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Original Article

Analysis of patients with adhesive capsulitis after COVID-19 vaccination: An observational study

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ABSTRACT

Objectives: This study aimed to increase the awareness of clinicians about shoulder injury related to vaccine administration (SIRVA) by analyzing 21 patients with adhesive capsulitis that developed after COVID-19 (coronavirus disease 2019) vaccination.

Patients and methods: In this observational study, 21 patients (11 males, 10 females; mean age: 60.7±7.3 years; range, 45 to 70 years) with incipient shoulder pain and limitation diagnosed with adhesive capsulitis due to SIRVA were evaluated between June 2021 and December 2022. Demographic and clinical data of the patients were recorded. Pain was evaluated with the Visual Analog Scale (VAS). The passive range of motion (ROM) of the affected shoulder was measured by a goniometer. The applied treatment methods (medical treatment, physical therapy, intraarticular steroid injection, hydrodilatation, and suprascapular nerve block) were recorded. The patients were called in for control two months later. Visual Analog Scale scores and passive shoulder ROMs were reevaluated.

Results: Symptoms started after the second dose in nine (42.9%) patients. The mean time between vaccination and onset of complaints was 8.0±6.4 days. Sinovac vaccine was administered to eight patients, BioNTech vaccine was administered to five patients, and Sinovac+BioNTech vaccine was administered to eight patients. Baseline to control ROM angle changes were 128.8±30.4° to 155.0±20.6° for flexion, 117.1±37.8° to 147.1±26.4° for abduction, 45.9±17.8° to 61.9±12.6° for internal rotation, and 43.4±21.9° to 56.3±18.3° for external rotation, respectively. The mean VAS scores were 7.0±1.2 (5-9) at baseline and 2.7±1.0 (1-5) at the control. There was a statistically significant difference between the baseline and control (two months after treatment) in terms of VAS scores and ROM angles ($p<0.001$).

Conclusion: Clinicians should be aware of adhesive capsulitis following vaccine administration since a significant improvement can be obtained by proper treatment for SIRVA.

Keywords: Adhesive capsulitis, COVID-19, shoulder, SIRVA, vaccine.

Shoulder injury related to vaccine administration (SIRVA) is a term used to describe shoulder pain and limited range of motion that occurs within 48 h of vaccine administration and persists for more than one week.[1,2] The relationship between the injection of the vaccine to the deltoid muscle with the wrong technique into the synovial tissue and the inflammation of the structures below the deltoid muscle is well known.[1,2-8]

In a patient with no previous history of chronic pain or inflammatory disease, there are findings consistent with the rapid onset of pain and local immune-mediated inflammatory reaction after intramuscular vaccination in the shoulder. Pain in SIRVA usually begins within 48 h of vaccination and may persist for months.[1,4] Bursitis, adhesive capsulitis, and glenohumeral synovitis may occur in the shoulder after vaccine injection.[2-8]

While reports on influenza and tetanus vaccines are the most common in the literature,[2,8-10] there have been case reports and case series describing SIRVA

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symptoms after COVID-19 (coronavirus disease 2019) vaccine administration.[1,11-20] In this study, we wanted to emphasize that clinicians should be aware of adhesive capsulitis after SIRVA by analyzing 21 patients who developed adhesive capsulitis after COVID-19 vaccine administration.

