

Post-vaccination SARS-CoV-2 axillary adenopathy. Differences with axillary metastases from breast cancer

Adenopatía axilar posvacunación contra el SARS-CoV-2. Diferencias con metástasis linfática del cáncer de mama

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Abstract

The differential diagnosis of the metastatic axillary lymphadenopathies of breast cancer with which they occur secondary to the Pfizer-BioNTech vaccine against COVID-19, is imperative. In a series of cases, we analyzed the characteristics of unilateral axillary lymphadenopathy in patients after Pfizer-BioNTech vaccination. Axillary lymphadenopathy were observed ipsilateral to the vaccination arm. The axillary ultrasound defined these as reactive and that they disappeared in 3 weeks. The pathological findings were benign. The anamnesis, the place and date of vaccination and the radiological findings, play an essential role to carry out a correct differential diagnosis and follow-up of these adenopathies.

Keywords: Axillary lymphadenopathy. Reactive adenopathies. COVID-19. Pfizer-BioNTech. Breast cancer. Vaccine.

Resumen

El diagnóstico diferencial de las adenopatías axilares metastásicas del cáncer de mama con las que se producen secundarias a la vacuna de Pfizer-BioNTech contra la COVID-19 es imperioso. Analizamos una serie de casos con las características de las adenopatías axilares unilaterales tras la administración de la vacuna de Pfizer-BioNTech. Se observaron adenopatías axilares homolaterales al brazo de vacunación. La ecografía axilar las definió como reactivas y que desaparecían en 3 semanas. Los hallazgos anatomopatológicos fueron de benignidad. La anamnesis, el lugar y la fecha de vacunación, así como los hallazgos radiológicos, desempeñan un papel esencial para realizar un correcto diagnóstico diferencial y el seguimiento de estas adenopatías.

Palabras clave: Adenopatías axilares. Adenopatías reactivas. COVID-19. Pfizer-BioNTech. Cáncer de mama. Vacuna.

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Introduction

The side effects of the Moderna and Pfizer-BioNTech COVID-19 vaccines are common: 85% of local reactions at the injection site, and 75% of systemic reactions. Benign reactive axillary lymphadenopathies are uncommon, yet known, reactions. The highly immunogenic clinical response of both vaccines could predict a higher percentage of unilateral axillary adenopathies¹⁻³.

In breast cancer, presence of metastatic axillary adenopathies is a factor that affects global survival. Macroscopic axillary metastases and affected levels II and III imply a worse prognosis and higher risk of recurrence⁴. The differences between these adenopathies and those that occur after administering the Pfizer-BioNTech vaccine are not widely described in the literature.

The purpose of this case presentation is to analyze the clinical and radiological characteristics of unilateral axillary adenopathies in patients who received the Pfizer-BioNTech vaccine, and their differential diagnosis with breast cancer metastatic pathological adenopathies.

Clinical cases

In February 2021, four patients with unilateral axillary adenopathies were referred to the breast pathology clinic of our center. They were all women, of an average age of 43 years, with no family history of breast cancer and recently vaccinated with Pfizer-BioNTech. An ultrasound study of the breast and armpit and a mammogram were performed. Suspicious adenopathies were biopsied with a thick needle (Table 1). Subsequently, a monthly ultrasound follow-up was performed after administering the second dose.

Clinically, they referred unilateral axillary adenopathies (node level I) painful during the physical exploration one week after the vaccination, coinciding with the same arm where it was administered, and with no other associated symptoms. They were described as rolling, moving, and 2 cm in size approximately, and palpable breast nodes were ruled out.

Radiologically, adenopathies of 1.5-3 cm were seen with fatty hilum, homogeneous cortical thickening, and reactive appearance. The contralateral armpit was normal in all cases. No imaging suggesting breast cancer was found in any of the patients. The mammograms were classified as BIRADS 3. In the anatomopathological study, cells with reactive hyperplasia were found. During the follow-up of the patients, the adenopathies had clinically disappeared

during the first week, and there were not present in the ultrasound two weeks after the last dose of the vaccine.

