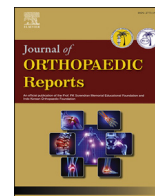




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Case Report

Musculoskeletal Sequelae following COVID-19 mRNA Vaccination: A Case Report

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A B S T R A C T

Background: COVID-19 is among the most deleterious pandemics the world has ever faced. With millions of people now having received the unprecedented COVID-19 vaccines and many millions yet to receive it, it becomes imperative to determine the side effect profile of these vaccines.

Case report: Herein, we present a case in which a patient developed inflammatory fasciitis of the shoulder girdle and sternoclavicular joint inflammation requiring hospital admission following COVID-19 vaccination. The patient is a South Asian male of Indian origin residing in the United States.

Conclusion: Our report aims to share the scenario in which a patient developed severe pain, muscle spasms, inflammatory fasciitis in the shoulder and inflammation in the SC joint in the post-vaccination setting following the second dose of the Pfizer-BioNTech COVID-19 vaccine. To our knowledge, this is the first such reported case, and therefore this contribution of the presentation and pathogenesis of this orthopaedic complication may provide further information regarding clinically adverse effects from this nascent immunological advancement.

1. Introduction

The coronavirus (SARS-CoV-2) disease has cemented its place among the most deleterious pandemics the world has ever faced. Almost 300 million people have already been infected around the world, resulting in over 5 million deaths.¹ Efforts to curtail the spread of this coronavirus have led to unparalleled measures by pharmaceutical companies to develop novel vaccinations.¹

Traditional vaccines with a history of longstanding public accessibility have been associated with certain predictable side effect panels, the vast majority of which are harmless.² These adverse reactions are the result of an immune-mediated reaction to the vaccine excipient, the active components of the vaccine, or are related to immunodeficiency in the host. Clinically, the most common manifestations of a vaccine-related side effect are pain, swelling, and erythema at the injection site.² More moderate symptoms commonly seen include systemic reactions such as fever, irritability, rash, and drowsiness. Rarer musculoskeletal side effects include swelling of the upper and lower extremities and inflammatory conditions such as myositis.^{2,3}

The introduction of new COVID-19 vaccines being offered through emergency use authorization in the U.S. as well as globally has revolutionized the landscape of vaccine science. Prior to this, the fastest that a vaccine had been developed and approved had been four years when the

mumps immunization was released in the 1960s.^{1,4} The arrival of these vaccines is also rendered unique through the mechanism of the vaccines themselves; the first two COVID-19 vaccines to be authorized by the FDA, by Pfizer-BioNTech and Moderna, both utilize messenger RNA (mRNA), which has never before been approved for general use in humans. Previous publicly accessible vaccines contained viral proteins or inactive forms of the virus.⁵ However, with the extremely high efficacy of these vaccines during their clinical trials, this technique seems to have been validated and may direct the future of vaccine research.

Early research on the adverse reactions of these COVID-19 vaccines has demonstrated delayed injection site reactions, fever, fatigue, headache, myalgia, nausea, and skin rash.^{6,7} These reactions were more frequently reported in females, younger individuals, and after the mRNA-1273 vaccine.^{7,8} A unique depiction of multisystem inflammatory syndrome (MIS) in both children and adults has also been outlined in a landmark study from Japan.⁹ As we see the gradual decline in vaccine hesitancy and allow for longer longitudinal studies following multiple doses, it is likely we will discover additional side effects.

With millions of people now having received these unprecedented COVID-19 vaccines and many millions yet to receive it, it becomes imperative to determine the side effect profile of these vaccines. Therefore, we introduce a report of a patient who developed inflammatory fasciitis of the shoulder girdle and inflammation of the sternoclavicular

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joint following administration of the second dose of Pfizer-BioNTech COVID-19 vaccine administration in January 2021. Included are data on the clinical presentation and treatment outcomes of the patient.

2. Case report

The patient is a 48 year old male from North Carolina of South Asian ethnicity, who works as a healthcare professional in a hospital system. His medical history prior to hospital admission in January was significant only for medication-controlled hypertension and hyperlipidemia. Surgical history consists of sublingual salivary cyst excision and nasal septum surgery. Home medications include rosuvastatin and olmesartan. He is a non-smoker, does not abuse alcohol or drugs, and his BMI was 23.7 upon admission.

