JCEWM 2023 ;1(1): 51-56

Case Series

COVID-19 Vaccination Related Lymphadenopathy as a Cause of Acute Shoulder Pain: A Report of Two Patients

Beshoy Ghaly, PT, DPT, ECS, RMSK[1]; Sarah Quintillan, PT, ECS[2]; Ryan Boggs, PT, DPT, DSc, Cert VRS[3]; Michael Ross, PT, DHSc, OCS, FAAOMPT[3]

1 Autonomy Diagnostics, New York, NY
2 Superior Quality Physical Therapy and Rehab Services, New York, NY
3 Daemen University, Amherst, New York.

Abstract

Introduction: Physical therapists have utilized ultrasound imaging for over three decades for cross sectional muscle thickness, age-related musculoskeletal changes, response of muscle to interventions, and for biofeedback. More recently, physical therapists have started to incorporate point of care ultrasound as a diagnostic tool for a variety of neuromusculoskeletal conditions including fractures, schwannomas, entrapment of neurovascular structures, and muscle disease. The purpose of this case report is to describe the evaluation and treatment of two patients with shoulder pain that was thought to be musculoskeletal in nature who were subsequently diagnosed with COVID-19 vaccination-related lymphadenopathy and also bring attention to lymphadenopathy as a potential side effect of the COVID-19 vaccination.

Case Description: The first patient case was a 26-year-old male with a chief complaint of right shoulder pain and heaviness who was referred for ultrasound imaging by his physician for a suspected rotator cuff tear. He reported that his symptoms started 2 days prior after playing basketball. The second patient case was a 33-year-old male with a chief complaint of left shoulder pain that was insidious in onset 5 days prior who was referred for ultrasound imaging by his physician. For both patients, the physical examination demonstrated full pain-free range of motion and normal muscle strength for their involved shoulders. Point of care ultrasound imaging performed by the physical therapist was also negative for tendon or bursa abnormalities for the involved shoulder in both patients. Upon further questioning, the first patient stated that he received his first of two COVID-19 vaccinations three days prior in his right deltoid region and the second patient stated that he received his first of two COVID-19 vaccinations six days prior in his left deltoid region. While both patients were afebrile, they did report a recent onset of fatigue after their vaccination. Their past medical histories were unremarkable. Ultrasound imaging of the axillary region for both patients revealed swollen lymph nodes with hilar vascularity on Doppler ultrasound imaging; the axillary nodes were also tender to palpation. Other lymph nodes in the same axillary region as well as the contralateral axillary region did not show any swelling for both patients.

Outcomes: Both patients were referred to their physicians and both were diagnosed with COVID-19 vaccination-related lymphadenopathy. Following the second of two COVID-19 vaccinations, both patients experienced fatigue, malaise, and fever that started about 8 to 12 hours after the second vaccination and resolved within 24 hours.

Discussion: Lymphadenopathy is a potential side effect of COVID-19 vaccination. This report suggests that this condition may manifest as shoulder pain that mimics musculoskeletal pathology; thus, it is important for physical therapists to be aware of this important side effect. If lymphadenopathy is suspected, appropriate screening and medical referral are necessary.

Citation: JCEWM 2023; 1(1): 51-56.

Corresponding Author:

Ryan Boggs ; rboggs1@daemen.edu

Daemen University

4380 Main Street

Amherst NY 14226

1. Introduction

In response to the COVID-19 pandemic that claimed the lives of more than 6 million people worldwide, three COVID-19 vaccines were developed and authorized by the Food and Drug Administration for emergency use.[1,2] Two of these vaccines, Pfizer and Moderna, demonstrated effectiveness rates of preventing symptomatic COVID and hospitalization of 88% and 93%, respectively. Despite the benefits of vaccination, adverse effects to the vaccines have been reported in 64% of individuals after 1 dose with adverse event rates increasing to 80% after both doses.[3] The most common adverse reactions to the vaccines, which are mild in nature and resolve within a few days, include the following: local injection site pain, fever, chills, myalgia, headache, and fatigue. Severe complications have been reported in 0.2-1.1% of cases including thrombocytopenia and allergic reactions/anaphylaxis.

