolerance and Cushing syndrome. During his follow-up after two months, oral MTX was substituted with subcutaneous MTX, and leflunomide was added. The decision to change therapy was made because decreasing the dosage of methylprednisolone immediately caused flares of fever and joint pain. After two months of therapy, the patient's condition had not changed significantly. As soon as steroids are not used, fever and joint pain are renewed. The previous therapy continued for another three months until the patient relapsed with sub-febrile fever, severe pain in the hip, knee, and shoulder joint. Therefore, observing the ineffectiveness of the therapy, it was decided to switch to the biological drug adalimumab every other week in combination with MTX subcutaneously per week and methylprednisolone, but leflunomide was discontinued.

Discussion

Vaccination against COVID-19 has become the most effective at preventing severe disease, hospitalisation, and death. Also, previous studies have shown that the benefits of vaccination outweigh the possible risks. However, several types of side effects have been observed, including those associated with autoimmune diseases such as AOSD [2]. At the time of writing this report, several cases of AOSD after receiving the mRNA COVID-19 vaccine had been published [3,4].

AOSD is a rare autoinflammatory disease characterised by high-spiking fever, a typical salmon-coloured skin rash, arthralgia and leukocytosis [5]. And there is no confirmatory test for AOSD, but symptoms can be used in clinical criteria for diagnostics. Most used are the Yamaguchi and Fautrel criteria [6]. Several clinical cases were reviewed, and it was found that the most common symptoms were fever, leukocytosis, a typical rash, joint pain, and a sore throat [2,7]. In most cases, the initial symptoms of the disease developed within 7 to 10 days after receiving the vaccine [4,8-10]. In one of the cases reported, the patient developed symptoms only 3 months after receiving the vaccine [7]. In contrast, there have been case reports in which the patient presented with symptoms as soon as one day after the vaccination [5]. And if we look at the gender division between the cases, then from the 14 cases reviewed in evidence-based medicine journals, 11 out of them reported female patients. The age division in these cases was between 30 and 50 years [3,7,8].

The exact pathogenic mechanism of AOSD is unknown, but it may involve innate immunity, including activation of innate immune cells, and elevated cytokine levels [11]. First-line treatment for AOSD is systemic corticosteroids, but in more serious and complicated cases, second-line drugs such as disease-modifying antirheumatic drugs, TNF-alpha inhibitors, and IL-1/IL-6 inhibitors can be added [12]. In the presented clinical case, the patient was treated with high-dose steroids at the early stage of the disease, but as the therapy was not showing the desired results, MTX, leflunomide, and later adalimumab were added. In case reports published earlier, patients in most of the cases were treated with corticosteroids [8], which was followed by a significant improvement in the patient's condition. However, there were cases when it was necessary to add drugs like anakinra [3] and tocilizumab [9] to achieve the

desired result. To maintain remission of the disease and prevent relapse, most of the patients were receiving corticosteroids with or without additional biological medications or disease modifying anti-rheumatic drugs [2,8,10].

Whether this syndrome is an extremely rare adverse reaction to the vaccine or coincidental, it is not known.

Conclusion

Early diagnosis of AOSD is difficult because there are no specific tests, and usually it is a diagnosis of exclusion. Also, in the reported case, the diagnosis was established only during the second hospitalisation, almost half a year after receiving the second dose of the vaccine. Physicians should consider this condition in patients who have prolonged fever after COVID-19 vaccination, and a diagnosis should be made for proper early management to avoid potentially serious complications.

Learning Points

1. Early diagnosis of AOSD is difficult because there are no specific confirmatory tests, and usually it is a diagnosis of exclusion.
2. Adult-onset Still's disease should be considered if patient develops prolonged fever after COVID-19 vaccine.

Conflict of Interest

The authors declare that they have no conflicts of interest regarding the publication of this case report.

Consent for Publication

Written and informed consent was taken from the patient to publish this case report.

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Ethical Approval

Ethical approval to publish an anonymous case report has been received at our institution.

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