Shoulder injury related to vaccine administration (SIRVA)

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1. Introduction

The Vaccine Injury Compensation Program (VICP) was created in 1988 to ensure an adequate supply of vaccines, stabilize vaccine costs, and establish and maintain an accessible and efficient forum for individuals found to be injured by certain vaccines. The VICP is a no-fault alternative to the traditional tort system for resolving vaccine injury claims and provides compensation to people found to be injured by specific covered vaccines [1]. At its inception, the vast majority of VICP cases involved evaluation of possible vaccine-related injuries in children. In recent years, however, the program’s demographics have shifted dramatically with more than 50% of submitted cases now involving adults [2].

Thousands of vaccinations are administered to children, adolescents and adults every day in the United States with transient pain at the vaccine injection site recognized as one of the more commonly seen side-effects of vaccination [3]. The experience at VICP suggests that vaccination may infrequently cause more severe, persistent shoulder pain with prolonged restriction of function. This report summarizes a series of cases in which persistent shoulder pain following vaccination was felt to be related to administration of the vaccine, proposes a mechanism by which such injuries may occur, identifies common historical and physical examination findings in patients with shoulder pain related to vaccine administration and offers considerations for reducing the risk of shoulder injury related to vaccine administration.

2. Materials and methods

The Vaccine Injury Compensation Program houses an administrative database containing information on recent claims submitted to the Program. A query of the database was conducted to identify potentially relevant cases based on a claimed injury of “shoulder pain,” “arm pain,” “shoulder dysfunction,” “frozen shoulder,” “adhesive capsulitis,” or “shoulder bursitis.” “Brachial neuritis” was also included since this injury is frequently claimed when the arm is involved regardless of the actual diagnosis. Case histories of all submitted medical records were reviewed in detail to verify vaccination date, symptom onset and clinical course.

Cases consistent with a diagnosis of brachial neuritis or complex regional pain syndrome were excluded, as were cases of superficial localized soft tissue swelling with pain and/or superficial scarring. Two cases claiming arm pain were excluded because the onset of arm pain was reported many months following vaccination and records lacked sufficient documentation to verify any association between the onset of symptoms and vaccination. Following the review, 13 potential cases submitted between 2006 and 2010 were identified for inclusion in this report.

A literature search was conducted using PubMed and search terms of “vaccination,” with “shoulder,” “shoulder dysfunction,” “arm pain,” “needle length,” and “BMI.” The literature search was limited to publications in English.
3. Results

In the course of reviewing claims submitted from 2006 through 2010, the VICP identified 13 claims in which it appeared that vaccine administration led to significant shoulder pain and dysfunction. The demographic and clinical characteristics of these 13 cases are shown in Table 1. All individuals in this case series were adults, 85% were women, and, with one exception, all received either influenza vaccine or a tetanus-containing vaccine prior to the onset of symptoms. The mean body mass index (BMI) of patients in the case series was 27.2 (range 19.4–41.3).

A history of prior immunization with the same vaccine was confirmed in 85% of the cases. Among patients in whom a history of previous vaccination was confirmed, the interval between vaccinations was no less than 10 years for those receiving tetanus-containing vaccines and no less than 11 months for influenza vaccine. One patient developed shoulder symptoms following administration of the third of a three dose series of human papillomavirus (HPV) vaccine which was administered three months following the second HPV vaccination.

### 3.1. History and physical examination

Shoulder pain was present in all patients. Onset of pain was reported as occurring less than 24 h after vaccination in 93% and occurred immediately following injection in 54% of our cases. Forty-six percent of the patients voiced concerns regarding vaccine administration, specifically that the vaccination had been administered "too high" in the deltoid. The most common findings on examination were limited and painful range of motion. Skin and local injection site reactions were not reported and sensory symptoms such as tingling and numbness in the affected extremity were uncommon. Weakness was not a common finding in any of the cases during the initial examination and when found was attributed to pain. Deep tendon reflexes, when tested, were noted to be normal.

