Shoulder Injuries Related to COVID-19 Vaccination

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ABSTRACT
Shoulder injury attributable to vaccination (SIRVA) is an adverse event secondary to inoculation. Its most frequent cause has been vaccination against influenza, but the current massive campaign against the SARS-CoV-2 pandemic makes it an injury whose knowledge is of importance for specialists. It includes different structural lesions and has a torpid and prolonged evolution. SIRVAs must be reported to the sanitary control agencies. Their treatment is based on the use of corticosteroids and rehabilitation.

Key words: COVID-19; bursitis; vaccine; shoulder pain.

Lesiones de hombro atribuibles a la aplicación de la vacuna contra la COVID-19

RESUMEN
Las lesiones de hombro atribuibles a la vacunación son aquellos efectos adversos secundarios a una inoculación. Su causa más frecuente ha sido la vacunación contra la gripe, pero la actual campaña masiva por la pandemia de SARS-CoV-2 determina que los especialistas conozcan este cuadro para un mejor diagnóstico y tratamiento. Estas lesiones tienen una evolución tórpida y prolongada. Deben notificarse a las agencias de control sanitario. Su tratamiento se basa en la administración temprana de corticoides y la rehabilitación.

Palabras clave: COVID-19; bursitis subacromial; vacuna; dolor de hombro.

Nivel de Evidencia: V

INTRODUCTION
The global emergency generated by the outbreak of the SARS-CoV-2 pandemic has determined the need for a massive vaccination campaign in order to achieve mass immunization quickly. This entails the daily application of millions of vaccines in all corners of the planet. 1

The site of inoculation is the deltoid muscle, as it is a safe area that allows a good immune response with low adverse effects, does not make ambulation difficult, and is easy for the patient to expose. 2-3 However, it is not complication-free. The most frequently reported adverse effect, regardless of the type of vaccine applied to the shoulder, is pain at the site of inoculation. 4-9 There may also be redness, itching, edema, tenderness, induration, and bruising. 4-12 All these symptoms are usually mild and transitory, disappearing two or three days after vaccination. 12

In a smaller percentage of cases, severe and persistent local symptoms occur that include severe pain, loss of active and passive range of motion, and functional disability. The acronym that identifies this situation is SIRVA (Shoulder Injury Related to Vaccine Administration), a term with medicolegal implications that was coined by Atanasoff in 2010. 4 We have not found reports in Spanish related to this condition. Our Spanish translation is “Lesiones de Hombro Atribuibles a la Vacunación” (LHAV).
The objective of this presentation is to provide information to the general traumatologist in order to properly diagnose, report, and treat these cases.

Definition

It would be a mistake to consider that any painful condition located in the shoulder after the application of a vaccine is attributable to it. A high percentage of people who receive the injectable flu vaccine report tenderness, swelling, and pain at the site of application, but this does not justify the SIRVA rating.

There is a very precise definition that includes a series of conditions to be able to consider a severe injury as attributable to the application of a vaccine: 13,14

1. Pain should begin within 48 hours after inoculation.
2. Symptoms must last at least seven days from their onset.
3. The condition includes the loss of active range of motion that can also be accompanied by a decrease in passive range of motion.
4. Symptoms taking place immediately before inoculation cast doubt on the existence of an event attributable to the act of vaccination.

SIRVAs most commonly present with subacromial and subdeltoid bursitis4,6,8,15 and rotator cuff injuries.4,5,8,13,15 Regarding the most affected tendons, supraspinatus, subscapularis, infraspinatus, and teres minor injuries have been reported.13,14 Szari et al.10 described a case of SIRVA with magnetic resonance imaging of tendinopathy in the four tendons of the rotator cuff and possible calcifying tendinopathy of the teres minor.

