Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Axillary adenopathy following COVID-19 vaccination: A single institution case series

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ABSTRACT

Axillary adenopathy is a potential side effect following COVID-19 vaccination. We report four cases of axillary adenopathy in the setting of recent COVID-19 vaccination (Moderna and Pfizer-BioNTech) at our institution. Our cases show unilateral axillary adenopathy, as well as adenopathy persisting for two to three weeks following vaccination. The Society of Breast Imaging (SBI) and Harvard University have each released guidelines for management of axillary adenopathy following COVID-19 vaccination. While SBI recommends short term imaging 4–12 weeks following the second dose, a group of physicians from Harvard suggest clinical follow-up with sonographic imaging if clinical concern persists beyond six weeks. As a larger percentage of the general population becomes vaccinated, it is important for radiologists to be aware of potential vaccine-induced ipsilateral axillary adenopathy on screening and diagnostic breast imaging to reduce the number of unnecessary biopsies performed in this patient population.

1. Introduction

As COVID-19 was declared a global pandemic in March 2020 by the World Health Organization, many hospitals and healthcare facilities began to limit the number of elective procedures, including cancer screenings, in order to decrease risk of transmission of the virus and conserve healthcare resources. Therefore, breast cancer screenings were delayed or canceled for many patients throughout the United States.[1] A study at a large healthcare provider group in Massachusetts also noted a decline in breast biopsies during the early months of the pandemic.[1] Postponing breast cancer screening and diagnostic procedures can lead to delayed cancer diagnoses, with reports of up to a 51.8% decreased incidence of new breast cancer diagnoses during the pandemic.[2]

In December 2020, the US Food and Drug Administration (FDA) authorized emergency use of two mRNA COVID-19 vaccines, Moderna and Pfizer-BioNTech. In February 2021, the Johnson & Johnson/Janssen adenovirus-based vaccine was also authorized for emergency use. This represents a necessary step towards reducing COVID-19 morbidity and mortality and allowing healthcare facilities to return to normal operations. As vaccination efforts increase, it is important for providers to be aware of potential side effects including the potential for axillary swelling/tenderness and adenopathy which have been reported with both mRNA vaccines and can present on routine breast imaging.

During the Moderna clinical trials, axillary swelling or tenderness was reported in up to 11.6% of patients following dose 1 and 16.0% of patients following dose 2.[3] Furthermore, axillary and/or cervical lymphadenopathy was reported in 1.1% of patients 2 to 4 days after vaccination versus 0.6% in the placebo group.[3] The average duration of lymphadenopathy was 1 to 2 days.[3]

During the Pfizer-BioNTech clinical trials, vaccinated patients reported an increased incidence of axillary and/or cervical lymphadenopathy was reported as an unsolicited adverse event in 64 of the vaccinated patients (<1%) with average duration of lymphadenopathy approximately 10 days.[4] Although, since lymphadenopathy was only reported as an unsolicited event in the clinical trials, the incidence rate is likely higher.

Axillary adenopathy in the setting of recent vaccination is not a new phenomenon. For example, there have been documented cases of ipsilateral axillary adenopathy following vaccination for BCG and influenza.[5,6]

Since March 2021, there have been multiple articles discussing ipsilateral axillary adenopathy following COVID-19 vaccination (specifically the mRNA vaccines), including a case series from an institution in New York reporting 4 cases of unilateral axillary lymphadenopathy following COVID-19 vaccination in the ipsilateral arm, although no interval follow-up had been reported at time of publication.[7] There have

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also been reports on multiple online physician and breast radiology forums, including the Society for Breast Imaging and the American College of Radiology, of either personal experiences or seeing an increased number of imaging cases of ipsilateral axillary adenopathy following COVID-19 vaccination.