3. Clinical findings

As a healthcare professional, he was offered the Pfizer-BioNTech COVID-19 vaccination by his hospital system in January 2021. Following his first dose, the patient did not have any symptoms. 21 days later, he received the second dose in his left shoulder, and only had mild soreness surrounding the injection site. Around noon the following day, he reported feeling a drop in his core internal body temperature. This subjective cold sensation lasted 8 h and subsided by the time the patient went to sleep that night.

However, the next day (two days after receiving the second dose), he began to have pain in his left neck, originating where it attached to the skull and radiating to his scapula, shoulder, and anterior pectorals. The pain intensified, and by the end of the day, he could barely lift his hand, and was having severe pain and spasms throughout the left upper quarter of his body. The patient tried heating and cooling packs, oral NSAIDs, lidocaine patches, but was not able to relieve his pain. Eventually, the pain localized to the left sternoclavicular (SC) joint. He was seen in clinic the following morning, where laboratory studies were drawn (Erythrocyte Sedimentation Rate, C-Reactive Protein, complete blood cell count with differential, and rheumatologic panel) and had an X-ray and ultrasound of his left SC joint taken. All laboratory studies were within reference range except for a CRP value of 4.34, marked elevated. His X-ray did not have any remarkable findings, but ultrasound revealed a fluid collection in the SC joint (Fig. 1).

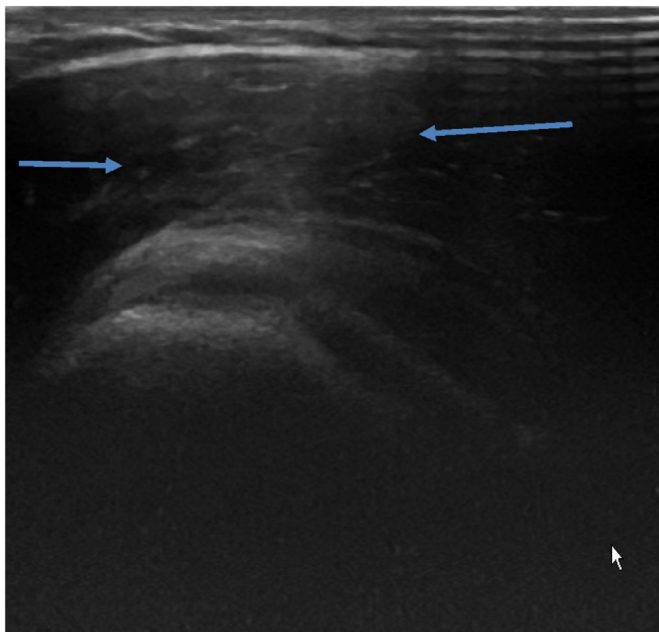


Fig. 1. Musculoskeletal ultrasound of the sternoclavicular joint showing slight swelling and fluid collection.



Fig. 2. MRI of neck and shoulder showing inflammatory fasciitis throughout the patient's left upper shoulder girdle, mild supraspinatus tendinitis, and enlarged cervical nodes.

4. Diagnostic assessment

Later that evening, his pain had exacerbated, and he developed spasms and a fever (Tmax 101.3 F), so he went to the Emergency Room. Due to his pain and spasming, he could not lay down for a physical exam until diazepam, ketorolac, morphine, and fentanyl were administered. Laboratory studies were drawn and an MRI of his left neck and shoulder were ordered, which showed inflammatory fasciitis throughout his left upper shoulder girdle, mild supraspinatus tendinitis, and enlarged cervical nodes (Fig. 2). He was admitted to the hospital, and pain was controlled with IV ketorolac and methocarbamol. Infectious Disease was consulted and performed a workup, ruling out an infectious source. Although wary of possibly blunting his COVID immune response, his managing physicians decided to administer a low-dose steroid for pain relief.