PATIENTS AND METHODS

Twenty-one adhesive capsulitis patients (11 males, 10 females; mean age: 60.7±7.3 years; range, 45 to 70 years) with new-onset shoulder after COVID-19 vaccination who applied to the physical therapy and rehabilitation outpatient clinic of the Health Sciences University, Ankara Training and Research Hospital between June 2021 and December 2022 were evaluated in this observational study. Patients who had no shoulder pain complaints before the vaccination and had new-onset shoulder pain and limitation after the vaccination were included in the study. Patients with history of trauma, fracture, shoulder surgery, or bilateral shoulder involvement, patients with abnormal findings on direct radiography as calcific tendinopathy, tumors, or advanced degenerative disease, and those with neurological, psychiatric, and rheumatological diseases were excluded from the study. Patients' age, sex, dominant extremity, affected extremity, time between the vaccine and the complaint, comorbid diseases, the name of the vaccine, the total number of vaccine doses, and the number of doses that started the complaints were noted. Shoulder pain during movement was evaluated with the Visual Analog Scale (VAS) on a scale of from 0 to 10. Zero represented "no pain," whereas 10 represented "most severe pain." The affected side's shoulder range of motion (ROM) angles were measured by the same clinician with a goniometer. First, the patient was asked to actively bring the shoulder to flexion, abduction, internal rotation, and external rotation, respectively, while lying in the supine position. Afterward, the clinician tried to passively complete the ROM, and the angle was measured with a goniometer at the end point.

A shoulder X-ray was requested from all patients. The patients were treated with either only medical therapy (nonsteroidal anti-inflammatory drugs) and exercise or various injection techniques and physical therapy agents, depending on the intensity of pain or limitation. A suprascapular nerve block (SSNB) was administered with a mixture of 6 mL of local anesthetic (bupivacaine) and 4 mL of saline under ultrasound guidance to patients with prominent shoulder pain. Physical therapy agents (hot pack, TENS [transcutaneous electrical nerve stimulation], and ultrasound), intra-articular steroid (1 mL/40 mg methylprednisolone acetate) treatment, or ultrasound-guided SSNB + hydrodilatation (4 mL bupivacaine + 12 mL saline) combination therapy was applied to patients with significant shoulder limitation. The treatment methods applied were recorded.

A home exercise program, including passive mobilization, stretching, Codman pendulum exercises, internal rotation, external rotation, adduction, abduction, flexion, and extension was given to all patients. The patients were asked to do these exercises for half an hour every day.

The patients were called for control two months after their treatment. The VAS score was reevaluated, and passive shoulder ROM angles were measured with a goniometer during the control.

Statistical analysis

Data were analyzed using IBM SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Data values of continuous variables were expressed as mean ± standard deviation (SD). Categorical variables were expressed as numbers and percentages. The normality of the distribution of the data was tested by the Shapiro-Wilk test. For baseline and two-month VAS and ROM comparisons, the paired t-test was used for data with normal distribution, and the Wilcoxon signed-rank test was used for data with nonnormal distribution. The significance level was set at $p<0.05$.

RESULTS

Eight (38.1%) of the patients had diabetes mellitus, and two (9.5%) patients had hypothyroidism. Symptoms occurred after the first dose in three (14.3%) patients, after the second dose in nine (42.9%) patients, after the third dose in eight (38.1%) patients, and after the fourth dose in one (4.8%) patient. The mean time between vaccination and the onset of symptoms was 8.0±6.4 (range, 1-28) days. The mean time for patients to apply to our outpatient clinic was 3.8±2.4 months. The mean number of vaccines administered to the patients was 2.9±0.9 (range, 2-5). Two doses of Sinovac were administered to six patients, while three doses of Sinovac were administered to two patients. Two doses of BioNTech were administered to three patients, three doses of BioNTech were administered to one patient, and

four doses of BioNTech were administered to one patient. Two doses of Sinovac with one BioNTech were applied to four patients, two doses of Sinovac with three BioNTech were administered to two patients, and two doses of Sinovac with two BioNTech were administered to two patients. The right hand was dominant in 20 (95.2%) patients, and the left hand was dominant in one (4.8%) patient. The vaccines were administered to the nondominant arm, and the vaccinated shoulder was affected in all patients. The demographic and clinical data of the patients and treatment methods applied to the patients are summarized in Table 1. No abnormal finding was detected in the direct radiographs of the patients.