One interesting adverse reaction noted following vaccination is vaccine associated reactive lymphadenopathy (VARL) which is a typical immune response but may present a diagnostic challenge during medical screening. This is of utmost clinical importance in individuals who may be seen with a history of malignancy as unilateral axillary lymphadenopathy (UAL) is frequently seen in patients with breast cancer. Determining the cause of UAL as benign or malignant is crucial following its presentation on multiple imaging studies including ultrasound, positron emission tomography, magnetic resonance imaging, mammography, and computed tomography.[8] Unilateral axillary lymphadenopathy may be seen on typical imaging for other conditions or during oncologic follow-up exams and present a diagnostic dilemma.

Physical therapists have utilized ultrasound imaging for over three decades for cross sectional muscle thickness, age-related musculoskeletal changes, response of muscle to intervention, and for biofeedback. More recently, physical therapists have started to incorporate point of care ultrasound as a diagnostic tool for a variety of neuromusculoskeletal conditions including fractures, schwannomas, entrapment of neurovascular structures, and muscle disease. Neuromusculoskeletal ultrasound is used as an extension of the physical examination to assist in the diagnosis and management of peripheral nerve and orthopedic conditions. Included in the roles of the physical therapist is medical screening to ensure symptoms are neuromusculoskeletal in nature and not a more serious medical condition that requires referral to another specialty. The purpose of this case report is to describe the evaluation and treatment of two patients with shoulder pain that was thought to be musculoskeletal in nature who were subsequently diagnosed with COVID-19 vaccination related lymphadenopathy. This case report was prepared following the CARE Guidelines.[12]

2. Patient Information, Clinical Findings, and Diagnostic Assessment

Case 1

The first patient was a 26-year-old male with a chief complaint of right shoulder pain and heaviness who was referred to a physical therapist for ultrasound imaging by his physician for a suspected rotator cuff tear. He reported symptoms started 2 days prior after playing basketball. Past medical and surgical history were unremarkable, and the patient was afebrile. The physical examination demonstrated full pain free range of motion and normal muscle strength of the right shoulder. Ultrasound imaging was negative for tendon, bursal, or joint abnormalities. Upon further questioning, the patient had received his first dose of the COVID-19 vaccination three days prior in his right deltoid region and was experiencing fatigue since the injection. Ultrasound imaging of the axillary region revealed a singular swollen lymph node with hilar vascularity (Figure 1 & Figure 2). The axillary nodes were also tender to palpation. Other lymph nodes in the same

JCEWM. **2023**, *1. 10.55566/JCEWM-D-22-00005*

axillary region as well as the contralateral axillary region did not show any abnormalities. The patient was referred to their physician and subsequently diagnosed with COVID-19 vaccination-related lymphadenopathy. The patient was advised by his physician to follow up after one week if the symptoms persisted. The patient did not show up for a follow up.

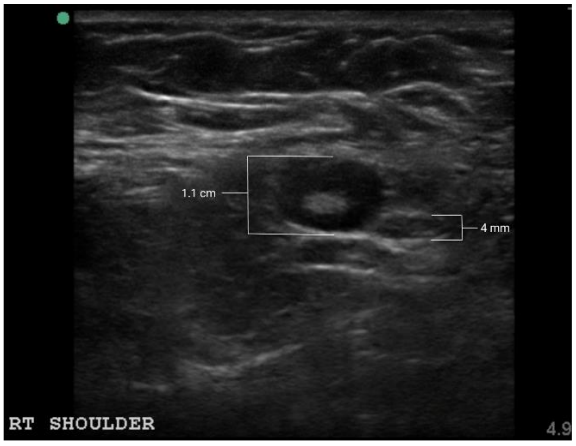

Figure 1 - Case 1. Diagnostic ultrasound assessment of the right axillary region revealing an anechoic thickened cortex ring around the hyperechoic hilum indicating a swollen lymph node which measured 1.1 cm. Note the normal appearance of the other lymph node which measured 4 mm.