There have been reports of biceps tendinopathy,4 glenohumeral effusion and synovitis,14-16 adhesive capsulitis,5,8,11,16 myositis,16 formation of sterile intramuscular abscesses,15 osteitis,16 accumulation of fluid in the deltoid16 (Figure 1) and in the rotator cuff,16 erosive arthritis,16 septic arthritis,4 osteomyelitis,15 and osteonecrosis.18

Figure 1. Fluid image in the thickness of the deltoid muscle after receiving the COVID-19 vaccine.
There have also been published reports of nerve injuries including the anterior branch of the axillary nerve, C6 radiculopathy, and complete radial palsy.\textsuperscript{19,20} Cases of Parsonage-Turner syndrome secondary to vaccination have also been reported.\textsuperscript{21}

The experience is more limited with vaccination against COVID-19 because its implementation is recent. So far, two cases of subacromial bursitis,\textsuperscript{12,15} one case of septic arthritis\textsuperscript{8}, and four cases of brachial plexitis\textsuperscript{21} have been reported. It should be noted that the case published by Chuaychoosakoon et al.\textsuperscript{12} is debatable because, in the radiographs, a previous advanced glenohumeral osteoarthritis is appreciated.

**Epidemiology**

The exact rate of severe local complications secondary to vaccination in the shoulder area is not known. There is undoubtedly a lower report of adverse effects.\textsuperscript{5,10} One of the factors that contribute to this is that the system, in most countries, is based on the voluntary reporting of suspected adverse reactions by healthcare professionals and patients, making it difficult to measure the actual incidence.

In the United States, there is the National Vaccine Injury Compensation Program (VICP) that, since 2010, has received claims related to injuries allegedly caused by vaccination. According to the Vaccine Adverse Event Reporting System (VAERS) of that country, between 2010 and 2016, there were 1,006 reports of shoulder dysfunction after the application of the inactivated influenza vaccine compared to an estimated 130 million doses of this vaccine administered each flu season in the US.\textsuperscript{10}

Although the percentage is very low, complaints have progressively increased. In 2011, seven complaints were filed with the VICP, while in 2016, there were 446.\textsuperscript{13}

The literature reveals that the majority of cases occur in women.\textsuperscript{4,5} Although the reports correspond to a wide age range (from 21 months to 90 years), they are most frequent in the middle age of life, averaging around 50 years.\textsuperscript{5} The most frequent cause is vaccination against influenza,\textsuperscript{4,5} but they can occur after any type of vaccine applied to the shoulder.

Almost half of the people with shoulder injuries reported that they had been vaccinated too high in the arm.\textsuperscript{4} Pain usually appears in the first 48 hours after vaccination.\textsuperscript{4,14,19}

**Mechanism of injury**

In most cases, the condition is generated by an inadequate inoculation technique.\textsuperscript{3,8,12-15} The safe areas of inoculation, the appropriate length of the needles according to the characteristics of the patient, and other technical details have been described in detail.

The technique can fail due to the vaccine being applied very high in the arm, which causes compromise of the subacromial-subdeltoid bursa, or very low, with possible neurological compromise, or very deep, with aggression on the periosteum or the joint,\textsuperscript{13} or very shallow, depositing the vaccine in the subcutaneous cellular tissue that is not sufficiently vascularized to facilitate an adequate immune response and is associated with an increase in local adverse reactions.\textsuperscript{17}

Beyond this, the injury caused by vaccination is usually greater than what would be expected from a simple trauma with a needle.\textsuperscript{5,15} When a vaccine is inoculated, an antigen-antibody reaction occurs in the muscle that causes discomfort, but in general, in a transitory and moderate way. When the vaccine solution is inadvertently injected into a synovial space, such as those in the shoulder, antibodies from previous infections or vaccination can lead to a much longer inflammatory reaction.\textsuperscript{4,15} Although COVID-19 is a new disease and the population is receiving vaccines for the first time, it is unlikely that an adult has not been exposed to adenovirus in the past.

Thompson and Ensrud\textsuperscript{11} published a case of adhesive capsulitis of both shoulders after the application of an influenza vaccine in one of them, this suggests an immune-mediated response.

Although the aforementioned studies support the possibility of an immune response, a definitive clinical study to support this theory has not yet been conducted.