The mean baseline VAS score was 7.0±1.2 (min-max, 5-9). The mean VAS score two months after the treatment was 2.7±1.0 (min-max, 1-5). The mean baseline affected side shoulder flexion angle was 128.8±30.4°, abduction angle was 117.1±37.8°, internal rotation angle was 45.9±17.8°, and external rotation angle was 43.4±21.9°. At the two-month control, the mean shoulder flexion angle of the involved side was 155.0±20.6°, abduction angle was 147.1±26.4°, internal rotation angle was 61.9±12.6°, and external rotation angle was 56.3±18.3°. The VAS score two months after treatment was statistically significantly lower than the initial VAS score ($p<0.001$). The mean ROM at the second month was statistically significantly increased compared to the baseline ($p<0.001$, Table 2).

TABLE 1
Demographic and clinical data of the patients

	n	%	Mean±SD
Age (year)			60.7±7.3
Sex			
Female	10	47.6	
Male	11	52.4	
Comorbidity			
Present	10	47.6	
Absent	11	52.4	
Affected shoulder			
Right	1	4.8	
Left	20	95.2	
Vaccines			
Sinovac	8	38.1	
BioNTech	5	23.8	
Sinovac + BioNTech	8	38.1	
Treatments			
Medical treatment + Exercise	7	33.3	
SSNB + Exercise	6	28.6	
SSNB + Hidrodilatation + Exercise	5	23.8	
Physical therapy + Exercise	2	9.5	
Physical therapy + Intra-articular steroid + Exercise	1	4.8	

SD: Standard deviation; SSNB: Suprascapular nerve block.

TABLE 2
The baseline and two-month VAS scores and ROM angles of the patients

	Baseline		2nd month		
	Mean±SD	Min-Max	Mean±SD	Min-Max	*p*
VAS score	7.0±1.2	5-9	2.7±1.0	1-5	
Flexion	128.8± 30.4°		155.0±20.6°		
Abduction	117.1±37.8°		147.1±26.4°		<0.001
Internal rotation	45.9±17.8°		61.9±12.6°		
External rotation	43.4±21.9°		56.3±18.3°		

VAS: Visual Analog Scale; SD: Standard deviation; ROM: Range of motion.

DISCUSSION

In the past years, millions of doses of COVID-19 vaccines have been administered worldwide due to the pandemic. This prospective observational study described the clinical features of 21 patients who developed adhesive capsulitis after COVID-19 vaccination and applied to our outpatient clinic. In the literature, there is no study with as many cases as ours on adhesive capsulitis after the COVID-19 vaccine. Vaccine inquiries must be made in patients presenting with adhesive capsulitis; if not, clinicians can easily overlook SIRVA. Since adhesive capsulitis after SIRVA is a condition with a good prognosis and responds well to treatment, early diagnosis and initiation of treatment are vital. We also achieved significant improvement in both pain and ROM of the affected shoulder in our patients two months after treatment.

Symptoms of SIRVA may develop if the intramuscular injection to the deltoid muscle is applied to the shoulder joint with the wrong technique.[19] Shoulder injury related to vaccine administration is thought to be induced by an inflammatory immune response to vaccines or adjuvants as a result of inappropriate injection techniques into the anatomical structures adjacent to the deltoid muscle. The most commonly reported cause is intrabursal injections, which can lead to subacromial and subdeltoid bursitis, as well as adhesive capsulitis. However, rotator cuff tears, tendinopathy, chondral lesions, septic arthritis, and nerve injuries have also been reported under the diagnosis of SIRVA.[20,21] The subdeltoid bursa is located between 0.8 and 1.6 cm below the skin surface, a distance easily penetrable by the standard 25-mm needle. Therefore, the appropriate needle length should be chosen, taking into account sex and weight, instead of the standard needle when injecting.[22]

Ghosh et al.[23] evaluated nine patients who developed adhesive capsulitis after the COVID-19 vaccine in their recent case series. Although the pathogenesis is not fully known, they drew attention to the SIRVA hypothesis, which causes local spread of the vaccine through microvascular structures and nerves in the deltoid muscle or secondary adhesive capsulitis. Five of the patients were male, four were female, and the mean age was 48.7±12.7 years. The time from vaccination to symptom onset was 12.3±3.1 days, and the mean symptom duration was 9.4±2.4 weeks. In our study, the mean time between vaccination and the onset of symptoms was shorter (8.0±6.4), and the duration of admission to our outpatient clinic was longer (3.8±2.4 months). The reason for this may be that the patients applied to different polyclinics, such as orthopedics and family medicine, before applying to us. This shows the importance of clinicians' awareness of adhesive capsulitis due to SIRVA. If clinicians had noticed this situation and referred the patient to a physical medicine and rehabilitation clinic earlier, early diagnosis and treatment of patients would have been possible.