### 3.2. Diagnostic evaluation

Among the 39% of patients who underwent electrodiagnostic studies, none had findings suggestive of a neurological disorder such as brachial neuritis. When performed, MRI findings varied but included fluid collections in the deep deltoid or overlying the rotator cuff tendons. The path of vaccine administration replicated by inserting a needle into the deltoid, area contained an inflamed and scarred bursa/thickened tissue around a damaged tendon.

### 3.3. Clinical course

The severity and duration of shoulder dysfunction varied among patients in this case series. More than half of the patients required at least one injection of a corticosteroid over time. Surgical intervention was performed in 31% of cases with half of those cases requiring a second surgical intervention. Review of the available records showed that shoulder symptoms persisted among our cases from six months to many years. All patients had symptoms for at least six months. Less than one third of patients had complete recovery while the majority of patients in this series had continuing symptoms including persistent pain, limited range of motion, and pain on range of motion at last follow-up.

### 4. Discussion

Bodor and Montalvo [4] reported two cases of shoulder pain, weakness, and reduced range of motion following vaccination with the onset of symptoms in both cases occurring two days after vaccination. Both patients had shoulder dysfunction and pain involving multiple structures of the shoulder with reduced range of shoulder motion. One patient developed adhesive capsulitis. Both required multiple steroid injections in locations including the subacromial bursa, bicipital tendon sheath and glenohumeral joint to reach complete resolution of pain. Using ultrasound the authors investigated the location and depth of the subdeltoid bursa in their two patients and in 21 healthy controls. They found that the bursa extended from 3.0 to 6.0 cm (1.18–2.36 in.) beyond the lateral border of the acromion and that it lay anywhere from 0.8 to 1.6 cm (0.31–0.62 in.) below the skin surface; depths easily reached by the 1 in. needle used in both patients. The authors hypothesized that the vaccine was injected into the subdeltoid bursa in both of their patients causing a robust local inflammatory and immune response. They further hypothesized that since the subdeltoid bursa is contiguous with the subacromial bursa, this led to bursitis, tendonitis, and inflammation of the shoulder capsule. We found no other case reports

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1 For consistency and to reduce confusion, we will use the term "subacromial bursa" to refer to both the subdeltoid bursa and subacromial bursa in the remainder of the paper.
or epidemiologic studies regarding shoulder dysfunction resulting from vaccination.

There have been several larger studies which utilized body weight, gender, and/or body mass index (BMI) together with ultrasound evaluation of deltoide fat pad and skin fold thickness to determine the appropriate needle length for intramuscular injection in different patient groups [5–7]. In one of the few studies addressing the risk of injecting into shoulder tissues underlying the deltoide muscle, Lippert and Wall [8] assessed the risk of over-penetration through the deltoide muscle in children ages 3–18 using the needle lengths recommended by the Centers for Disease Control. They reported a risk of over-penetration ranging from 11 to 61% when using the needle lengths recommended for each age group. We found no publications regarding the risk of over-penetration due to needle length in an adult population. However, considering the ultrasound measurement findings by Bodor and Montalvo, it is conceivable that a needle length of one inch or greater could reach the bursa or other tissues in some patients, particularly adults with a lower BMI (Fig. 1).

The act of inserting a needle or injecting a non-antigenic substance into the deltoid muscle would not be expected to cause an immune-mediated inflammatory response. Even when an individual is vaccinated in the deltoid muscle with a previously administered vaccine any local injection site reaction caused by vaccine antigen–antibody interaction is expected to be relatively brief and resolve as the antigen is cleared from the soft tissues over a period of several days. If, however, a vaccine is inadvertently injected into the synovial space of the shoulder (bursa or joint), pre-existing antibody in the synovial tissues, present as a result of earlier naturally occurring infection or vaccination, may lead to a more prolonged inflammatory response [9,10]. A study by Dumonde using rabbits demonstrated that antigen injected into the synovial space was bound to existing antibody in the connective tissues of the joint leading to formation of antigen–antibody complexes and acute inflammation which lasted for six weeks [11].

