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Reactive Lymphadenopathy: Triggering False Positives on Magnetic Resonance Imaging

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Case Report

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Abstract

There are numerous etiologies of reactive lymphadenopathy on radiological imaging. Lymph node evaluation is critical for screening high risk patients for new pathology, and for the planning of systemic chemotherapy and radiation therapy. Although ultrasonography (US) is useful for screening and staging illness, it is not completely reliable. In addition to being subjective, there is also poor accessibility of deeply located lymph nodes. Breast Magnetic Resonance Imaging (MRI) offers the advantages of provision of a larger field of view, increased capability of comparison of right and left axillary areas, and increased sensitivity and specificity. It is reported that pandemic H1N1v and seasonal influenza vaccinations cause alteration in fluorodeoxyglucose avidity in positron emission tomography (PET)/CT scans. There were no identified scientific publications documenting the possibility of false positives on MRI due to the Shingrix vaccine, nor any universal recommendations for patients to avoid vaccinations for a specified period of time prior to imaging. The following is a case report of false positive reactive lymphadenopathy found in a healthy patient during breast MRI screening due to high risk status.

Keywords: Magnetic Resonance Imaging; MRI; Reactive Lymphadenopathy; PET Scan, Shingrix; Herpes Zoster; varicella-Zoster Virus (VZV); Axillary Lymph Node

Abbreviations: US: Ultrasonography; MRI: Magnetic Resonance Imaging; PET: Positron Emission Tomography; VZV: Varicella-Zoster Virus.

Introduction

Herpes Zoster (HZ; 'shingles') represents a decline in cell-mediated immunity to varicella-zoster virus (VZV) associated with immunosuppression and is increasingly common with advance in years [1-3]. The vaccine HZ/su (Herpes Zoster subunit) consists of a single recombinant VZV protein, glycoprotein E antigen, combined with the AS01B adjuvant system able to stimulate T cell immunity, and is shown ~90% efficacy in prevention of HZ in controlled trials in patients over the age of 50 years [1-3].

HZ may occur at any age, but the risk increases dramatically over the age of 50 years, as natural immunity to pathogens declines [1,2]. More than 90% of individuals are infected with the virus at some point, and immunosenescence causes more than 50% of individuals over the age of 85 years to experience HZ. However, HZ may occur at any age due to numerous medical and pharmacological etiologies of impaired cell mediated immunity [2,3]. HZ represents the reactivation of lifelong latent infection with VZV in the paraspinal dorsal root ganglia/cranial nerve ganglia years following initial infection. Shingrix is approved for the prevention of herpes zoster (EU, USA, Japan, Canada and Australia) and postherpetic neuralgia (EU and Australia) in adults aged > 50 years. HZ/su demonstrated an overall vaccine efficacy of 97.2% among participants 50 years of age or older, indicating a significantly reduced risk of HZ in this group. Shingrix was approved by the United States Food and Drug Administration in October 2017 as HZ prophylaxis [1,2,4].

The most commonly reported reactions to Shingrix include injection site reactions, myalgia and fatigue. Most adverse reactions are transient and mild/moderate in severity [1,3]. Shingrix is recommended to be injected via two intramuscular injections spaced two to six months apart. Less than 10% of subjects had transient (1-2 days) injection site pain, swelling or redness.

Although ultrasonography (US) is useful for screening and staging illness, it is not completely reliable. Not only is there the factor of subjectivity, there is poor accessibility of deeply located lymph nodes [5,6]. It is reported that the sensitivity and specificity of breast US range from 27.4% to 92% and from 55.6% to 98.1%, respectively. Breast MRI offers the advantages of provision of a larger field of view, increased ability for comparison of right and left axillary areas, and increased sensitivity and specificity from 78-96% and 75% to 96%, respectively. Shirone, et al. reported that recent influenza vaccines prior to FDG-PET/CT may cause ipsilateral axillary lymph node accumulations, especially within 7 days of the vaccination; the authors suggested that questionnaires about vaccination may assist in avoidance of false interpretations by radiologists [5]. Thomassen, et al. [6] cited multiple studies of PET scan hypermetabolic and F-FDG uptake related to influenza vaccinations. In addition, they reported that influenza vaccination may lead to FDG-avid draining lymph nodes beyond 1 month. The FDG avidity was more evident in the H1N1v group versus the seasonal group; the recovery period was approximately 45 days, respectively. The authors proposed a restraining period of 30-50 days from influenza vaccine to PET scan.

With the current worldwide pandemic and mass global vaccinations with the COVID-19 vaccine, many patients have reported lymphadenopathy. According to Wolfson, et al. [7] 46% of patients who received the Moderna vaccine reported lymphadenopathy, and 38% and 39%, for those receiving Pfizer and Johnson & Johnson, respectively. Due to the significance of these numbers, it would serve patients well report recent vaccines during the screening process for medical imaging.