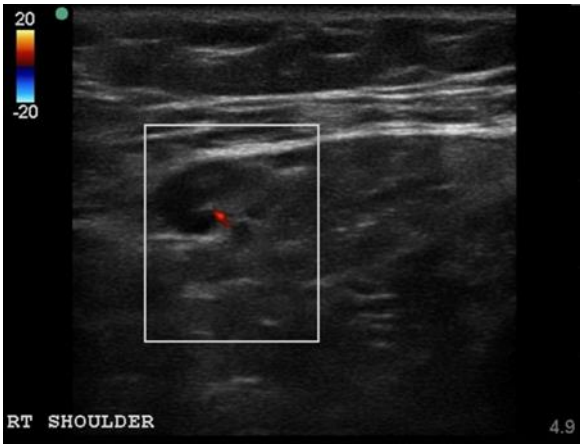

Figure 2 – Case 1. Color Doppler ultrasound assessment of the right axillary region revealing positive color Doppler findings of the swollen lymph node.

Case 2

The second patient was a 33-year-old male with a chief complaint of insidious left shoulder pain that started 5 days prior. This patient was referred to a physical therapist for ultrasound imaging by his physician. Past medical and surgical history were unremarkable, and the patient was afebrile. The physical examination demonstrated full pain free range of motion and normal muscle strength of the left shoulder. Ultrasound imaging was negative for tendon or bursa abnormalities. Upon further questioning, the patient had received his first dose of the COVID-19 vaccination six days prior in his left deltoid region and was experiencing fatigue since the injection. Similar to the first case, ultrasound imaging of the axillary region revealed a singular swollen lymph node with hilar vascularity (Figure 3 & Figure 4). The axillary nodes were also tender to palpation. Other

JCEWM. **2023**, *1. 10.55566/JCEWM-D-22-00005*

lymph nodes in the same axillary region as well as the contralateral axillary region did not show any abnormalities. The patient, much like the first patient, was referred to their physician and subsequently diagnosed with COVID-19 vaccination-related lymphadenopathy. The patient consulted the physician after 3 weeks for a regular follow up. The symptoms were resolved with no complaints of any shoulder pain or discomfort. A follow up ultrasound scan of the lymph node showed the same findings as previously noted with absent tender points using sono-palpation. The physician did not recommend a follow up visit.

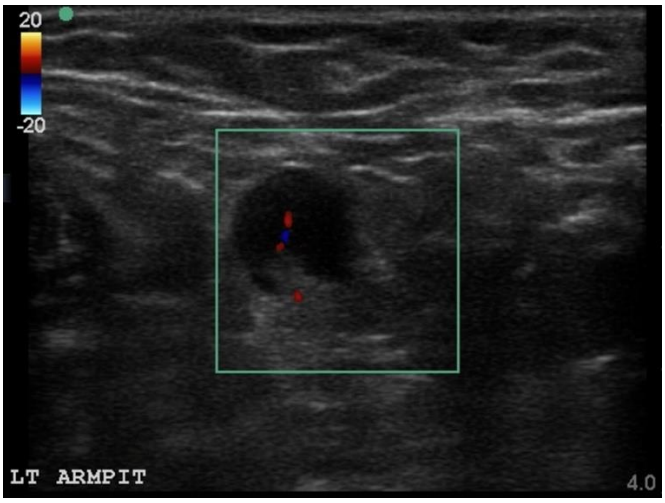

Figure 3 – Case 2. Color Doppler ultrasound assessment of the left axillary region revealing positive color Doppler findings of the swollen lymph node.