The patient's pain was controlled until his second day of admission, when his IV ketorolac was replaced with oral meloxicam. This change resulted in a pain score of 10 out of 10, and the patient required IV fentanyl for relief. His physicians then put him on a regimen of IV ketorolac, methocarbamol, gabapentin, and a hydromorphone patient-controlled analgesia pump. Although pain was controlled, the patient developed more severe spasms between his scapula and the medial border of his rhomboids. Eventually, his physicians gave him 60 mg of methylprednisolone and started him on a standing dose of 800 mg ibuprofen TID, 1000 mg acetaminophen TID, and gabapentin, methocarbamol, and oxycodone PRN. Four days after he was admitted to the hospital, the patient was discharged with a short course of prednisone, ibuprofen, and acetaminophen, which he took for one week before finally being free of pain and spasms.

At final follow up 12 months later, patient had no residual pain or lingering symptoms in the shoulder girdle or upper arm. No weakness or neurologic deficits were noted, and patient had made a full recovery.

5. Discussion

Understanding the side effect profile of these novel mRNA vaccines designed to curtail COVID-19 will allow physicians to better identify, isolate and treat patients. Our report aims to share the scenario in which a patient developed severe pain, muscle spasms, inflammatory fasciitis in the shoulder and inflammation in the SC joint in the post-vaccination setting following the second dose of the Pfizer-BioNTech COVID-19 vaccine. To our knowledge, this is the first such reported case, and therefore this contribution of the presentation and pathogenesis of this orthopaedic complication may provide further information regarding clinically adverse effects from this nascent immunological advancement.

Our current recognition of the adverse reactions following vaccination comes from decades of research on accessible vaccines. Thus, we have come to expect mild to moderate pain, swelling, and erythema at the injection site following each dose of routine vaccinations such as influenza and hepatitis.^{2,5,10} However, very little is currently known about the effects of mRNA vaccines. In a recent study on 134 patients with cancer being actively treated by checkpoint inhibitors, Waissengrin et al. found that administration of the Pfizer BNT162b2 mRNA vaccine was most associated with pain, rash, and local swelling, whereas the most common systemic reactions were myalgia, fatigue, headache, fever, chills, and gastrointestinal complications.⁴ Kadali et al. investigated the side effects of the Moderna mRNA-1273 vaccine. After surveying 432 healthcare workers who had received the vaccine, authors disclosed many of the same side effects as the ones reported by Waissengrin et al. with the addition of muscle spasms, decreased sleep quality, brain fogging, flushing, heat/cold intolerance, and palpitations.¹¹ Interestingly, the authors of both studies stated that none of the reported side effects from either vaccine required admission to the hospital or any other special intervention, unlike the patient in our report.

One possible explanation for the shoulder pain following vaccination is a rare condition called Parsonage-Turner Syndrome (PTS). PTS is characterized by an inciting event like infection, medication, surgery, or vaccination resulting in sudden unilateral shoulder pain that quickly amplifies in severity.¹² The pain is associated with neurological ischemia, resulting in brachial plexopathy or neuralgic amyotrophy, confirmed through nerve conduction studies or electromyography. This nerve insult then causes weakness in the muscles of the upper extremity. PTS is usually self-limiting, with resolution of pain within a week and full neurological recovery within months. Though very uncommon, there has been one reported case of Parsonage-Turner Syndrome following the Pfizer COVID-19 vaccine.¹³ Mahajan et al. describe a 50 year old male patient who developed pain and weakness in his left hand grip and left wrist extension one week after his second dose.¹³ Diagnosis was made by electromyography, showing decreased motor unit recruitment, and the patient recovered fully with one dose of oral prednisone 40 mg/day followed by a five-week taper down to 5 mg/day.

The patient in our study was seen by neurologists at our institution out of concern for possible PTS. Upon their examination, they found no evidence of brachial plexus involvement, as the patient had no numbness or weakness. Additionally, the pain of Parsonage-Turner syndrome is usually a deep aching pain more towards the shoulder and sometimes around the scapula, which was different than his pain. Finally, the pain of Parsonage-Turner does not usually respond as well as his pain did to steroids. Their final recommendation stated that there was no need for further imaging or an EMG nerve conduction study.