The Society of Breast Imaging (SBI) released guidelines for the management of axillary adenopathy in patients with recent COVID-19 vaccination. SBI recommends that unilateral axillary adenopathy on screening mammography be assigned BI-RADS 0 to further assess the ipsilateral breast and document vaccination history.[8] Following appropriate diagnostic work up in women who received the COVID-19 vaccine in the ipsilateral arm in the preceding four weeks, short term follow-up in 4–12 weeks after the second vaccine dose may be considered. Lymph node sampling is recommended if the axillary adenopathy persists on short term follow up.[8]

More recently, Harvard Medical School/Massachusetts General Hospital Department of Radiology reported an alternative approach regarding management of ipsilateral axillary adenopathy in the setting of recent COVID-19 vaccination.[9] The recommendations suggest reporting isolated ipsilateral axillary adenopathy in the setting of recent vaccination (within 6 weeks) as benign (BI-RADS 2) for screening and diagnostic breast imaging (excluding patients with recent breast cancer diagnosis).[9] Clinical follow-up of the axilla is recommended for all patients with palpable axillary adenopathy, and if clinical concern persists beyond six weeks, then axillary ultrasound is suggested for further evaluation.[9] Recommendations from both SBI and Harvard suggest obtaining COVID-19 vaccination history at time of exam.[8–9]

2. Case descriptions

2.1. Case 1

A 50-year-old female presented for routine screening mammography. The patient reported no personal or family history of breast cancer. The patient reported receiving the Moderna COVID-19 vaccine in her left upper extremity 15 days earlier.

Bilateral screening mammography demonstrated an enlarged left axillary lymph node. Measuring 2.6 cm in greatest dimension, with cortical thickening (Fig. 1). There was also a questioned asymmetry in the left breast. The right breast was unremarkable. Comparison with prior outside breast imaging was recommended.

2.2. Case 2

A 45-year-old female presented for diagnostic evaluation of a palpable right axillary abnormality and follow up of a probably benign left breast mass. The patient reported receiving the Pfizer COVID-19 vaccine two days prior to imaging.

Targeted ultrasound of the right axilla demonstrated a lymph node with normal morphology in the region of the patient's palpable abnormality. Additionally, in the right axilla, not directly in the region of palpable abnormality, there was a 1.7 × 1.1 × 1.4 cm lymph node with cortical thickening and mildly effaced fatty hilum (Fig. 2). Targeted left breast ultrasound demonstrated a stable probably benign mass. The patient was advised to return for short term 3-month follow-up targeted ultrasound of the right axilla to ensure resolution.

2.3. Case 3

A 40-year-old female presented for diagnostic evaluation of left breast asymmetries. The patient reported a family history of breast cancer in her paternal grandmother. The patient noted recently receiving the COVID vaccine, however the exact injection date and arm injected are not disclosed.

Left breast diagnostic mammogram demonstrated asymmetries which persisted on spot compression views. Left breast ultrasound showed probably benign clusters of cysts likely corresponding to the mammogram findings. Additionally, there was an enlarged left axillary lymph node measuring 1.5 × 1.1 × 1.4 cm with a heterogeneous hyperechoic and thickened cortex (Fig. 3), as well as several adjacent smaller left axillary lymph nodes. A 3-month follow-up left breast/axillary ultrasound was recommended.

2.4. Case 4

A 54-year-old with history of right breast cancer status post right mastectomy and tram flap reconstruction greater than 15 years prior presents for high-risk screening breast MRI. Additional pertinent history includes a benign left breast mass biopsy about 8 months prior. The patient reports COVID vaccination in the left arm 23 days prior to screening MRI. Contrast-enhanced breast MRI shows multiple enlarged level 1 and 2 left axillary lymph nodes with cortical thickening (Fig. 4). No suspicious findings were identified in either breast or right axilla. Follow-up left axillary ultrasound in 4–12 weeks after final vaccination dose was recommended.