Finally, aluminum compounds in the adjuvant of some vaccines may also have contributed to severe inflammatory reactions.\textsuperscript{5}
Clinical presentation

Patients typically present severe pain and decreased range of motion after inoculation of the vaccine. In many cases, the pain begins immediately, especially when the needle entered the subacromial bursa or caused an injury to the peripheral nerves. In the latter situation, the presentation begins with burning pain in the very act of inoculation. In cases of sepsis, there may be fever and even chills.¹⁸

The pain is moderate to severe and is localized in the deltoid area spreading to the arm. Over time, this leads to cervicodorsal compromise.

In the acute stage, it is important to assess and document the area of needle entry. Erythema, swelling, and bruising may be seen. In chronic stages, this disappears and muscle atrophy prevails. The deltoid region usually presents pain upon palpation.

The active range of motion is severely limited by pain; over time, adhesive capsulitis can develop, with loss of passive range of motion.

The cervical spine and cardiovascular status of the patient should always be evaluated.

Complementary studies

The images of complementary studies will vary according to the type of injury. Radiographs are nonspecific and generally do not provide useful diagnostic information.

Initial findings indicate inflammatory changes in soft tissues. It is common to detect an increase in fluid within the subacromial/subdeltoid bursa on ultrasound and magnetic resonance imaging (Figure 2). Salmon et al.²² compared these initial images with those after five months and observed a regression of joint effusion and a decrease in bursitis, so these studies may not be very conclusive in chronic conditions.¹⁴

Figure 2. Distension of the subacromial-subdeltoid bursa after the application of the vaccine against COVID-19.
Vaccine-related myositis manifests as focal or diffuse edema within the muscle at the injection site, most commonly the deltoid. It is possible to detect signs of tendinopathy or even a partial and full-thickness tear of the rotator cuff, but these are usually previous injuries.

Bone changes include focal spinal edema, typically on the lateral aspect of the proximal humerus. Cortical bone erosion has also been described.

A case of osteonecrosis was reported that manifested with typical findings on imaging studies, such as hyperemia, bone marrow edema, and collapse of the humeral head. Likewise, focal bone marrow signals were observed within the humeral head, probably due to the injection of the vaccine substance directly into bone structures, which could lead to focal osteitis.

It is always a good idea to request laboratory tests, such as CBC, ESR, and acute phase reactants, when the patient consults for the first time.

If there are doubts regarding peripheral neurological involvement, it must be taken into account that at least one month must elapse for an electrophysiological study to be meaningful. If there are signs consistent with Parsonage-Turner syndrome, it is helpful to request an MRI of the brachial plexus with and without contrast.

**Differential diagnosis**

More than 90 causes of shoulder pain have been described. The possibility of SIRVA should be suspected in a patient presenting with acute shoulder pain after administration of a deltoid vaccine.

If the patient has a confirmed disease, previous symptoms, or images of chronic lesions before the event, these findings will cast doubt on SIRVA but do not rule it out.

The first thing to rule out is sepsis. Distinguishing infectious from vaccine-related bursal disease is particularly difficult on imaging alone. Although shoulder radiographs are very likely to appear normal, there may be cortical irregularity of the humerus. On MRI, the fluid-filled bursa will appear hyperintense on the T2 sequence. On ultrasound, it will be seen as a fluid-filled anechoic structure surrounded by hyperechoic walls. In these cases, the medical history and the results of laboratory tests are the most useful elements to distinguish these etiologies.

The diagnosis of a lesion secondary to the administration of a vaccine in the deltoid region may seem very obvious and simple, but the patient is not always initially evaluated by a traumatologist. A case has been published of a patient diagnosed with Parsonage-Turner syndrome, treated with gabapentin by a neurologist, although, in reality, it was osteomyelitis of the proximal end of the humerus. One of our patients was treated by a neurologist with pregabalin for four months, without clinical response; in fact, it was a case of bursitis secondary to an improperly administered inoculation.

SIRVA is a situation that can determine a long list of musculoskeletal disorders that we have already mentioned; for this reason, we consider that the participation of a specialist in Orthopedics and Traumatology is essential for its diagnostic and therapeutic management.

