Coronavirus Disease (COVID-19) Vaccination Associated Axillary Adenopathy: Imaging Findings and Follow-Up Recommendations in 23 Women

Shabnam Mortazavi, MD

Susana Bracewell, MS4

Journal Club – April 20, 2021
In Recent News

The New York Times

Women and the Covid-19 Vaccine: What You Need to Know
Can it affect mammograms or the timing of fertility treatments? What side effects should you look out for? Experts weigh in.
5 days ago

New York Post

COVID-19 vaccine can impact mammogram with 'false positive'
Getting a mammogram soon after getting the COVID-19 vaccine? Be warned: The vaccine might cause your lymph nodes to swell, which may ...
5 days ago

The Washington Post

A harmless vaccine side effect could mimic cancer in mammograms. Here’s what to know.
Enlarged lymph nodes can be a side effect of vaccination for some people. As harmless as vaccine-swollen nodes are, those in the armpit may ...
1 month ago
Learning Objectives

By the end of this journal club, participants will be able to:

• Review the basic anatomy of the female breast and axillary lymph nodes
• Recognize the radiographic findings of benign vs. pathologic lymph nodes
• Formulate a differential for unilateral vs. bilateral axillary lymphadenopathy
• Understand BI-RADS assessment categories
• Provide a guideline for COVID-19 vaccinations and mammography
Module Outline

I. Case
II. Background
III. Article Overview
IV. Clinical Questions
V. Key Points
Case Presentation

68-year-old female with a past medical history significant for right breast cancer status post breast conserving therapy and adjuvant chemotherapy and recent left arm COVID vaccination presents for her diagnostic mammogram
Case Imaging – Mammogram

What do you notice about the mammogram?
Case Imaging – A Better Look
Case Imaging – Ultrasound

What is your impression of the ultrasound?

Do you have a differential for what is going on?

What would your recommendations be?
Case Resolution

• BI-RADS category 3 (probably benign)
• Short interval follow-up
  • Repeat mammography in 6 weeks to evaluate for decrease in size of left axillary lymph node
Case Questions

• What is the BI-RADS assessment scale?

• What are the features of a pathologic lymph node?

• What causes axillary lymphadenopathy?

• What should the recommendations be concerning mammograms and COVID-19 vaccinations?
Module Outline

I. Case

II. Background

III. Article Overview

IV. Clinical Questions

V. Key Points
Anatomy of the Female Breast
Anatomy of a Lymph Node
Normal Ultrasonographic Appearance of Lymph Nodes

- **C** = cortex, **P** = paracortex, **H** = hilum
- Cortex appears hypoechoic with slightly hyperechoic paracortex
- Hilum is hyperechoic, representing central sinus, medullary cords, blood vessels, and fat
Normal Mammographic Appearance of Axillary Lymph Nodes

- Well-defined
- Relatively low density
- Fatty hila or a fatty center
Differential of Axillary Lymphadenopathy

- **Bilateral**
  - Autoimmune diseases, such as rheumatoid arthritis, Sjögren syndrome, systemic lupus erythematosus, etc.
  - Lymphoma
  - Leukemia
  - HIV and HIV-associated conditions
  - Granulomatous diseases, such as sarcoidosis or tuberculosis
  - Lymphoid hyperplasia from infections/inflammation, for instance with infectious mononucleosis
  - Axillary nodal metastases from breast cancer (uncommonly), lung cancer, and melanoma

- **Unilateral**
  - **Benign**
    - Mastitis
    - Cellulitis
    - Tuberculosis
    - Post-vaccination
  - **Malignant**
    - Metastasis from breast malignancy
    - Metastasis from melanoma
    - Metastasis from primary malignancy in ipsilateral arm
    - Lymphoma (uncommonly)
Mammographic Appearance of Pathologic Axillary Lymph Nodes

- Dense
- Large
- Round
- Loss of fatty hilum
Abnormal Sonographic Appearance of Axillary Lymph Nodes

- Larger size
- Rounded or irregular shape
- Loss of fatty hilum
- Cortical thickening
Breast Imaging-Reporting and Data System (BI-RADS)

<table>
<thead>
<tr>
<th>BI-RADS® ASSESSMENT CATEGORIES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Category 0:</strong> Mammography: Incomplete – Need Additional Imaging Evaluation and/or Prior Mammograms for Comparison Ultrasound &amp; MRI: Incomplete – Need Additional Imaging Evaluation</td>
</tr>
<tr>
<td><strong>Category 1:</strong> Negative { } 0% PPV for malignancy ➔ Routine mammography screening</td>
</tr>
<tr>
<td><strong>Category 2:</strong> Benign</td>
</tr>
<tr>
<td><strong>Category 3:</strong> Probably Benign { } &lt;2% ➔ Short interval follow-up or continued surveillance</td>
</tr>
<tr>
<td><strong>Category 4:</strong> Suspicious</td>
</tr>
<tr>
<td><strong>Category 5:</strong> Highly Suggestive of Malignancy { } &gt;95% ➔ Biopsy should be performed</td>
</tr>
<tr>
<td><strong>Category 6:</strong> Known Biopsy-Proven Malignancy { } 100% ➔ Surgical excision when clinically appropriate</td>
</tr>
</tbody>
</table>
Module Outline

I. Case
II. Background
III. Article Overview
IV. Clinical Questions
V. Key Points
Article Specifics

I. **Purpose:** To promote radiologists' familiarity with this new phenomenon and to provide evidence-based guidelines in order to avoid unnecessary workup.

II. **Journal:** *American Journal of Roentgenology*, published online in February 2021.

III. **Study Type:** Retrospective study of electronic medical record from December 2020 to February 2021.

IV. **Cases:** 23 women displayed axillary adenopathy ipsilateral to the vaccinated arm on screening or diagnostic breast imaging.

