

Case Report

Long-Term Autoimmune Polyarthrititis due to COVID-19 Vaccine

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Abstract

Background

Vaccinations for COVID-19 have played a pivotal role in controlling the global pandemic, with most adverse events being mild and transient. However, rare post-vaccination autoimmune responses have been reported. The understanding of long-term rheumatologic sequelae, particularly autoimmune polyarthrititis following COVID-19 vaccination, remains limited.

Case Presentation

We report the case of a 41-year-old previously healthy man who developed progressive polyarthrititis and systemic symptoms following the Johnson & Johnson COVID-19 vaccine. The initial symptoms of joint swelling and arthralgia appeared within a week of the first vaccine dose, subsiding temporarily with medication. After receiving a booster dose, the patient experienced worsening polyarthrititis affecting multiple joints including knees, elbows, wrists, shoulders, and neck, along with low-grade fever, fatigue, and functional decline. Despite outpatient anti-inflammatory therapy, symptoms persisted and worsened over the next six months, prompting hospitalization. Workup revealed elevated inflammatory markers (ESR 77 mm/hr, CRP 193.2 mg/L), synovial fluid consistent with inflammatory arthritis, and infectious serologies. Imaging showed joint effusions and calcified pulmonary granulomas. He was diagnosed with vaccine-induced reactive arthritis. Treatment with intravenous corticosteroids led to partial symptom relief, and he was discharged on oral steroids and initiated on methotrexate for long-term management.

Conclusion

Clinicians should maintain a high index of suspicion for autoimmune phenomena such as reactive polyarthrititis following COVID-19 vaccination, especially in patients with new-onset joint symptoms. Early recognition and referral to rheumatology may improve outcomes. Further studies are needed to clarify the pathophysiology, risk factors, and long-term prognosis of such vaccine-associated autoimmune conditions.

Keywords

COVID-19; SARS-CoV-2; pandemics; COVID-19 vaccines; vaccines adverse events and reactions; vaccination; autoimmune disorders; arthritis

Introduction

COVID-19 infection has been associated with proinflammatory impact and activation of autoimmune processes.^{1,2} COVID-19 vaccines are related to multiple transient side effects including fatigue, drowsiness, muscle/joint pain, and other side effects with a significant association with older age, history of rheumatoid arthritis, or nonsteroidal anti-inflammatory drug

(NSAID) usage,³ but the understanding of the long-term impact of the vaccines is still limited. We report a case of acute onset of autoimmune polyarthrititis post COVID-19 vaccination followed by a prolonged course of symptoms.

Case Presentation

A 41-year-old man with no significant medical history presented to the hospital with worsen-

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ing polyarthrititis and fever. The patient initially had a low-grade fever, increasing to 101.9 degrees Fahrenheit. The patient also reported having swelling and limitation of range of motion in multiple joints, specifically shoulders, knees, and elbows, that started in late 2021. The patient noticed similar symptoms (knee swelling, polyarthralgia) 1 week after getting the Johnson & Johnson COVID-19 vaccine in late 2021, which were relieved with medications. He later received a booster Johnson & Johnson COVID-19 vaccine dose early in 2022, after which he noticed diffuse swelling and pain in both knees, followed by involvement of both elbows, wrists, neck, and shoulders with a gradual worsening of symptoms from intermittent to constant for 4 weeks, before presenting to the hospital about 6 months after the booster dose. The patient reported being on a progressive regimen of anti-inflammatory agents started by his primary care provider without any relief. He further reported generalized weakness, feeling that he lost muscle mass, and noted to have worsening knee pain on standing. A review of systems was positive for neck pain, occasional headaches, and chills. Negative pertinent history included lack of cough, night sweats, and tuberculosis exposure. The patient denied prior adverse reactions to vaccines, prior history of joint pain, or autoimmune disorders.

