

**Case Report**

**Calcific Tendinitis of the Shoulder Induced by an mRNA Vaccine for COVID-19: A Case Report**

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**Abstract**

Coronavirus disease 2019 (COVID-19) vaccines have been widely used and have been shown to be effective in combating the pandemic. However, various side effects have been reported following vaccination. For instance, a condition called “shoulder injury related to vaccine administration” (SIRVA) is characterized by shoulder pain and limited range of motion after intramuscular injection of a vaccine into the deltoid muscle of the shoulder.

Despite an increase in SIRVA cases, the exact incidence of the disease is unclear, and there are a few reports of SIRVA about the COVID-19 vaccine. Here, we report a rare case of an 83-year-old woman who was diagnosed with calcification in her left shoulder one year ago and developed calcific tendinitis after receiving an mRNA vaccine for COVID-19 (Pfizer-BioNTech). Radiographs showed calcification of the supraspinatus tendon, and magnetic resonance images showed continuous inflammatory findings from the subdeltoid bursa to the subacromial bursa. We treated the patient with celecoxib and acetaminophen, and she recovered after about two months. In order to prevent SIRVA, the presence of shoulder joint disease should be carefully asked during a pre-vaccination assessment. The puncture point should be chosen with the median point of the deltoid muscle or

the anterior-posterior axillary line as landmarks, because the more cephalad the puncture position, the greater the chance of causing SIRVA.

Keywords: calcific tendinitis; shoulder injury related to vaccine administration; COVID-19; vaccine; mRNA

## Introduction

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection remains unabated and widespread. There has been a significant increase in the number of deaths caused by coronavirus disease 2019 (COVID-19) infection [1]. COVID-19 vaccines have been widely adopted and have proven efficacious in fighting this pandemic [2]. Various side effects have been reported after vaccination, and these side effects include fatigue, headache, chills, local swelling and discomfort, anaphylaxis, and thrombosis, but the most common are local symptoms [3,4]. Shoulder pain and limitation of range of motion after intramuscular administration of a vaccine to the deltoid muscle of the shoulder is called shoulder injury related to vaccine administration (SIRVA) and is mainly reported after influenza vaccination [5]. Despite an increase in SIRVA cases [6], the exact incidence of the disease is unclear, and there are a few reports of SIRVA about the COVID-19 vaccine [7–11]. Here, we described a patient who developed calcific tendinitis after receiving an mRNA vaccine for COVID-19 (Pfizer-BioNTech). The patient had severe local inflammation following the injection.

## Case presentation

After being diagnosed with calcification in her left shoulder one year ago, an 83-year-old woman had her first COVID-19 injection (mRNA vaccine from Pfizer-BioNTech) in the left deltoid muscle. During the procedure, a puncture was made 8 cm caudal to the acromion. For two days, left shoulder pain appeared and then improved. The second injection (mRNA vaccine from Pfizer-BioNTech) was performed 26 days later at a point 4 cm caudal to the acromion. She experienced worse discomfort, swelling, and heat compared to the first injection, and the pain did not improve; thus, she went to an orthopedic department on the eighth day after the second injection. Her fever was 37.1 degrees at the time. According to radiographs, calcification in the left supraspinatus tendon had increased over the previous year (Fig. 1(A) and (B)). A blood test revealed elevated C-reactive protein (CRP) of 4.72 mg/dL. Calcium and phosphorus levels were within normal limits at 9.5 mg/dL and 4.0 mg/dL, respectively.

We diagnosed calcific tendinitis induced by COVID-19 vaccination and treated the patient with celecoxib on a regular basis and acetaminophen as needed. On the 14th day after the second vaccination, the pain and swelling in the shoulder tended to improve, and the calcification seen in the supraspinatus tendon on radiographs had almost disappeared, leaving only a small amount of calcification around the supraspinous muscle (Fig. 1(C)). The magnetic resonance images (MRIs) taken 17 days after the second vaccination revealed a high-signal lesion on the short T1 inversion recovery image and was continuous from the subdeltoid bursa to the subacromial bursa (Fig. 2). A blood test taken 21 days after the second vaccination revealed that the CRP level had improved to 0.15 mg/dL; however, the limitation of range of motion associated with pain remained. Two months after the second injection, calcification had disappeared (Fig. 1(D)). The pain in her left shoulder improved, and the range of motion was 170 degrees in flexion and abduction.

