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## Development of Seronegative Rheumatoid Arthritis after Covid-19 Vaccination: A Case Report

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### Abstract

Over a billion people around the world have received COVID-19 vaccines. Widespread vaccination is critical in stemming the pandemic. Several vaccine side effects have been reported. Most side effects are self-limited and resolve within days. Serious side effects, although rare, have been reported including anaphylactic reaction, cerebral venous sinus thrombosis, myocarditis and pericarditis.

This case report describes the development of Seronegative Rheumatoid Arthritis in a 71 years old female, after receiving the of Pfizer COVID-19 vaccine.

The patient was a previously healthy 71-year-old white female who began getting joint pain, numbness and painful tingling in her hands days after receiving her Pfizer COVID-19 vaccine.

She was initially diagnosed with carpal tunnel syndrome.

Her symptoms progressed to include joint swelling and pain in the hands, wrists, and feet with generalized fatigue.

The patient was diagnosed with seronegative rheumatoid arthritis and started on prednisone and methotrexate which greatly improved her symptoms.

**Keywords:** COVID-19, Seronegative Rheumatoid Arthritis, Vaccination reaction.

### 1. Introduction

COVID-19 Vaccinations will be given to billions of people worldwide in the next several months to years. The vast majority of side effects from the vaccine are self-limited and seen immediately or within days of the immunization. These include pain at the injection site, myalgia, fatigue, metallic taste, and injection syncope. [1] Other rare but more serious effects include cerebral venous sinus thrombosis with thrombocytopenia. [2] Myocarditis and pericarditis have been reported in younger population.

With the sheer number of vaccines being given, surveillance will be important to identify autoimmune disorders and other long-term effects that may be initiated by the vaccine stimulating the immune system.

In the United States, all significant events from vaccines are to be reported to the Vaccine Adverse Event Reporting System (VAERS). [3] Other countries have their own reporting systems in place.

## **2. Case Report**

A healthy 71 year old female presented to our institution for the Pfizer COVID-19 vaccination. She had no significant past medical history and maintained a healthy lifestyle by eating a well-rounded diet and exercising most days of the week through cycling. She did not take medications and had no chronic illnesses. She had a family history of essential hypertension and giant cell arteritis in her father.

On January 02, 2021, she was given the initial dose of the Pfizer COVID-19 vaccine and advised to follow up 21 days later for her second immunization. She had no side effects from the initial vaccine, except mild soreness of the injection site lasting one day. She returned for her second dose at the 21-day interval without incident.

Within 2 days of the second dose, she began to experience pain, tingling, and numbness in her hands. She was evaluated by her primary care physician who suspected a cervical impingement. The patient was sent for a non-contrast MRI of the cervical spine. The results of the MRI did not correlate with the patient's symptoms. Over the next 2 weeks, the numbness and tingling in her hands began to affect her function, limiting her ability to grip or twist items with her hands. Nerve conduction studies were performed and she was diagnosed with carpal tunnel syndrome.

The patient was referred to Neurosurgery and was recommended to have a carpal tunnel release. Over the next weeks, her symptoms began to affect other small joints including those in her feet and ankles and she began getting joint swelling in the affected joints. She was also experiencing fatigue.

Her surgery was postponed until further testing could be performed.

Her primary care physician ran several tests including a complete blood count which showed mild anemia with a Hemoglobin of 10.3 g/dl (reference interval 12.0-16.0 g/dl), Antinuclear Antibody <1:80 (reference interval 1:80), Rheumatoid Factor was <10.0 IU/ml (reference interval 0.0-14 IU/ml) and Cyclic Citrullinated Peptide Antibody IgG 2 Units (reference interval 0-19 Units).

High-sensitivity C-Reactive Protein (hs-CRP) value was elevated at 21.81 mg/l (reference interval 0.00-5.00 mg/l). A decision was made to refer the patient to Rheumatology where she was diagnosed with Seronegative Rheumatoid arthritis. This clinical diagnosis was made based on her having more than 6 weeks of symptoms with pain, tenderness, and soft swelling of more than 10 small joints including her proximal interphalangeal of her hands and feet. She had pain and decreased range of motion of her wrists ankles, and shoulders. Her laboratory testing more specifically for rheumatoid arthritis was negative including Rheumatoid Factor and Citrullinated Peptide Antibody IgG.

### **3. Differential Diagnosis**

The patient presenting symptoms at the beginning of the process was numbness and tingling in her hands. The differential diagnosis included cervical radiculopathy which was excluded through a non-contrast MRI of the cervical spine. She was diagnosed with carpal tunnel syndrome, which was confirmed by nerve conduction studies. This was found to be part of the symptomatology of the seronegative rheumatoid arthritis and subsequently resolved with treatment of prednisone and methotrexate.

Viral arthropathy was considered in the differential diagnosis and was excluded because she had no history of viral exposure or viral symptoms predating the onset of joint complaints. Viral arthropathies such as those caused by Parvovirus usually resolve within one to three weeks and have an associated generalized rash which was absent in this patient. [4,5]

### **4. Treatment**

Initial treatment with acetaminophen, oral nonsteroidal anti-inflammatory medications, and supportive care did little to improve her condition. Once the diagnosis of seronegative rheumatoid arthritis was reached and the patient tested negative for underlying infections including tuberculosis and hepatitis she was started on Methotrexate and prednisone. Her symptoms decreased significantly. Within weeks, her swelling and fatigue improved, and the tingling and numbness nearly resolved.