In the emergency department, the patient was noted to have a low-grade fever, total bilirubin 0.4 mg/dl, alkaline phosphatase 236 IU/L, aspartate aminotransferase 62 IU/L, alanine transaminase 135 IU/L, uric acid 6.3 mg/dl, white blood cell count 11.47 K/UL, platelet count 935 K/UL, erythrocyte sedimentation rate 77 mm/hr, and C-reactive protein 193.2 mg/L. An electrocardiogram was noted to be unremarkable and a COVID-19 polymerase chain reaction test was negative. Serological workup also revealed negative rheumatic factor, cyclic citrullinated peptide, and antinuclear antibody. An abdominal ultrasound was significant for fatty liver and a knee X-ray showed mild degenerative osteophytes, moderate effusion on the right knee, minor effusion on the left knee, and preserved joint space bilaterally. A right elbow X-ray showed joint effusion with bulging intra-articular fat pads. A computed tomography (CT) chest/abdomen/pelvis revealed small pleural calcification in the right posterior mid-hemithorax, calcified granuloma at the left apex, border-

line retroperitoneal and pelvic lymph nodes, and evidence of old granulomatous disease (**Tables 1 and 2**).

The patient was started on intravenous (IV) steroids with some symptom relief. The rheumatology and infectious disease specialist evaluated the patient. The patient was incidentally noted to have a positive interferon gamma release assay test. The patient was started on rifampin treatment for latent tuberculosis as the patient was planning to initiate immunosuppressive therapy for symptom control. The final diagnosis was long-term reactive arthritis related to the COVID-19 vaccine.

The patient's joint swelling and tenderness were improving but still present while on IV steroids. The patient was transitioned to oral steroids at discharge and was later started on methotrexate.

Discussion

Vaccination is an important tool in prevention; however, vaccines have adverse effects and can develop into autoimmune syndromes.⁴ COVID-19 infection and vaccination have been associated with autoimmune conditions.⁵ Viral vaccinations may trigger autoimmunity leading to auto-immune rheumatic diseases and inflammatory syndromes, which are believed to be caused by overstimulation of the immune response against self-antigens.⁶ Vaccinations have been associated with many local and systemic reactions ranging from erythema in the injection site to serum sickness-like syndrome involving different systems. The mRNA COVID-19 vaccine, as opposed to a placebo, has resulted in localized and systemic reactions ranging from local pain, heat, swelling, and redness to systemic effects like fever, fatigue, arthralgias, and myalgias within 1 to 2 days after the vaccination and rare cases of anaphylaxis have been reported.^{7,8} Immediate and delayed-type hypersensitivity plays a role in vaccination reactions. However, the immediate reactions are usually related to the vaccine ingredients, not the viral components, eg, polyethylene glycol and cross-reactive polysorbate 80 are found to be the causal factors for immediate reactions.⁹

The viral infections and vaccinations may trigger autoimmunity and the post-vaccine syn-

Table 1. Serological and Rheumatological Test Results

Lab test	Results and comments	Reference range
ANA	Negative	Negative
Lyme IgG/IgM	Negative	Negative
Rheumatoid factor	Negative (<10 U/mL)	Negative
HLAB27	Positive	Negative
C-ANCA: P-Abnormal with diffuse cytoplasmic pattern with Serine Protease 3 positive	94 U/mL, Note: Can suggest granulomatous polyangiitis	0-20 U/mL
Myeloperoxidase antibody	Negative	Negative
CCP	6 U/mL	<20 U/mL are negative
Anti-smooth muscle antibody	25 U/mL	20-30 U/mL weak positive, <20 units/mL - negative
Complement C3	225.1 mg/dL	87-200 mg/dl
IgA	186 mg/dL	68-408 mg/dl
IgG	1452 mg/dL	768-1632 mg/dl
IgM	140 mg/dL	35-263 mg/dl
Chikungunya IgG/ IgM	Negative	Negative
Ehrlichia and anaplasma (PCR)	Negative	Negative
<i>B Burgdorferi</i> C-10 peptide IgM, IgG antibodies	Negative	Negative
14-3-3 eta protein (marker of inflammation)	<0.2 ng/mL	<0.2ng/ml >0.2 indicative of RA or erosive arthritis
Serum iron	24 ug/dL	50-160 ug/dl
TIBC	217 ug/dL	240-400 ug/dl
Percent saturation	11.1 %	20-40%