Similar to our study, Ghosh et al.[23] applied nonsteroidal anti-inflammatory drugs, intra-articular steroid injection, and SSNB in the treatment of patients with adhesive capsulitis after the COVID-19 vaccine and found a decrease in pain and an increase in ROM after eight weeks.

Bass and Poland[20] recently published a review examining 333 cases who developed SIRVA after COVID-19 vaccination. In these patients, the sex ratio was 76% female and 24% male. However, in our study, the female-to-male ratio was almost one (10/11). In Bass and Poland[20] study, 62 patients commented the onset of their symptoms in relation to vaccine administration. Nineteen patients reported immediate onset, 22 patients reported onset within 24 h, five patients reported onset between 24 and 72 h, and 16 patients reported onset over days to weeks. Of patients with imaging-confirmed SIRVA (n=95), the most common diagnoses were adhesive capsulitis (37.9%) and bursitis (34.7%), and the most common symptom was pain. The most common diagnostic modality was X-ray (n=49) in the study; X-ray was also utilized in our study to exclude other shoulder pathologies, and we did not detect any abnormality. All of our patients had pain and limitation of movement. We diagnosed adhesive capsulitis with history and clinical findings. In this case, an expensive imaging method such as MRI was not required.

Although SIRVA is well-established in the literature, the pathogenesis of adhesive capsulitis due to COVID-19 vaccination is still unclear. Sporadic adhesive capsulitis cases have been reported after other vaccines.[24,25] Bass and Poland[20] determined that adhesive capsulitis secondary to COVID-19 vaccination is under the umbrella of SIRVA. Sahu and Shetty[26] reported 10 patients with adhesive capsulitis after COVID-19 vaccination. The authors explained that adhesive capsulitis may be due to vaccine transfection to local capsular tissue or nerves, which leads to an autoimmune response. The other reason for SIRVA is that the antigen-antibody reaction due to the injection of the antigen into the subacromial/subdeltoid bursa

leads to acute and prolonged hyperinflammation.[10] Overpenetration, wrong injection site, and inappropriate vaccination technique have also been referred as possible causes.[26]

Biglia et al.[27] presented a case of a 50-year-old female patient who developed adhesive capsulitis and subacromial/subdeltoid fibroadhesive bursitis 48 h after the second dose of COVID-19 vaccination. When the patient did not benefit from nonsteroidal anti-inflammatory drugs, they applied capsule hydrodistension two times with an interval of two weeks under ultrasound guidance, and after one month with exercise therapy, they achieved almost complete improvement in pain and shoulder ROM.

Adhesive capsulitis is a clinical condition frequently observed in our daily practice. However, adhesive capsulitis after vaccine administration is underreported and a significant cause of postvaccine morbidity. Therefore, the symptoms of SIRVA should be recognized by clinicians and the patients must be immediately directed to the relevant outpatient clinics for treatment.

This study has some limitations. One limitation is the short follow-up period of the patients, and the absence of a control group. There may be a need for randomized controlled prospective studies in which patients can be followed and evaluated for a longer period of time.

In conclusion, adhesive capsulitis may rarely manifest after vaccination and may not be noticed by clinicians. It is crucial to know the relationship between adhesive capsulitis and vaccine administration due to the need for early diagnosis and treatment. Significant improvement can be obtained in the treatment ofpatients with adhesive capsulitis after SIRVA secondary to the COVID-19 vaccine.

Ethics Committee Approval: The study protocol was approved by the Health Sciences University Ankara Training and Research Hospital Clinical Research Ethics Committee (date: 29.12.2022, no: E-93471371-514.99.209942406). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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