Discussion

The differential diagnosis of unilateral axillary adenopathies is very wide, including benign pathology (concurrent lymphadenopathy in breast parenchyma, inflammatory arthritis, infectious or traumatic etiology), and malignant pathology (breast cancer or lymphoma)^{5,6}. Historically, unilateral axillary adenopathies have been described after the administration of the smallpox, influenza virus, bacille Calmette-Guérin (BCG), human papilloma, and anthrax vaccines. This side effect is more common in vaccines that cause a significant immune response, such as the Moderna and Pfizer-BioNTech COVID-19 vaccines. It primarily appears 2-4 days after the vaccine is administered, and the duration is between 2 and 4 weeks. Although, in our series of cases we only found adenopathies at the node level I, they have also been found at levels II and III⁵⁻⁸.

When palpable unilateral axillary adenopathies are found, or incidentally, during a breast screening study, it is imperative to rule out a homolateral malignant pathology. The presence of metastatic adenopathies in breast cancer is the most significant survival and recurrence predictor, decreasing the survival rate of 5 years from 98.8% to 85.8%^{9,10}.

The ultrasound has a sensitivity of 26-76% and a specificity of 88-98% when evaluating the morphological characteristics of axillary adenopathies. Using the ultrasound, a normal lymph node is described as oval, with well-defined smooth edges and a hypoechoic, even cortical with thickness of less than 3 mm. On the contrary, lymph nodes that suggest metastasis have focal hypoechoic cortical thickening, absence of fatty hilum or complete replacement of the node by an ill-defined mass^{4,9,10}.

In our series, lymph nodes after vaccination are defined as reactive: well-defined, with fatty hilum, and homogeneous cortical thickening (Fig. 1). These characteristics, which make us suspect benignity, allow us to make a differential diagnosis with those with pathological characteristics⁵⁻⁸.

With the implementation of the immunization plan in the general population, these adenopathies will become more frequent during early detection screenings for breast cancer. Therefore, we propose including the COVID-19 vaccination date and the side where the injection was administered in the clinical history of each patient. Some center, after finding unilateral axillary adenopathies,

Table 1. Characteristics of the studied patients

Case	Age (years)	Vaccine	Arm injected	Symptoms	Start of symptoms after vaccination	Ultrasound description of adenopathy	Biopsy with thick needle
1	34	Pfizer	Left	Left axillary adenopathy	7 days	Reactive, 2.5 cm, fatty hilum	Reactive hyperplasia cells
2	53	Pfizer	Left	Left axillary adenopathy	2 days	Reactive, 2.9 cm, fatty hilum, homogeneous cortical thickening	Reactive hyperplasia cells
3	43	Pfizer	Left	Left axillary adenopathy	3 days	Reactive, 1.7 cm, fatty hilum, homogeneous cortical thickening	Reactive hyperplasia cells
4	42	Pfizer	Right	Right axillary adenopathy	5 days	Reactive, 1.4 cm, fatty hilum	Reactive hyperplasia cells

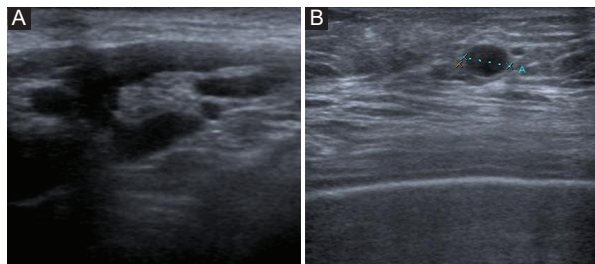


Figure 1. A: axillary ultrasound after receiving the Pfizer-BioNTech vaccine where a reactive lymph node of 2.9 cm with fatty hilum can be observed. **B:** axillary ultrasound indicating a 9 mm node with no fatty hilum, suggestive malignancy.

recommend an ultrasound at the time of the diagnosis in order to define their characteristics, and repeat the ultrasound 6-8 weeks after the second dose of the vaccine. If adenopathies persist, an ultrasound-guided biopsy is recommended in order to rule out malignancy^{5,6}.

Conclusions

The anamnesis, the place and date of vaccination and the radiological findings, play an essential role to carry out a correct differential diagnosis and follow-up of these adenopathies. These findings should be sufficient to decrease the number of false positives in breast cancer screenings.

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Conflicts of interest

The authors declare not to have any conflicts of interest.

Ethical disclosures

Protection of people and animals. The authors declare that the procedures followed were in accordance with the ethical standards of the responsible human experimentation committee and with the World Medical Association and the Declaration of Helsinki.

Data confidentiality. The authors declare that they have followed the protocols of their work center regarding the publication of patient data.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

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