3. Discussion

We have described four cases of axillary adenopathy with recent history of COVID-19 vaccination. As demonstrated through our cases, this finding may present on routine screening breast imaging, as an incidental finding on diagnostic exams, or on targeted diagnostic workup as a response to direct complaint from the patient. Thus, radiologists must consider this etiology for unilateral axillary adenopathy across all patients, and not just those who present with clinical complaint of axillary pain or palpable abnormality. Current recommendations suggest obtaining COVID-19 vaccination history at the time of exam,[8] and as more of the population becomes vaccinated it is prudent to adopt this as a routine measure for any patient presenting for breast imaging.

Ultrasound appearance of the lymph nodes varied across our patients. Cases 2 and 4 demonstrated lymph node enlargement as well as a thickened cortex. Case 3 demonstrated unusual appearance of a heterogenous, hyperechoic, thickened cortex. It is unclear whether these differences in appearance have any clinical implications, and thus follow up imaging is appropriate in all cases to document resolution and exclude malignant etiology.

It is also worth noting that the axillary adenopathy was detected greater than 2–3 weeks following vaccination in cases 1 and 4. This is longer than the reported average duration of adenopathy in the Moderna and Pfizer-BioNTech clinical trials.[3,4] This suggests that adenopathy may persist for two or more weeks following vaccination, and it is important for radiologists to recognize the possibility of this extended duration when considering the patient's history and making decisions about appropriate follow up. For the cases presented, short term imaging follow-up was recommended to ensure resolution of axillary adenopathy, with the exception of case 1 which recommended comparison to outside imaging.

Due to the COVID-19 pandemic, nearly all imaging centers have implemented new practice measures to protect healthcare workers and patients, including universal masking, decreasing the number of scheduled patients, social distancing in waiting areas, and utilizing more extensive disinfection protocols.[10] While these measures allow for continued breast cancer screening and management during the pandemic, they also create limitations in scheduling and resources. Thus, it is necessary to ensure that care is utilized in a judicious manner. As widespread vaccination efforts take effect, it is important to recognize recent COVID-19 vaccination as a potential etiology for axillary adenopathy so that appropriate follow-up may be recommended and unnecessary lymph node biopsies can be avoided. Clinicians and breast imagers are still learning about vaccine-induced adenopathy as a greater percentage of the population becomes vaccinated against COVID-19 and

additional studies with patient follow-up are needed to determine criteria for biopsy. Imaging follow-up will also help determine the expected duration of axillary adenopathy in asymptomatic and symptomatic patients.

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Appendix A

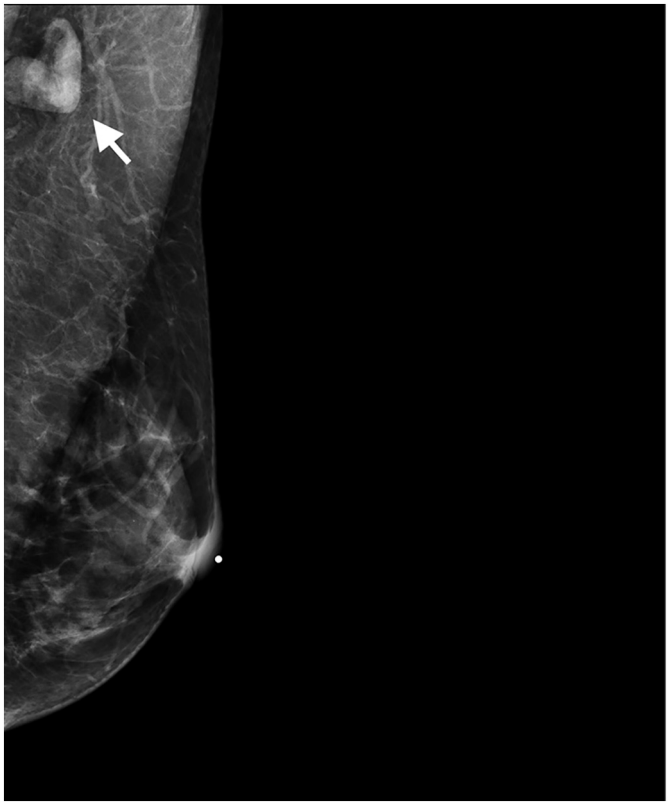

Fig. 1. A 50 year old female presented with unilateral right axillary adenopathy on screening mammogram 15 days after receiving the Moderna COVID-19 vaccine.