As is known, the prevalence of rotator cuff injuries is extremely high in the asymptomatic population; therefore, its mere presence in a SIRVA does not necessarily imply that it is the product of inoculation.

**Treatment**

At present, there is no consensus in the literature on how to manage these vaccination-related injuries. After ruling out infection and considering that it is an acute inflammatory process that can affect different structures of the shoulder, the ideal is to begin immediately with the administration of corticosteroids.

Atanasoff et al. reported that more than half of a series of 13 patients with SIRVA required at least one corticosteroid injection at some point.

The administration of corticosteroids in the subacromial space has been proposed, but there is no scientific evidence to support it in this condition. Taking into account that it is a situation of intense pain in the shoulder, adding another mechanical aggression in the area is not a good idea. According to our experience, the use of depot corticosteroids in the gluteal region has the same analgesic effect as that applied in the subacromial space, with much less risk.

In cases of Parsonage-Turner syndrome, in addition to the initial use of corticosteroids, the administration of immunoglobulins has been proposed based on the neuroallergic hypothesis of the syndrome. In patients with peripheral neurological lesions, it is also common to administer vitamin B complexes.
Rehabilitation with gentle exercises including a home exercise program is essential and recommended by all authors. Its early and progressive implementation contributes to controlling pain and preventing the development of frozen shoulder conditions.

In chronic cases, it may be indicated to administer myorelaxant agents when there is cervicodorsal involvement. In cases that do not respond to conservative treatment, surgery has been indicated. Notably, in the series by Atanasoff et al., 31% of the patients required surgical intervention, and half of them required a second surgery.

**Prognosis**

The recovery of these conditions is not easy or fast. Definitive improvement can take weeks to years. In the first published series, which included 13 patients, less than a third made a full recovery. Most suffered persistent symptoms, such as pain and long-term limited range of motion, and all had symptoms for at least six months.

**Health report**

In the December 2020 document called “Technical Guidelines for the National Vaccination Campaign against COVID-19”, the Directorate for the Control of Vaccine-Preventable Diseases of the Ministry of Health defines the concept of Adverse Event Supposedly Attributable to Vaccination and Immunization (ESA VI). ESA VI is considered to be “any unexpected health situation (unfavorable or unintended sign, abnormal laboratory finding, symptom, or disease) that occurs after vaccination and that does not necessarily have a causal relationship with vaccination or with the biological product.”

A serious ESAVI is “any event that leads to hospitalization or prolongs it, results in significant or persistent disability, congenital anomaly, or death. Serious events must be reported to the surveillance system immediately.” We consider that SIRV A is a serious ESAVI because it implies, in many cases, a significant and persistent disability.

All ESAVIs must be notified. All “vaccination errors” that may or may not have generated an adverse effect, e.g. errors during the application, use of inappropriate diluents, wrong needles, wrong routes of administration, or overdose, must also be reported. If, by mistake, the vaccine has been administered by another route than intramuscular, the dose should be considered invalid and reported as ESAVI.

To report an ESAVI, a notification form that can be obtained online must be completed and sent to the competent authority in accordance with each jurisdiction. In the case of the Autonomous City of Buenos Aires, to the email: reportesesavicaba@gmail.com. This information will finally be communicated to the SIISA platform (Sistema Integrado de Información Sanitaria Argentino, Integrated Argentine Health Information System).

**Final considerations**

SIRVAs are rare, but when they do occur, their evolution is torpid and their management complicated. The possibility of SIRVA does not outweigh the enormous advantages of vaccination. This condition should be suspected in all people without a history of shoulder pain or dysfunction who experience sudden pain and reduced range of motion after deltoid inoculation.

The best procedure in this case includes: 1) early diagnosis, 2) ruling out infection and neurological lesions, 3) detecting which musculoskeletal structures are compromised, 4) initial treatment with corticosteroids, 5) mild rehabilitation that includes a home exercise program, 6) mandatory notification to the health authorities.
REFERENCES