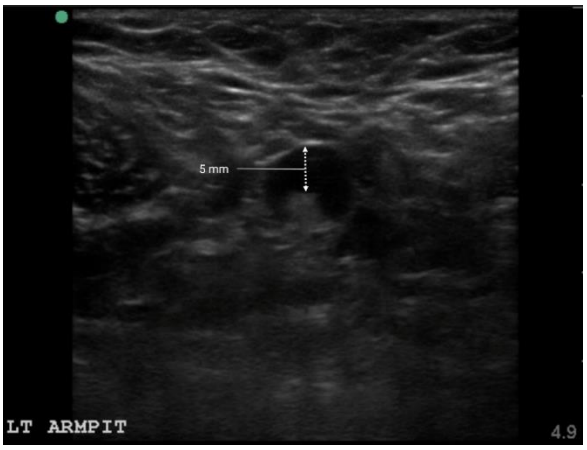

Figure 4 – Case 2. Diagnostic ultrasound assessment of the left axillary region revealing an anechoic thickened cortex ring measuring 5 mm around the hyperechoic hilum.

3. Discussion

The patients described in this report were referred to a physical therapist for ultrasound imaging for suspected orthopedic conditions of the involved regions. Both patients were subsequently sent back to the referring physician due to signs of lymphadenopathy on routine ultrasound imaging.

Vaccine associated reactive lymphadenopathy (VARL) is considered a mild adverse reaction to the COVID-19 mRNA vaccines, which depend on the migration of antigen-presenting cells to regional lymph nodes to elicit a cellular (T-Cell) and humoral (B-Cell) immune response.[4] Additionally, mRNA vaccines elicit a more robust B-Cell proliferation in the lymph node, which increases the incidence of UAL.[4] The reported duration of VARL is typically 10 days with positron emission tomography and computed tomography scans demonstrating trace duration of up to 32 days.[5,6] As previously mentioned, it is reasonable to expect an increased frequency of UAL on imaging after vaccination which may persist for 1 month after the dose.

A normal lymph node appearance on ultrasound is of oval or lobulated shape with a well-defined margin. The node has a hyperechoic representation of the fatty hilum and a thin uniform hypoechoic cortex surrounding the hilum. A hypoechoic cortex measuring 3 mm or less is considered normal.[11] Morphologic criteria, such as cortical thickening, hilar effacement and non-hilar cortical blood flow, are more important than size criteria in the identification of metastases.[10]

Of interest, sonographic evaluation of the axillary lymph nodes in both patients demonstrated cortical thickening as well as positive vascularity patterns. Hilar vascularity refers to color doppler signals originating symmetrically from the nodal hilum of the lymph node and is typically seen in benign or reactive lymph nodes as seen in lymphadenopathy. Evaluation of lymph node vascularization is an important tool which allows the sonographer to classify vascular patterns as either normal/reactive or consistent with metastatic involvement. The first patient's compromised lymph node measurement was 1.1 cm versus 4 mm for a normal adjacent lymph node. The second patient's compromised lymph node had a cortical thickness that was measured at approximately 5 mm.

Several guidelines have been developed to direct patient care when working with patients with UAL. The Society of Breast Imaging has proposed guidelines especially when working with patients with recent or past breast cancer or malignancy.[7] These guidelines have been endorsed by several international organizations including the Canadian Society of Breast Imaging.[8] The most comprehensive algorithm to assist with guiding management of UAL across specialty settings, inclusive of the oncology specialty, was proposed and published by Lehman et al.[9] In the proposed management plan, patients should be classified into one of the following three categories: 1) as an isolated finding on imaging, 2) in conjunction with another finding on imaging, and 3) in a patient undergoing cancer staging and/or treatment.

