JAMA Clinical Challenge

Axillary Lymphadenopathy After COVID-19 Vaccination in a Woman With Breast Cancer

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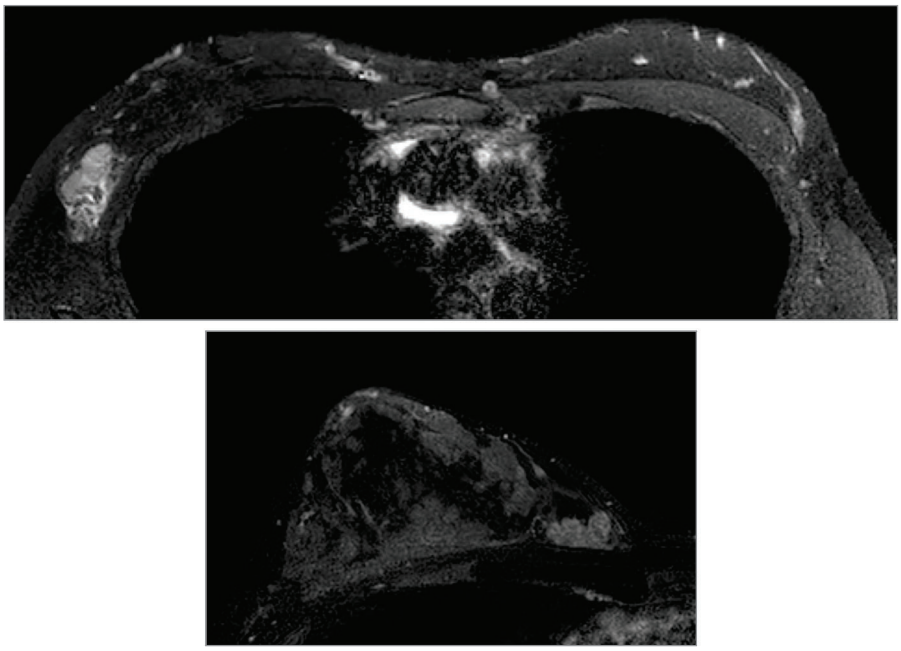

Figure. Top, Axial T2-weighted magnetic resonance imaging (MRI) at the level of the axilla. Bottom, Axial postcontrast T1 fat-saturated MRI of the right breast.

A 39-year-old healthy woman without family history of malignancy found a mass in her right breast at 38 weeks of pregnancy. Prior to delivery, she underwent diagnostic ultrasound of the right breast, which showed a possible mass in the location of the palpable lesion that was most consistent with a normal island of fibroglandular tissue. Follow-up mammogram and ultrasound of the right breast (without axillary evaluation) were performed 6 months later, which showed an irregular 17-mm mass with associated pleomorphic calcifications in the same area. Ultrasound-guided biopsy was performed. Pathology showed high-grade, estrogen receptor–positive ductal carcinoma in situ (DCIS). On postbiopsy physical examination, the patient had a palpable 2.5-cm right breast mass at the 3-o'clock position without palpable axillary lymphadenopathy.

Surgical treatment with lumpectomy was recommended, and breast magnetic resonance imaging (MRI) was performed prior to surgery to evaluate the extent of disease (**Figure**). Axial T2-weighted MRI at the level of the axilla revealed edema surrounding 2 enlarged, morphologically abnormal right level-1 axillary lymph nodes; axial postcontrast T1 fat-saturated MRI of the right breast revealed an irregular mass with irregular margins at the site of biopsy-proven DCIS. The patient reported receiving her second dose of COVID-19 vaccine (Pfizer-BioNTech) in the right arm the day before the breast MRI.

WHAT WOULD YOU DO NEXT?

A. Perform repeat breast MRI 4 to 6 weeks after vaccination

B. Perform right axillary ultrasound 4 to 6 weeks after vaccination

C. Perform an axillary sentinel lymph node biopsy at the time lumpectomy is performed

D. Perform right axillary ultrasound now, with intent to biopsy enlarged lymph nodes

Quiz at jamacmelookup.com

Diagnosis

Vaccination-associated reactive lymphadenopathy

What to Do Next

D. Perform right axillary ultrasound now, with intent to biopsy enlarged lymph nodes

The keys to the correct diagnosis in this case were the recent receipt of COVID-19 vaccine 1 day prior to MRI, in conjunction with the lack of palpable axillary lymphadenopathy prior to vaccination. This presentation raised suspicion for vaccination-associated reactive lymphadenopathy; however, because of the patient's recent diagnosis of ipsilateral breast cancer, a targeted axillary ultrasound