Recently, case reports have described the clinical course of Rheumatic-Immune-Mediated Inflammatory Disease (R-IMD) following severe acute respiratory syndrome coronavirus SARS-CoV-2 vaccinations. For instance, one paper found a new diagnosis of systemic lupus erythematosus with necrotizing lymphadenitis in a previously healthy, 24 year old Caucasian male following his second dose of Pfizer-BioNTech SARS-CoV-2 vaccine.¹⁴ As some of the symptoms our patient was experiencing could be attributed to autoimmune or rheumatological etiologies, a rheumatologic panel was also performed on the patient,

including IgG and IgM studies and vaccine specific antibodies. The results of the studies returned unremarkable for any rheumatological or auto-immune workup.

A new term, but not phenomenon, may provide us with yet another link explaining our patient's clinical picture. Shoulder injury related to vaccine administration (SIRVA) is a medicolegal term first introduced in 2010 to describe "shoulder pain with limited range of motion within 48 hours after vaccine receipt in individuals with no prior history of pain, inflammation, or dysfunction of the affected shoulder before vaccine administration."¹⁰ The pathophysiology is not understood, though consensus suggests an inflammatory response is generated when a vaccine is injected into tissues containing a preexisting antibody, resulting in bursitis. Though physical exam elicits severe pain and limited range of motion about the shoulder, neurological findings of weakness and sensory loss are less common. Imaging may be nonspecific in cases of SIRVA, and as such it remains a primarily clinical diagnosis. Treatment of SIRVA includes NSAIDs, corticosteroid injections, and physical therapy, with some cases requiring surgical intervention.¹⁰ SIRVA has been most discovered in cases of inactivated influenza vaccination, finding rates of up to 2.5%. Given both the novelty and the rampant global-scale distribution of the COVID-19 mRNA vaccines, rates of SIRVA are expected to rise sharply in the following years.

Initially, our patient's managing physicians postulated that his sternoclavicular pain might be due to SC joint arthropathy, given localized pain and presence of fluid on ultrasound. However, this seems unlikely given absence of swelling and redness on physical exam, negative radiographic changes on X-ray, and lack of soft tissue swelling in the SC joint on MRI. Furthermore, arthropathy symptoms often last for a few months and are alleviated by NSAIDs, rarely requiring corticosteroids, neither of which are consistent with our patient's presentation.¹⁵ Finally, while SC joint arthropathy has been linked to traumatic and infectious etiologies, there is currently no post-vaccine association.^{10,15}

Herein, we present a case in which a patient developed inflammatory fasciitis of the shoulder girdle and sternoclavicular joint inflammation requiring hospital admission following COVID-19 vaccination. Initial concern was for infectious source given fever and mild systemic symptoms, although this was ruled out following workup by his physicians. Parsonage-Turner Syndrome may explain the pain and spasms, but our patient did not have any neurological sequelae such as weakness or sensory loss. The patient's clinical manifestations could possibly be attributed to SIRVA, as he experienced new onset shoulder and scapular pain shortly after the second dose and developed an inflammatory picture. Yet, the patient's intricate pain regimen including oscillating between IV opioids, NSAIDs, and steroids, as well as the presence of unexplained SC joint pain and inflammation makes the diagnosis more complex. The Pfizer representative at the patient's institution was equally perplexed, saying he had never seen any case like this one.

Of course, these vaccines have proven efficacy against COVID-19 and we wholeheartedly advocate for those who are able to get vaccinated against this virus that has uprooted so much. Nonetheless, the full array of the musculoskeletal side effect profile carried by these novel COVID-19 mRNA vaccines requires further investigation and monitoring as people continue to receive their doses and more cases begin to present themselves.

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Informed consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for patient images and other clinical information to be reported in the journal. The patient understands that his names and initials will not be published and

due efforts will be made to conceal his identity.

Authors contribution

AS was the primary author and gathered the information regarding the case and did the majority of the writing for the manuscript.

SGP was the principal investigator and wrote part of the manuscript, as well as providing editing and revision help.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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