The guidelines suggest if UAL is noted less than 6 weeks after last vaccination in an individual with no other additional findings, this should be treated as a benign finding and no further imaging should be performed. As seen with the two patients mentioned in this case report, this was the only finding on clinical or ultrasound examination. As this can be a clinical finding in serious disease, both patients were promptly referred to the provider for medical examination, diagnosis, and management. It is recommended, however, that axillary ultrasonography should be performed after 6 weeks of vaccination if clinical concern still exists. Patients who fit into categories 2 and 3 as mentioned above are encouraged to undergo prompt recommended imaging. Management of categories 2 and 3 is tailored to the specific patient and is beyond the scope of this report but the decision making and referral steps for the physical therapist performing ultrasound imaging in patients with suspicious lymphadenopathy are the same. The role of the physical therapist who performs ultrasound imaging is the following: 1) perform a clinical examination, 2) perform an ultrasound imaging examination as an extension of the clinical exam, 3) document relevant and potential incidental findings, and 4) refer the patient back to the referring provider.

4. Conclusion

To further clarify the clinical picture in patients undergoing ultrasound imaging who may demonstrate signs of lymphadenopathy, we recommend documenting at a minimum, the dates of vaccination administration and laterality of each injection. Vaccination brand should also be recorded as the rate of VARL is higher with certain vaccine manufacturers. This documented information may help paint a clearer picture of the patient's case and provide crucial information to the referring physician when they are determining the medical management of the patient.

References

1. US Food and Drug Administration. Pfizer-BioNTech COVID-19 vaccine emergency use authorization. Accessed March 9 2022. https://www.fda.gov/media/144412/download
2. US Food and Drug Administration. Moderna COVID-19 vaccine emergency use authorization. Accessed March 9 2022. https://www.fda.gov/media/144636/download
3. Beatty AL, Peyser ND, Butcher XE, et al. Analysis of COVID-19 Vaccine Type and Adverse Effects Following Vaccination. JAMA Netw Open. 2021;4(12):e2140364.
4. Lam DL, Flanagan MR. Axillary Lymphadenopathy After COVID-19 Vaccination in a Woman With Breast Cancer. JAMA. 2022;327(2):175–176.
5. Polack FP, Thomas SJ, Kitchin N, et al; C4591001 Clinical Trial Group. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Caccine. N Engl J Med. 2020;383(27):2603-2615.
6. Adin ME, Isufi E, Kulon M, Pucar D. Association of COVID-19 mRNA Vaccine with Ipsilateral Axillary Lymph Node Reactivity on Imaging. JAMA Oncol. 2021;7(8):1241-1242.
7. Society of Breast Imaging. SBI Recommendations for the Management of Axillary Adenopathy in Patients with Recent COVID-19 Vaccination. Reston, Va: Society of Breast Imaging, 2021.
8. Tu W, Gierada DS, Joe BN. COVID-19 Vaccination-Related Lymphadenopathy: What To Be Aware Of. Radiol Imaging Cancer. 2021 May;3(3):e210038
9. Lehman CD, D'Alessandro HA, Mendoza DP, Succi MD, Kambadakone A, Lamb LR. Unilateral Lymphadenopathy After COVID-19 Vaccination: A Practical Management Plan for Radiologists Across Specialties. J Am Coll Radiol. 2021;18(6):843-852.
10. Dialani V, James DF, Slanetz PJ. A Practical Approach to Imaging the Axilla. Insights Imaging. 2015;6(2):217-29. doi: 10.1007/s13244-014-0367-8. Epub 2014 Dec 23. PMID: 25534139; PMCID: PMC4376818.
11. Park JY, Lee JY, Yi SY. Axillary Lymphadenopathy on Ultrasound after COVID-19 Vaccination and Its Influencing Factors: A Single-Center Study. J Clin Med. 2022;11(1):238. doi: 10.3390/jcm11010238. PMID: 35011979; PMCID: PMC8746129.
12. Gangier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley DS, CARE Group. The CARE Guidelines: Consensus-based Clinical Case Reporting Guideline Development.