V. **Data:** Type of vaccine, time between first dose and imaging, presentation, imaging showing abnormal node, number of abnormal lymph nodes, maximal lymph node cortical thickness (mm), follow up recommendations.
Study Cohort

• Women with image-proven axillary adenopathy

• Detected during screening or diagnostic breast imaging from December 2020 to February 2021

• Recently received COVID-19 vaccination
Materials and Methods

• Axillary adenopathy was found during review of electronic medical record

• No new interpretations of the imaging were made
Materials and Methods (cont)

• What did the author classify as an abnormal lymph node?
  • For mammography, if the size, shape or density was disproportionate to others (ipsilateral and/or contralateral)
  • For ultrasound, based off subjective assessment of cortical abnormalities, including focal or diffuse thickening greater than 3 mm
    • Overall node size was not a criterion given lack of consensus for axillary node assessment on ultrasound
  • For MRI, if asymmetric in size and/or number to the contralateral axilla
Results

- 23 women (age 49 ± 21 years) with axillary adenopathy ipsilateral to the vaccinated arm
- Only 13% of women were symptomatic
- Median interval between vaccine and abnormal imaging was 9.5 days (range of 2-29 days)
- 57% of women had only one abnormal node
- The cortical thickness of the largest node was >6 mm in 13%

| Table 1-Summary of 23 women with COVID-19 vaccination associated axillary adenopathy |
|---------------------------------|---|
| **Feature**                     | **n (%)** |
| Type of vaccine                 |          |
| Pfizer                          | 12 (52)  |
| Moderna                         | 5 (22)   |
| Not reported                    | 6 (26)   |
| **Time between first dose and imaging (d)** |          |
| 2-6                             | 7 (35)   |
| 7-13                            | 2 (15)   |
| 14-20                           | 3 (15)   |
| >20                             | 1 (5)    |
| **Presentation**                |          |
| Symptomatic (axillary lump with possible tenderness) | 3 (15) |
| Asymptomatic, screening         | 10 (43)  |
| Asymptomatic, diagnostic (reason unrelated) | 10 (43) |
| **Modality demonstrating abnormal node** |          |
| Mammography                     | 3 (22)   |
| US                              | 12 (52)  |
| Mammography and US              | 4 (17)   |
| **MRI**                         | 2 (9)    |
| **Number of abnormal lymph nodes** |          |
| 1                               | 13 (57)  |
| 2                               | 2 (10)   |
| 3                               | 3 (13)   |
| >3                             | 2 (9)    |
| **Maximal lymph node cortical thickness (mm)** |          |
| 4                               | 10 (43)  |
| 5-6                             | 10 (43)  |
| >6                             | 3 (13)   |
| **Imaging follow-up recommendation (weeks)** |          |
| No imaging follow-up (BI-RADS 2) | 1 (4)   |
| 4-6 (BI-RADS 3)                 | 5 (22)   |
| 7-12 (BI-RADS 3)                | 13 (57)  |
| 13-24 (BI-RADS 3)               | 3 (13)   |
| US-guided biopsy (BI-RADS 4)    | 1 (4)    |

*Excludes 5 patients for whom adenopathy was first detected after 2nd dose (interval of 1, 7, or 9 days after 2nd dose)*
Results (cont)

- BI-RADS 2 was assigned in one woman
- BI-RADS 3 was assigned in 21 women
  - Median recommended ultrasound follow-up of 8 weeks (range of 4-24 weeks)
- BI-RADS 4 was assigned in one woman
  - The patient had left breast pain and past medical history of left breast cancer, ipsilateral to the vaccination
  - Ultrasound-guided core needle biopsy yielded reactive lymphoid process
- Follow-up imaging or biopsy was recommended in all but one patient
Discussion

• The largest known sampling of axillary adenopathy secondary to COVID-19 vaccinations seen on imaging

• Society of Breast Imaging recommends
  • Initial BI-RADS 0 assessment to allow further assessment of the ipsilateral breast
  • After appropriate diagnostic workup, consider a follow-up examination 4-12 weeks after the second dose (BI-RADS 3)
  • If axillary adenopathy persists, consider lymph node sampling to exclude malignancy

• Another recommendation would be to follow the affected axilla 4-to-12 weeks after the second dose with targeted ultrasound to demonstrate resolution
Discussion (cont)

- Axillary adenopathy ipsilateral to the vaccinated arm may be a reactive process
- Recommendations for follow-up imaging may not be warranted
- Incorporating the patient’s COVID-19 vaccination history is critical to optimize management in women with otherwise normal breast imaging
- Concurrent assessment of the contralateral axilla for comparison may be helpful
Limitations

- Small study size
- Short study period
- Single institution
- Retrospective design
- Evolving information
- Only mentioned Pfizer and Moderna vaccinations
- Unaware of the total percentage of women with adenopathy after COVID-19 vaccinations
- No comparison between women with and women without vaccinations
Module Outline

I. Case

II. Background

III. Article Overview

IV. **Clinical Questions**

V. **Key Points**
Clinical Questions Now. . .

• What percentage of women have unilateral axillary lymphadenopathy after COVID-19 vaccinations?

• How many callbacks are benign?

• Should women be turned away from screening if recently vaccinated?
Key Points

- On imaging, lymph nodes should be reniform, small, and retain their fatty hilum

- It is important to realize that unilateral reactive lymphadenopathy in the era of COVID-19 vaccinations may be normal
  - At the same time, malignancy should always be on the differential

- If possible, screening/nonemergent breast imaging should be postponed after COVID-19 vaccination to avoid abnormal results and unnecessary invasive workup
References


4. Case courtesy of Dr Garth Kruger, Radiopaedia.org, rID: 21438