Abbreviations: ANA = Antinuclear antibodies; B Burgdorferi = *Borrelia burgdorferi*; C-ANCA = antineutrophilic cytoplasmic autoantibody; CCP = cyclic citrullinated peptide; HLAB27 = human leukocyte antigen B27; IgA = immunoglobulin A; IgG = immunoglobulin G; IgM = immunoglobulin M; PCR = polymerase chain reaction.

drome by an autoimmune/inflammatory syndrome induced by adjuvants (ASIA syndrome).¹⁰ The ASIA syndrome associated with COVID-19 vaccination includes several endocrinopathies, including Graves' disease.⁹

Literature showed that the COVID-19 vaccine spike glycoprotein might cause cross-reactivity due to molecular mimicry. Patients with a history of autoimmune disorders or strong immune responses are more vulnerable to this phenomenon.¹¹ In our patient, without a history of autoimmunity, the occurrence of polyarthritis after COVID-19 vaccination was supported by the possibility of auto-immune reactions to vaccinations.¹² Furthermore, the presentation

of new onset of arthritis and arthralgia after COVID-19 vaccination is usually presented with swelling, pain, stiffness, and decreased range of motion in the affected patient within a week of receiving the vaccination.¹³ Our patient-reported symptoms within a week of receiving the first dose and re-presentation and worsening of similar symptoms after the second dose. He presented with pain, diffuse swelling in multiple joints, joint stiffness with fever, and chills. In addition, the patient had difficulty ambulating and generalized weakness over 4 weeks, with a CT scan of the chest, abdominal, and pelvis suggestive of borderline retroperitoneal and pelvic lymph nodes. Romeo et al prospectively evaluated the incidence of lymphadenopathy

Table 2. Synovial Fluid Analysis

Synovial fluid analysis	Result	Reference
Crystal, synovial/joint F1	None seen	None
Color	Yellow	Yellow
Clarity	Cloudy	Clear
Nucleated cells	27 523 x 10 ⁹ /L	0-200 x 10 ⁹ /L
RBC, fluid	Rare	Not established
Neutrophil	71 cells/uL	Not established
Lymphocytes	19 cells/uL?	Not established
Macrophages	10 cells/uL?	Not established
Eosinophils, fluid	0 cells/uL?	Not established
Lining cells, synovial	0 cells/uL?	Not established
Biopsy cultures	Negative	Negative
Smear for acid-fast bacilli	Negative	Negative

in healthy subjects after the COVID-19 vaccine. They concluded that there was a high incidence of axillary, supra-clavicular, and lateral-cervical lymphadenopathy, which are considered benign.¹⁴ However, there is limited literature that can explain retroperitoneal lymphadenopathy after the COVID-19 vaccination.

After ruling out the most common autoimmune conditions and considering auto-immune polyarthritis, we concluded it was reactive arthritis due to the COVID-19 vaccine. Reactive arthritis is classically considered inflammatory arthritis that occurs after gastrointestinal or genitourinary infection and is considered a subtype of spondyloarthritis. However, the term has been widely used as immune-mediated arthritis that occurs after infection. It is understood to be aseptic arthritis that occurs after infection due to changes in the immune system. As our patient's joint symptoms started after COVID-19 vaccination, but not after viral infection, and symptoms persisted for several months, viral arthritis was excluded.¹⁵ In a recent case, Roux et al reported reactive sacroiliitis after the COVID-19 vaccine.¹⁶

Conclusion

Our case provides further evidence that COVID-19 vaccination is associated with long-term rheumatological conditions such as polyarthritis. Reactive arthritis is a rare presentation after COVID-19 vaccination, resulting from multiple pathogenic mechanisms, in-

cluding hypersensitivity reactions triggered by the vaccine components. ASIA syndrome is an autoimmune inflammatory reaction caused by vaccine adjuvants or arthritis that occurs after any infection or vaccination. We recommend caution when counseling prospective vaccine recipients regarding these side effects, especially in those with prior rheumatological illnesses. In addition, early identification of these possible side effects and seeking an evaluation by a rheumatologist or immunologist would result in improved patient morbidity.

