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A Look at the Impact of mRNA Vaccination on Imaging Studies

Announcer:
Welcome to VacciNation on ReachMD, sponsored by Moderna. Here's your host Dr. John Russell.

Dr. Russell:
This is *VacciNation* and I'm Dr. John Russell. Joining me today to investigate the links between COVID-19 vaccines and abnormal mammogram findings and how to address this in practice is Dr. Randy Miles, Assistant Professor of Radiology at the Harvard Medical School and Interim Service Chief of the Division of Breast Imaging at the Massachusetts General Hospital.

Dr. Russell:
Dr. Miles, thanks for being here today.

Dr. Miles:
Thank you for the invite.

Dr. Russell:
So, let's dive in, Dr. Miles. What can you tell us to start about this unexpected intersection between your world of breast imaging and the entrance of the mRNA vaccines with the associated lymphadenopathy into broad circulation?

Dr. Miles:
Your lymph nodes are activated to produce white blood cells in reaction to the vaccine so that the body is better prepared to keep you healthy if you're exposed to the actual virus. So with that, we can actually see this interaction of the vaccine and the lymph nodes on our imaging. We can see that the lymph nodes actually enlarge on our imaging studies, and that's kind of what's gotten us into this dilemma that we'll be talking about today.

Dr. Russell:
So how prevalent would you say these axillary findings are turning up in these imaging studies that you're doing?

Dr. Miles:
It's very hard to give an exact number since every patient reacts to the vaccine slightly different. A study out of Yale recently showed that reactive ipsilateral axillary lymph nodes occurs in about 13% of cases following the administration of the COVID vaccine. So, we do believe it's a small percentage of patients where we actually see this. In general, the closer to the vaccination date the higher likelihood that you will have enlarged lymph nodes in your axillary region if the vaccine is given in the arm.

We definitely saw this more frequently when vaccines were first rolled out to the general public. But anecdotally, we've been seeing this less and less, which may reflect a few things. One, it may reflect that doctors are now encouraging patients to obtain their mammography exams prior to vaccinations or they may be encouraging them to have their exams performed at least six weeks following the vaccination. Also, we're moving further and further away from that period in which most people were initially vaccinated. So I think that also contributes to this observation.

Dr. Russell:
So, for your whole career in breast imaging, though, patients have been receiving some type of vaccine. Have you seen this before with other vaccines over the years?

Dr. Miles:
Yes, lymphadenopathy due to vaccinations is not unique to COVID. We have seen this with other vaccines, particularly those that are

given in the arm. It's like the basis of vaccination inducing an immune response so that the body is prepared to fight off a virus so some of that we expect to see, or I guess the better way to put it is it's something that we're not surprised to see once someone has been vaccinated.

Dr. Russell:
So, Dr. Miles, it's never been more important I think in medicine for us to have absolute clarity, especially when it comes to issues around vaccines. So just to speak the obvious for a second, I'd love you to clarify it, when we say someone had an abnormal mammogram and the findings were seen soon after receiving a COVID-19 vaccine, research has found no link between the COVID-19 vaccine itself and breast cancer, correct?

Dr. Miles:
That is correct. There is no link between COVID-19 vaccine administration and the development of breast cancer itself.

Dr. Russell:
So, to get a better understanding of these reactions to vaccines that overlap with cancer indicators on imaging studies, you've got a lot of different imaging studies now at your disposal, what do you see specifically and with which of the diagnostic modalities?

Dr. Miles:
First, I'll say I think it's important to note that it is always difficult to differentiate between malignant versus reactive lymphadenopathy. Enlarged lymph nodes mimicking cancer as I've kind of alluded to before is not specific to administration of the COVID vaccine. COVID vaccination is just one of the causes of reactive lymphadenopathy, which is a benign etiology of enlarged lymph nodes. When we are evaluating these examinations, where we do see enlarged lymph nodes in the axillary region; we have traditionally just looked for reasons that may cause that lymphadenopathy and some of the things that we routinely look for is there a presence of inflammatory diseases such as rheumatoid arthritis, has this patient had a recent illness or infection in that region so that's always been a part of our diagnostic evaluation and in this era of COVID, recent COVID vaccination is one of those things that is now a part of everyday life and some of that will have to evaluate going forward as long as we're administering the vaccine.