with intent to biopsy enlarged lymph nodes (choice D) is the best answer. In the setting of newly diagnosed ipsilateral DCIS, the asymmetrically enlarged right axillary lymph nodes identified on MRI could represent an invasive tumor in addition to DCIS with potential axillary lymph node metastasis. Therefore, waiting 4 to 6 weeks (choices A and B) is not recommended. In the setting of DCIS, where less than 25% of patients are found to have invasive carcinoma on final pathology after surgical excision, sentinel lymph node biopsy is performed only in patients for whom the procedure cannot be technically performed as a second operation (eg, mastectomy or those in whom the DCIS excision is in an anatomical location that would compromise the breast lymphatics). For this patient, without a diagnosis of invasive carcinoma and in the setting of a planned medial breast lumpectomy that would not alter the lymphatic pathway to the axilla, sentinel lymph node biopsy (choice C) would not be recommended.

Discussion

Vaccination-associated reactive lymphadenopathy is considered a local adverse reaction to vaccination (similar to pain and swelling) and is more commonly observed after receipt of the novel COVID-19 mRNA vaccines compared with other vaccines.[1-4] Similar to many vaccines, mRNA vaccines depend on antigen-presenting cells migrating to regional lymph nodes to elicit both a cellular (T-cell) and humoral (B-cell) immune response. Compared with protein-based vaccines, mRNA vaccines elicit a more robust and rapid B-cell proliferation in the germinal center of the lymph node, likely increasing the incidence of lymphadenopathy.[5,6]

In the US, the first COVID-19 vaccines (Moderna and Pfizer-BioNTech) to receive Emergency Use Authorization from the US Food and Drug Administration were mRNA vaccines. For recipients of the Moderna vaccine, 11.6% (1322/11 401) reported axillary swelling or tenderness in the ipsilateral vaccination arm after the first dose, and 16% (1654/10 357) reported this reaction after the second dose.[7] The median duration of reported lymphadenopathy was 1 day after the first dose and 2 days after the second dose.[7] For recipients of the Pfizer-BioNTech vaccine, 0.3% (64/21 720) reported lymphadenopathy in the vaccine group, compared with less than 0.1% (6/21 728) in the placebo group.[8] The average reported duration of lymphadenopathy was approximately 10 days.[8] The expected duration of vaccination-related lymphadenopathy remains unclear, but increased axillary nodal fludeoxyglucose F 18 uptake on positron emission tomography/computed tomography scans has been observed for up to 32 days after receipt of the Moderna vaccine in a cohort of women with cancer.[9]

In asymptomatic patients with a history of cancer who are undergoing monitoring for cancer recurrence, imaging should be performed either before or at least 4 to 6 weeks after COVID-19 vaccination to allow adequate time for resolution of vaccine-related lymphadenopathy. This avoids unnecessary workup, procedures, or both, as well as undue anxiety stemming from cases of reactive lymphadenopathy that cannot easily be distinguished from recurrent or metastatic disease. However, in patients with a new or active diagnosis of cancer, or for acute symptoms, active-treatment monitoring, or urgent treatment planning, imaging should not be delayed.[3,10]

Patient Outcome

The patient returned for right axillary ultrasound with intent to biopsy 8 days after her breast MRI (9 days after receipt of her second COVID vaccine dose). The right axillary lymphadenopathy originally seen on MRI had resolved on ultrasound; therefore, the axillary lymph node biopsy was canceled. The patient underwent lumpectomy, and pathological examination of the excised tissue showed DCIS with a single focus of microinvasion. Given upgrade to invasive disease, a sentinel lymph node biopsy was performed for staging, and 2 sentinel nodes were negative, consistent with the diagnosis of vaccination-associated reactive lymphadenopathy.

ARTICLE INFORMATION

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Section Editor: Kristin Walter, MD, Associate Editor.

Published Online: December 23, 2021. doi:10.1001/jama.2021.20010

Conflict of Interest Disclosures: None reported.

Additional Contributions: We thank the patient for providing permission to share her information.

Submissions: We encourage authors to submit papers for consideration as a JAMA Clinical Challenge. Please contact Dr Walter at kristin.walter@jamanetwork.org.

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