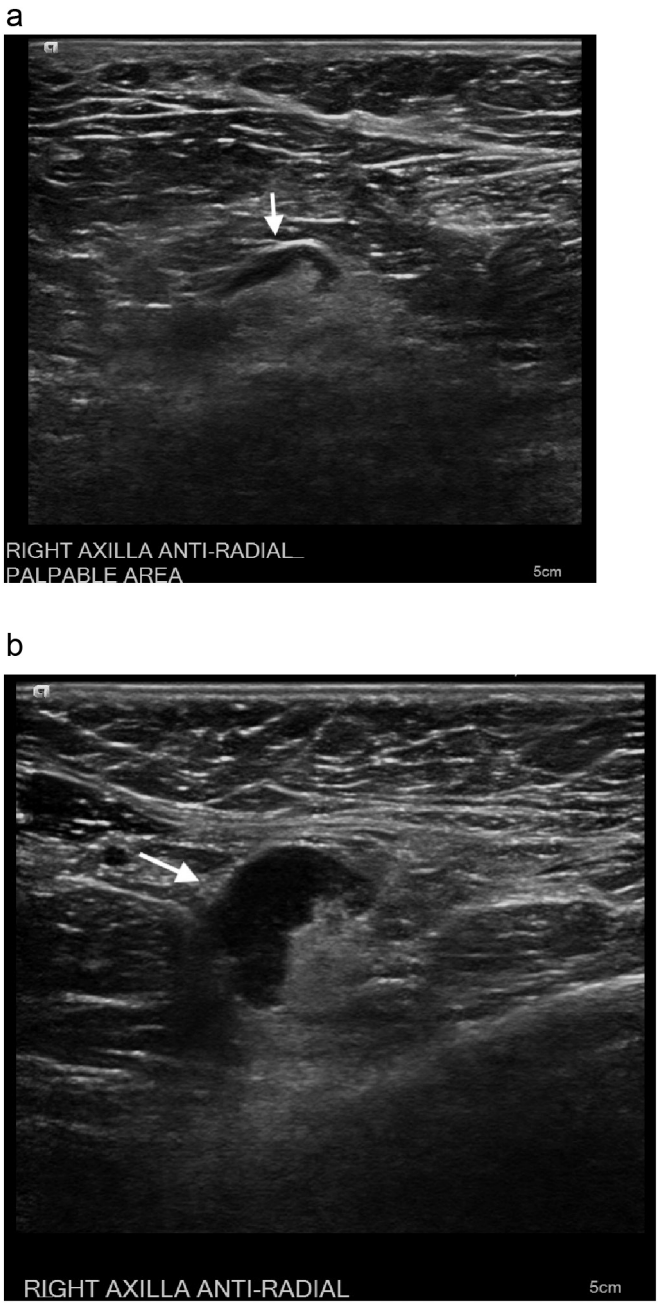

Fig. 2. A 45 year old female presented with a right axillary palpable abnormality two days after receiving the Pfizer COVID-19 vaccine. Right axillary ultrasound images demonstrate a) a normal lymph node in the area of palpable abnormality, however b) a nearby enlarged lymph node with cortical thickening.