In terms of a normal lymph node, it's typically kidney-bean shaped with a central fatty hilum and surrounding thin cortex. So, there's two components: an abnormal lymph node loses that central fatty hilum and that thin cortex becomes thickened. When we see these findings, this is when we start looking for those causes that may lead to a reactive lymph node that I've discussed before in terms of the

inflammatory conditions, prior to illness, prior to infection. If we do see a concurrent suspicious breast finding or cannot find one of these reasons to explain the reasoning behind that lymph nodes being enlarged, that's when we typically recommend further evaluation. If the finding is on a mammogram or if we see it on cross-sectional imaging, such as the CT or MRI, we typically will follow-up with an ultrasound of the axilla and if the finding remains indeterminate on that ultrasound, that's when we'll performed an ultrasound-guided biopsy.

Dr. Russell:
For those just tuning in, you're listening to *VacciNation* on ReachMD. I'm Dr. John Russell, and today I'm speaking with Dr. Randy Miles about the landscape of cancer imaging in the context of COVID-19 vaccinations.

Dr. Russell:
So Dr. Miles, if we consider patients with an unknown vaccine status, does that ambiguity affect imaging approaches, interpretations, or follow-up protocols in any way?

Dr. Miles:
It does not. Like I said, we really are very pragmatic when we are evaluating axillary lymphadenopathy. In the scenario where we do know about the vaccination status, I would say that the recommendations are diverse, including biopsy, immediate additional imaging with ultrasound, short interval imaging and clinical follow-up. So, I think there can be some more consensus among breast imaging centers in terms of having standard recommendations. Our center at MGH has really taken a pragmatic approach which we have published in the *American Journal of Radiology*. So, what we typically do in the setting of screening mammography, screening MRI, or any diagnostic imaging workup for breast symptoms, if the patient only has unilateral, axillary lymphadenopathy on the same side where they received the vaccine in the arm within the past six weeks, we report that as benign lymphadenopathy with no further imaging indicated. If these lymph nodes were palpable or if the patient or the doctor can feel them, then we just recommend clinical follow-up so that we can follow-up and make sure that the lymph nodes just resolve, just go back to normal based off of clinical exam. If there are any persistent concerns, such as in the case where you could palpate or feel those lymph nodes, if you feel those six weeks after the vaccination then the patient can still come in for a follow-up axillary ultrasound but is based off persistent findings, not based off those initial findings of axillary lymphadenopathy.

And any patient that has a recent breast cancer diagnosis is in that pre or peri-treatment setting we continue our protocol and we're very vigilant about assessing these lymph nodes, ensuring that no cancer has spread so we would image appropriately, and biopsy based off of the breast findings.

So, our recommendations align with ACR BI-RADS Atlas that if there is an explanation to explain ipsilateral axillary lymphadenopathy, such as inflammatory causes such as vaccine administration, then you can deem that examination benign. By following this pragmatic approach, we're able to reduce patient anxiety, provide a burden cause of unnecessary evaluation of enlarged lymph nodes in the setting of recent vaccinations and we are also able to avoid you know patients having a delayed vaccination or breast cancer screening which you know is not as big of an issue now, but as we were closer to that peak pandemic period, it was a real issue as women had delayed their routine screening.

Dr. Russell:
So, it certainly sounds like you and your team have given a lot of thought to this and have really though through protocols. What would be some of your recommendations to other healthcare institutions and imaging departments for establishing some best practices to reduce the risk of false-positives?