Conflicts of Interest

The authors declare they have no conflicts of interest.

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References

1. Castanares-Zapatero D, Chalon P, Kohn L, et al. Pathophysiology and mechanism of long COVID: a comprehensive review. *Ann Med*. 2022;54(1):1473-1487. doi:10.1080/07853890.2022.2076901
2. Szekanecz Z, Balog A, Constantin T, et al. COVID-19: autoimmunity, multisystemic inflammation and autoimmune rheumatic patients. *Expert Rev Mol Med*. 2022;24:e13. doi:10.1017/erm.2022.10

3. Nassar RI, Alnatour D, Thiab S, Nassar A, El-Hajji F, Basheti IA. Short-term side effects of COVID-19 vaccines: a cross-sectional study in Jordan. *Hum Vaccin Immunother.* 2022;18(5):2082792. doi:10.1080/21645515.2022.2082792
4. Aytekin ES, Şekerel BE, Şahiner ÜM. Allergic reactions during childhood vaccination and management. *Turk J Pediatr.* 2021;63(6):941-954. doi:10.24953/turkjped.2021.06.001
5. Yazdanpanah N, Rezaei N. Autoimmune complications of COVID-19. *J Med Virol.* 2022;94(1):54-62. doi:10.1002/jmv.27292
6. Safary A, Esalatmanesh K, Eftekharsadat AT, Jafari Nakjavani MR, Khabbazi A. Autoimmune inflammatory rheumatic diseases post-COVID-19 vaccination. *Int Immunopharmacol.* 2022;110:109061. doi:10.1016/j.intimp.2022.109061
7. Pandit T, Pandit R, Goyal L. Uncommon Side Effects of COVID-19 Vaccination in the Pediatric Population. *Cureus.* 2022;14(10):e30276. doi:10.7759/cureus.30276
8. Mushtaq HA, Khedr A, Koritala T, Bartlett BN, Jain NK, Khan SA. A review of adverse effects of COVID-19 vaccines. *Infez Med.* 2022;30(1):1-10. Published 2022 Mar 1. doi:10.53854/liim-3001-1
9. Gambichler T, Boms S, Susok L, et al. Cutaneous findings following COVID-19 vaccination: review of world literature and own experience. *J Eur Acad Dermatol Venereol.* 2022;36(2):172-180. doi:10.1111/jdv.17744
10. Unal Enginar A. Arthritis following COVID-19 vaccination: report of two cases. *Int Immunopharmacol.* 2021;101(Pt B):108256. doi:10.1016/j.intimp.2021.108256
11. Mohamed K, Rzymiski P, Islam MS, et al. COVID-19 vaccinations: the unknowns, challenges, and hopes. *J Med Virol.* 2022;94(4):1336-1349. doi:10.1002/jmv.27487
12. Asakawa J, Kobayashi S, Kaneda K, et al. Reactive arthritis after influenza vaccination: report of a case. *Mod Rheumatol.* 2005;15(4):283-285. doi:10.1007/s10165-005-0399-5
13. Dawoud R, Haddad D, Shah V, et al. COVID-19 vaccine-related arthritis: a descriptive study of case reports on a rare complication. *Cureus.* 2022;14(7):e26702. doi:10.7759/cureus.26702
14. Romeo V, Stanzione A, D'Auria D, et al. COVID-19 vaccine-induced lymphadenopathies: incidence, course and imaging features from an ultrasound prospective study. *J Ultrasound.* 2022;25(4):965-971. doi:10.1007/s40477-022-00674-3
15. Bekaryssova D, Yessirkepov M, Zimba O, Gasparyan AY, Ahmed S. Reactive arthritis before and after the onset of the COVID-19 pandemic. *Clin Rheumatol.* 2022;41(6):1641-1652. doi:10.1007/s10067-022-06120-3
16. Roux N, Poussing S, Maurier F. Case of reactive sacroiliitis possibly induced by an mRNA coronavirus disease vaccine. *BMJ Case Rep.* 2022;15(7):e249063. doi:10.1136/bcr-2022-249063