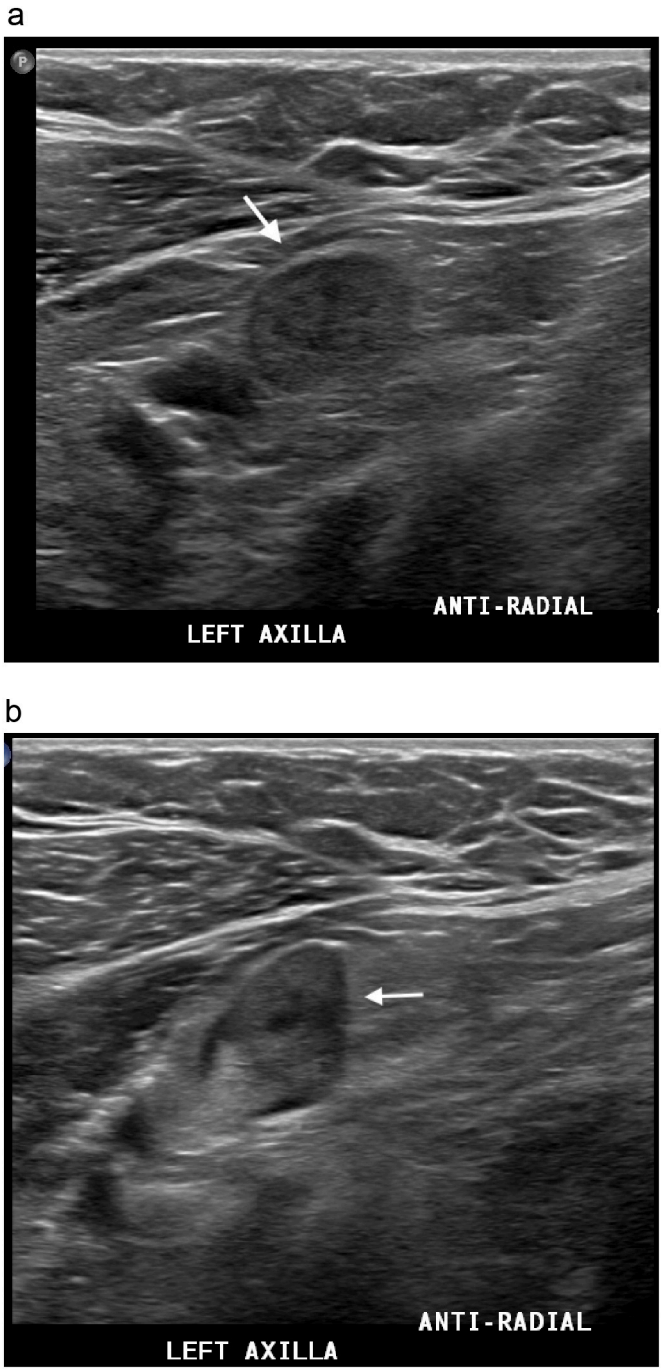

Fig. 3. A 40-year-old female presented with enlarged left axillary lymph nodes with heterogenous hyperechoic cortex after recently receiving a COVID-19 vaccine (although exact injection date and arm injected are not disclosed).

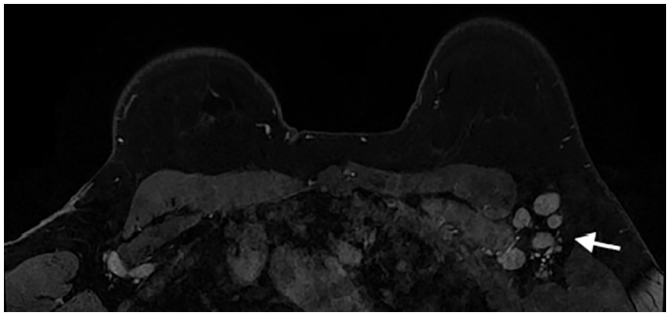

Fig. 4. A 54-year-old female with history of right breast cancer status post right mastectomy and flap reconstruction presented for high-risk breast cancer screening MRI. On the T1 fat suppressed post contrast series, there are abnormal level 1 and 2 left axillary lymph nodes 23 days following COVID-19 vaccination in ipsilateral arm.

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