Current Screening Guidelines for Women at Normal Risk

The United State Preventive Services Task Force Recommendation Statement (USPSTF) recommends every other year screening mammography for women aged 50 to 74 years. The decision to start screening mammography in women prior to age 50 years should be an individual one. Women who place a higher value on the potential benefit than the potential harms may choose to begin biennial screening between the ages of 40 and 49 years. The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women aged 75 years or older. The USPSTF concludes that the current evidence is insufficient to assess the risks versus benefits of adjunctive screening for breast cancer using breast ultrasonography, magnetic resonance imaging (MRI), or other methods in women identified to have dense breasts on an otherwise negative screening mammogram.

Current Screening Protocols for Women at High Risk

A woman is considered at higher risk if she has one factor that greatly increases risk or several factors that together, greatly increase risk. Your healthcare provider may use different tools to assess your risk and help you make a personalized breast cancer screening plan. Factors that greatly increase breast cancer risk include but are not limited to:

- A *BRCA1* or *BRCA2* gene mutation (and first-degree relatives of people with *BRCA1/2* mutations who personally have not been tested for *BRCA1/2*mutations)
- A personal history of invasive breast cancer, ductal carcinoma in situ, lobular carcinoma in situ or atypical hyperplasia
- Radiation treatment to the chest area between ages 10-30
- A greater than 20 percent lifetime risk of invasive breast cancer based mainly on family history

Case Description

Patient is a 55-year-old Caucasian female with history of fibrocystic breast disease, Status/Post right side excisional biopsy breast (2015) and Status/Post left side excisional biopsy breast (2016), both with benign pathology. Significant family history includes sister with Intraductal Carcinoma (breast) diagnosed at age 60 years; sister passed away of metastasis of same diagnosis at age 67 years. Patient's sister had metastasis to pelvis, vertebrae, liver, and chest cavity.

Screening protocol for this patient to monitor for breast cancer includes 3D mammography annually and breast MRI at the six-month mark (annually).

Indications: Elevated risk for breast cancer. Previous benign excisions. Sister with history of breast cancer diagnosed at age 60; passed away at age 67 years.

Patient received second administration of the Shingrix vaccine in the right deltoid 48 hours prior to the annual breast MRI.

Findings

New right axillary adenopathy. Multiple enlarged lymph nodes present. Edematous changes in the axilla, mostly, in the level 1 region although there are abnormal lymph nodes in the level 2 and level 3 regions as well. The largest level 1 lymph node measures 1.6 x 1 cm, The is a 1 cm short axis level 2 lymph node posterior to the pectoralis minor muscle and there are several level 3 lymph nodes which are all sub-centimeter in short axis, although appear larger when compared to prior imaging. No left axillary pathology noted. No suspicious enhancement in either breast; images of the mediastinum are unremarkable. No internal mammary adenopathy is seen. Limited images of the upper abdomen are unremarkable.

Ultrasound (right axillary region) and 3D mammography (right breast) at one week follow up were unremarkable. Ultrasound of the right axillary region at 8-week follow up was unremarkable.

Discussion

Currently the registration questions prior to MRI do not include inquiries regarding recent vaccinations. As in the case outlined, should there be a universal protocol instituted prior to imaging of various types? If so, what should be included (influenza; shingrix; pneumococcal etc.)? Should there be different protocols for different types of imaging and for various vaccines?.

Given that Shirone, et al. reported that influenza vaccines within 7 days of imaging, and Thomassen, et al. [6] cited multiple studies affected of PET scan hypermetabolism and F-FDG uptake due to influenza vaccinations, universal screening prior to imaging should be considered. In addition, they reported that influenza vaccination may lead to FDG-avid draining lymph nodes beyond 1 month. Prior studies have proposed a restraining period of 30-50 days from influenza vaccine to PET scan [8,9].

There are financial expense and emotional consequences of false negatives, false positives, and false interpretations. Universal screening measures would be relatively simple to institute; at the very least screening questions for imaging should include questions regarding recent vaccination status.

Radiologists at some institutions and health care organizations are cautioning physicians regarding the frequency of lymphadenopathy following vaccines. Swollen lymph nodes after the COVID-19 vaccine are commonly reported; this is secondary to a strong immune response in some patients. This can mimic serious conditions, including cancer [10,11]. Screening prior to MRI and Pet scans, among other imaging, should include questions such as, “Have you received vaccinations of any type within 6 weeks of the date of the imaging or procedure?” Imaging should be performed either prior to the imaging, or at least six weeks afterward to reduce the need for additional testing. That said, if the patient has active symptoms or findings, any delay in evaluation of the symptoms should be avoided. The cost savings and decrease in false positives justify this consideration.

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