Dr. Miles:
I think first step just looking ahead to document COVID-19 vaccination data, that's status, date of the vaccination, the dose, injection site of all patients presenting for breast imaging, no matter the modality. So, this should be collected and presented to radiologists who are interpreting these examinations. I think radiologists need to work with the primary care doctors, because a lot of these issues can be prevented just by clear communication and coordination with doctors ordering the examination. If possible, if patients can receive their breast imaging prior to their vaccination or booster that helps prevent these issues. If they are going to have their vaccination, if you can schedule their exam greater than six weeks after their last dose of the vaccination, that can also help prevent any confusion from ipsilateral axillary lymphadenopathy that we're seeing on the imaging examination.

If you're not able to arrange the breast imaging examination perfectly around the vaccines, I think you can use this pragmatic approach to evaluate breast imaging in the setting of vaccination so that you're not bringing women back unnecessarily for additional imaging or performing any unnecessary biopsies.

Dr. Russell:
So certainly, you and I realize the emotional impact for our patients who suddenly get a report that they have an abnormal mammogram. How do we balance this for our patients without leading to really negative patient experiences and perhaps change in what they'll do going forward?

Dr. Miles:
I think that's something that can be handled on both the primary care and the radiology side. I think first, preparing patients before they come into the breast imaging suite if they've had a recent vaccination that they may have enlarged lymph nodes and that it almost can be expected if they've had the vaccine recently and not to be alarmed.

I think once women come into the breast imaging suite if it is something that we do see on their examination I think it's something that we need to really just inform them what we're seeing and to either explain to them why we think we're seeing it or to include it as a part of the report. We have a caveat that we add to our reports in which we see ipsilateral axillary lymphadenopathy in women that have recently been vaccinated. We provide a summary of the findings that we're seeing, enlarged lymph nodes, and then we have a statement there that says that we are seeing these findings due to recent vaccination.

I think it's also important for women to understand their options so based off the literature or based off practiced and established guidelines we're comfortable sending women back to routine screening after seeing the enlarged lymph nodes on the ipsilateral side after vaccination if the vaccine was on that same side in terms of injection in the same arm. But if a woman is very anxious about this, really wants to have follow-up imaging and to see that lymph node return to normal size, there's always an option that she can return for follow-up imaging in six to eight weeks just to have imaging documentation that the lymph nodes has returned to normal size. So that's something that every woman should realize that she has the option. But it's not something that is absolutely necessary.

Dr. Russell:
So, Randy, just to finish up, to clarify some of the recommendations you would give to me, if I have a patient I'm going to refer on for a mammogram, they should either get their mammogram before they get a COVID vaccine or wait six weeks after, to tell them that there might be some incidental stuff that's found on the side that they got their vaccine and not necessarily to panic about that, for institutions to take into account some of the vaccine date, side, arms side, etc, when taking in information like everything else before doing a mammogram. Anything else that I'm kind of missing as the 30,000 foot view of this?

Dr. Miles:
No, I think you hit most the points. I just think it's really important to recognize that we're still dealing with the pandemic, but we're really coming out of this phase where a lot of women delayed their screening examinations just because of government mandates that we stop non-emergent care during the peak pandemic period. And we had this period where a lot of women were afraid to come to the hospital just because of the COVID risk. So now that women are coming back, we really don't want to exacerbate any loss of women not returning for their routine screening by scaring them with findings that we may see following a vaccine administration. If they have to come in soon after their vaccine, that's something that we can take into account and really reduce any instances of where we're over imaging or performing unnecessary procedures. But before we're sending women, really stepping back and trying to prevent that from the beginning by scheduling exams around the vaccine. But either way, we really need to encourage women to come in when they can and just be smart on both sides in terms of the best methods and getting them into the breast imaging suite.

Dr. Russell:
Well, with those forward-looking thoughts in mind, I want to thank Dr. Randy Miles for sharing insights on the intersection between COVID-19 vaccines and breast imaging. Dr. Miles, it was great speaking with you, today.

Dr. Miles:
Thank you so much.

Announcer:
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