We took these publications into consideration as we analyzed our case series to determine whether the injuries could be caused by vaccine administration. Since it is usually not possible to attribute causation from a case series, we took Sir Austin Bradford Hill’s proposed set of nine criteria or “viewpoints” into consideration in determining whether a causal relationship might exist between vaccine administration and shoulder dysfunction in some cases [12]. The clinical details of the patients in this series together with the published research literature on this subject meet many of Hill’s suggested criteria for a causal relationship including specificity, temporal association, biological plausibility, coherence, and experimental evidence. Of the patients in our series, none had a history of symptomatic shoulder problems prior to vaccination. They all received a vaccine to which they had previously been exposed. They all experienced the rapid onset of shoulder pain (range: immediate to four days) following vaccination. They all developed shoulder symptoms limited to the vaccinated shoulder. They all had symptoms and physical findings consistent with a local immune-mediated inflammatory musculoskeletal shoulder injury.

One of our cases provided additional evidence to support vaccine administration as a causal element in this type of injury. In this case, surgeons replicated the path of vaccine administration by inserting a needle into the deltoid area at the location identified by the patient as the injection site during reparative arthroscopic shoulder surgery. The path of the needle led through an area containing an inflamed and scarred bursa and thickened tissue around a damaged tendon. Beneath the tendon the needle came into contact with abnormally friable bone on the greater tuberosity of the humerus that gave way with pressure from the needle. We believe it is likely that this patient as well as the other patients in our series developed shoulder pain and dysfunction through the mechanism proposed by Bodor and demonstrated experimentally by Dumonde. Although shoulder dysfunction due to mechanical or overuse injury is always a diagnostic consideration, the rapid onset of pain with limited range of motion following vaccination in our series of patients is consistent with a robust and prolonged immune response within already-sensitized shoulder structures following injection of antigenic substance into the subacromial bursa or the area around the rotator cuff tendon. We believe that this type of phenomenon is not due to a specific vaccine but results from injection of a vaccine antigen to which a person has previously been sensitized as a result of previous naturally occurring infection or past vaccination. This concept is consistent with the vaccines which were given in this case series, namely influenza and tetanus vaccines which are given repeatedly over time and HPV vaccine which is given as a series of injections. We confirmed that almost all of our cases had received at least one dose of the same vaccine in the past. The two cases for which prior vaccination could not be confirmed by the medical records included one case of influenza vaccine administration and one case involving administration of a tetanus-containing vaccine. It is likely that an adult patient would have received a prior tetanus-containing vaccination at some point in their lifetime. Although it is possible that an adult may receive a first-time influenza vaccine, it is unlikely that an adult would not have had exposure to influenza virus or an influenza infection in the past. The immune response to both vaccines and infections wanes over time and may explain some of the variation in severity and duration of symptoms in our case series.

In general, chronic shoulder pain with or without reduced shoulder joint function can be caused by a number of common conditions including impingement syndrome, rotator cuff tear, biceps tendonitis, osteoarthritis and adhesive capsulitis [13]. In many cases, these conditions may cause no symptoms until provoked by trauma or other events. Reilly et al. [14] reviewed a series of shoulder ultrasound and MRI studies obtained in asymptomatic persons past middle age and found partial or complete rotator cuff tears in 39% of those individuals. Therefore, some of the MRI findings in our case series, such as rotator cuff tears, may have been present prior to vaccination and became symptomatic as a result of vaccination-associated synovial inflammation. Other findings such as fluid collections, localized tendon inflammation, and bursitis are more

Fig. 1. Anatomy of the shoulder girdle. The relationships of the subdeltoid/subacromial bursa and shoulder joint space to the supraspinatus tendon and to the greater tuberosity on which it inserts.
consistent with the vaccine needle over-penetration mechanism proposed here.