## Discussion

Since SIRVA occurs regardless of the vaccine type, such as mRNA, adenovirus and inactivated viral vaccine, it is due to the procedure of intramuscular injection. SIRVA occurs when a vaccine for intramuscular injection is accidentally administered into the subdeltoid bursa, causing inflammation within the bursa [6,12]. When measured using ultrasound, a study showed that the extent of the subdeltoid bursa from the acromion ranged from 3.0 cm to 6.0 cm, while the depth from the skin to the subdeltoid bursa was between 0.8 cm and 1.6 cm [12]. Due to its location, a 2.5 cm long needle or even a shorter 1.6 cm long needle can readily enter the bursa. The subdeltoid bursa is continuous with subacromial bursa, allowing inflammation to extend more proximally, causing tendinitis and capsulitis [6,12]. Because the second vaccine injection in our patient was proximal (4 cm caudal to the acromion) than the first, we think it is more likely that the vaccine was injected into the subdeltoid bursa. Based on the results of the MRI of continuous inflammation from the subdeltoid bursa to the subacromial bursa and radiographs of the calcification of the supraspinatus tendon, it is likely that the vaccine fluid travelled through the bursa and reached the supraspinatus area, causing inflammation.

For the optimal site of vaccine injection, several methods have been recommended. One of the insertion positions is 2-3 finger-widths (about 3–5 cm) from the acromion [13,14]; however, as mentioned earlier, when inserted into a patient, the subdeltoid bursa may extend 3.0–6.0 cm caudal to the acromion, which may overlap the insertion point. The anterior branch of the axillary nerve is also nearby, making it an unsuitable location for the nerve. In studies utilizing cadavers, the reported average distance from the acromion to the nerve was 53.2 mm [15] or 62 mm [16]. For these reasons, we do not recommend using the 2-3 finger width method.

The middle of the deltoid muscle (the midpoint between the acromion and the deltoid tuberosity) is another often used insertion point (Fig. 3). One anthropometric study showed that men and women might safely administer intramuscular vaccines at the midpoint of the acromion and deltoid tuberosity (6.8–8.5 cm from the acromion for men, and 5.5–7.3 cm for women, respectively) [17]. However, the bursa is immediately proximal so that this method may not avoid subdeltoid bursa when acromion or deltoid tuberosity are difficult to recognize, and needle insertion at an oblique angle may puncture the bursa. Using the anterior axillary line as a landmark is another way to target the caudal side of the body [18]. A study using ultrasound revealed that the posterior circumflex humeral artery (PCHA), with the axillary nerve, was located  $7.6 \pm 1.0$  cm caudal to the median lateral margin of the acromion in males and  $6.2 \pm 0.8$  cm caudal in females [18]. They concluded that the intersection between the anteroposterior axillary line and perpendicular line from the mid-acromion is far enough away from the PCHA to be safe. Conversely, caution should be exercised in this method because if the puncture is made distal to the anterior axillary line, the tendon component of the deltoid muscle will increase, resulting in poor blood flow, which may decrease immune induction [17], or the risk of radial nerve injury will increase due to the proximity of the nerve [19]. We recommend either the middle of the deltoid muscle (midpoint of the acromion and deltoid tuberosity) or the intersection of the anterior-posterior axillary line and a perpendicular line from the mid-acromion (Fig. 3). We should care not to point the needle proximally when using the mid-deltoid method and not to point the needle distally when using the anterior axillary line method.