She has returned to cycling 6 days per week and to maintaining a regular exercise program.

She currently is continuing working to taper her prednisone and continues on methotrexate. She is now able to use acetaminophen for pain control.

### **5. Outcome and Follow up**

Her hs- CRP has decreased with treatment. Her fatigue has resolved. The joint swelling, numbness, and tingling in her hands have nearly resolved.

### **6. Discussion**

It may not be possible to know if there is a cause and effect of this case of seronegative rheumatoid arthritis and the administration of the COVID vaccine. Other post-immunization reactions have been observed after these vaccines have been administered including myocarditis and pericarditis in the younger population. [6,7]

The criteria for diagnosis of rheumatoid arthritis uses a point system based on the American College of Rheumatology and the European League Against Rheumatism. (see Table 1) The classification assigns points for factors including the number of joints involved, especially small joints, serologic testing including rheumatoid factor and anti-cyclic citrullinated peptide, acute phase reactants such as sedimentation rate, and C-reactive protein. A score of 6 points or higher is diagnostic for rheumatoid arthritis.

Nonsteroidal anti-inflammatory medications (NSAIDs) and prednisone are not disease-modifying anti-rheumatic drugs (DMARDs) but can bridge patients' symptoms by decreasing the inflammatory process until the DMARDs take effect. Methotrexate is usually the initial drug of choice because of its efficacy and low cost. [8] Other older medications which may be effective in treatment include Hydroxychloroquine, Sulfasalazine, and Leflunomide. For those unable to tolerate Methotrexate or other medications, several biologics are now available. These are tumor necrosis factor-alpha inhibitors that are administered either through infusion or injection and are at a much higher cost. More recently small molecule/Janus inhibitors which are oral medications have been approved to treat rheumatoid arthritis.

Before starting patients on DMARDs testing for underlying infections such as Tuberculosis and hepatitis should be performed and recommended immunizations recommended for age should be administered.

Health care providers should be on alert for autoimmune reactions in patients who have received the COVID-19 immunization.

The risk of these reactions is small. The personal and social benefits of receiving the vaccine far outweigh the potential risks.

Rheumatoid arthritis should be suspected in patients with inflammatory small joint symptoms. Diagnosis is made through using the American Academy of Rheumatology and the European League Against Rheumatism criteria. Specific laboratory testing can assist in the diagnosis but is not required to reach a diagnosis.

Disease-modifying agents (DMARDs) should be started as soon as possible once a diagnosis of rheumatoid arthritis is made and underlying infections are excluded. This decreases the likelihood of synovitis and joint destruction.

Methotrexate is the initial drug of choice for the treatment of rheumatoid arthritis, and there are many other agents available if methotrexate is not effective or not tolerated.

Table 1. Diagnostic criteria for Rheumatoid Arthritis.

<b><u>Joint Involvement</u></b>	<b><u>Points</u></b>
1 Large joint	0
2-10 Large joints	1
1-3 Small joints	2
4-10 Small joints	3
10 Joints with at least 1 small joint	5
<b><u>Serology</u></b>	
Negative RF and anti-CCP	0
Low positive RF and/or anti-CCP	2
High positive RF and/or anti-CCP	3
<b><u>Acute phase reactants</u></b>	
Normal CRP and/or ESR	0
Abnormal CRP and or ESR	1
<b><u>Duration of Symptoms</u></b>	
< 6 weeks	0
> 6 weeks	1
<p><b><u>Rheumatoid Arthritis</u></b> is diagnosed based on:</p> <ol style="list-style-type: none"> <li>1. Synovitis in at least 1 joint.</li> <li>2. Absence of alternative diagnosis that better explains diagnosis of synovitis.</li> <li>3. Total score of at least 6/10 points from above criteria.</li> </ol> <p>Ref.[8]</p>	

### **7. Patient`s Perspective**

Throughout my life, I have been an extremely active person: running, hiking, cycling, and exercising daily. I am a professional artist, an avid photographer, and a gourmet cook. Since my retirement 7 years ago, I have cycled 6 to 12 miles daily, gardened (tilling, digging, planting, raking) 4 hours a day, and maintained an hour exercise program daily. I have also taken thousands of photographs and made thousands of meals.

After I received my second Covid-19 vaccination, I began to develop swelling, pain, numbness in my wrists, hands, ankles, and feet. In the following several weeks, pain radiated through my arms, shoulders, hips, thighs, and legs. I lost the ability to use my hands, raise my arms, grip objects, or lift the lightest objects. My ability to walk was greatly diminished. I was not able to cycle or garden. I couldn't operate my camera or do mundane tasks in my kitchen. I was incapacitated and in extreme pain.

Once treatment was started my symptoms diminished significantly. In the next three months, my labs showed incredible improvement. I am now able to return to my active lifestyle and have improved about 85 to 90 percent.

I feel that rare cases like mine should not discourage anyone from receiving their Covid vaccination. I completed a VAERS report in April to let healthcare providers know about similar possibilities of auto-immune responses to the vaccine so they can diagnose and treat patients more effectively.

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