The fact that six patients in our case series reported vaccine administration “too high” in the shoulder indicates that in some of our cases the injury may have been the result of improper injection technique. Given that 62% of our cases were overweight or obese based upon BMI and that no case was considered underweight, needle length alone may not have been the cause of injection into tissues other than the deltoid. Bodor’s ultrasound findings revealed that the subacromial bursa can extend over 2.36 in. laterally from the acromion in some cases. Therefore, we agree with Bodor that avoiding the top third of the deltoid would help to reduce the risk of penetrating the bursa. In addition, while patients are often seated for vaccinations, the standing position of the provider administering the injection may also contribute to injecting inadvertently high into the deltoid. A seated patient may help to reduce the risk of injury during a syncopal episode, but an awareness of proper injection technique on the part of the vaccine administrator should also be emphasized. Thus, concurrent seating positions for both the administrator and the receiver may minimize the risk of the injection being “too high”. Additional considerations for possible future study would include the benefit of abducting the arm a few degrees laterally so that the bulk of the bursa is protected by the acromion process and possibly exploring alternate injection sites in patients with little shoulder muscle mass.

There is a notable absence of children in our case series despite the fact that they have exposure to a broad range of vaccine antigens in the first decade of life. A number of factors may explain their lack of representation in this case series. The thigh is the preferred site of vaccination in toddlers and infants thus eliminating the risk of shoulder injury in this group. In older children and adolescents, the subacromial bursa may not be as developed or as extensive as those in adults. Vaccine administration in older children may more commonly include techniques such as “bunching” of the subcutaneous and deltoid tissue prior to vaccination thus increasing the distance between the skin and subacromial bursa. Children, as a group, have a much lower likelihood of pre-existing asymptomatic shoulder injuries which might be aggravated as a result of an inflammatory reaction related to vaccination. Finally, annual influenza vaccination, the most common vaccine associated with shoulder injury in this series, may have been more selectively encouraged for children at higher risk for influenza-related complications in past years thus reducing the possibility of vaccine-related shoulder injury in children by chance alone.

Our study is limited by the absence of a control group to allow comparison of outcomes. Additionally, patients submitting petitions to the Vaccine Injury Compensation Program may not be representative of the general public, leading to the possibility of a reporting bias similar to that which might be seen with the Vaccine Adverse Event Reporting System (VAERS) [15]. The strength of our case series is that the medical records in VICP petitions are typically voluminous and comprehensive, allowing detailed analysis of each case. Thus, although there is no specific diagnostic test for shoulder dysfunction due to vaccine needle over-penetration, we are able to describe clinical qualifications and aids to diagnosis for this entity allowing identification of possible cases of shoulder injury related to vaccine administration (SIRVA).

5. Conclusions

The medical literature supports the possibility that a vaccine can be unintentionally injected into structures underlying the deltoid muscle due to inappropriate needle length and/or injection technique [4–8]. The research literature supports the potential for inducing a prolonged immune-mediated inflammatory reaction if a vaccine antigen is injected into synovial tissue structures underlying the deltoid muscle [9–11].

Our clinical case series provides additional evidence supporting the report by Bodor and Montalvo [4] that vaccine administration in the upper third of the deltoid area can have long-lasting consequences unrelated to the specific vaccine administered. Commonalities of history and physical examination among patients in our case series may be helpful in identifying patients who may have developed shoulder pain and dysfunction as a result of inadvertent vaccination into the bursa or other tissues beneath the deltoid muscle.

Soft tissue atrophy including tendon atrophy or rupture is a recognized side effect of corticosteroid injection. In situations where recent vaccination is suspected as a possible cause of shoulder pain we suggest consideration of non-invasive imaging such as MRI or high resolution musculoskeletal ultrasonography, prior to steroid injection to define any pre-existing anatomic abnormalities. Non-invasive imaging might assume greater importance if symptoms persist and additional steroid injections are being considered.

The risk of vaccine administration-related shoulder injury may be reduced by giving careful consideration to appropriate needle length based on individual patient characteristics such as gender and body mass index. Care should be taken to insure that the needle is not inserted into the upper third of the deltoid muscle.

References