It is unknown whether the specific types of vaccine increase the risk of SIRVA. However, injecting vaccine antigens into humans who have been sensitized due to a previous natural infection or vaccination may be more susceptible to the onset of SIRVA [20]. Preexisting antibodies in the synovial tissue due to previous infection or vaccination may prolong the inflammatory response in the case of accidental injection of a vaccine into the synovial space (bursa or joint) of the shoulder [20,21]. In this case, the mRNA vaccine, which contains a nucleoside-modified RNA encoding the SARS-CoV-2 full-length spike [2], might be accidentally injected into the subdeltoid bursa, which may have generated spike proteins in the synovial space, triggering robust antigen-specific CD8+ and Th1-type CD4+ T cell response [2]. mRNA vaccinations would have the same risk of SIRVA occurrence as other vaccines because of this mechanism.

One reason for the particularly intense inflammation in our patient was a history of calcific tendinitis. After vaccination, degeneration of the shoulder joint, which had been previously asymptomatic or mildly symptomatic, may become symptomatic [20]. Patients with degenerative diseases of the shoulder joint may benefit from the vaccination of the opposite shoulder. However, there are no clear criteria for which side of the

shoulder should be vaccinated when there is a history of shoulder joint disease, making it difficult to decide how to manage. The presence of a shoulder joint disease should be duly enquired during pre-vaccination assessment.

The recommended treatments for SIRVA include non-steroidal anti-inflammatory drugs (NSAIDs) medication, physical therapy, and corticosteroid injections (CSIs) [22], but the study suggests that it is necessary to consider the acute and chronic phases separately. Active inflammation occurs in the acute phase, so NSAIDs are good to use to reduce inflammation. CSIs are also effective in reducing inflammation but should only be administered if the possibility of infection is low, as infection can occur after vaccination in rare cases [23,24]. In the acute phase of inflammation, aggressive physical therapy may be difficult, and rest and cooling of the shoulder joint are crucial. Physical therapy should be considered in the chronic period to keep the range of motion of shoulders intact [14].

SIRVA remains not widely recognized, especially in Japan. The reason for this is that Japan has a history of many quadriceps femoris contractures caused by intramuscular injections, and even today, intramuscular injections tend to be avoided. In fact, the influenza vaccine is often administered intramuscularly worldwide, but in Japan, it is injected subcutaneously for fear of muscle contracture. The COVID-19 vaccine is administered intramuscularly in principle, so we need to raise awareness of SIRVA.

One of the limitations of this report is that it is difficult to determine whether the calcific tendinitis is due to a side effect of the vaccine or an "accidental" occurrence. To the best of our knowledge, there have been no reports of calcific tendinitis after vaccination, suggesting that the COVID-19 vaccine is not particularly prone to calcific tendinitis.

In conclusion, we described a case of calcific tendinitis caused by an mRNA vaccine for COVID-19 that resolved with medical therapy. During a pre-vaccination assessment, the presence of shoulder joint disease should be carefully asked. The puncture point should be chosen with the median point of the deltoid muscle or the anterior-posterior axillary line as landmarks, because the more cephalad the puncture position, the greater the chance of causing SIRVA.

#### **Patient consent**

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

#### **Ethical approval**

Not applicable.

## Conflict of interest

None.

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### Figure legends

Fig. 1

The radiograph of the left shoulder taken on the eighth day from the vaccination (**B**) showing larger calcification than one year ago (**A**) (arrow). Most of the calcification disappeared on the 14th day (**C**) (arrowhead), and finally disappeared (**D**).



Fig. 2

**(A)** Coronal and **(B)** axial magnetic resonance images taken 17 days after the second vaccination showing a high-signal lesion on the short T1 inversion recovery image continuous from the subdeltoid bursa to the subacromial bursa (arrowhead). An arrow represents the presumed injection site.



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Fig. 3

Appropriate locations for vaccine administration: the middle of the deltoid muscle (midpoint of the acromion and deltoid tuberosity; blue star) and the intersection of the anterior-posterior axillary line and a perpendicular line from the mid-acromion (yellow star).

