



**Original Research Article**

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## **Axillary Lymphadenopathy after first dose of covid-19 vaccine**

**Mr. Ehsanur Rahman**<sup>\*</sup>, RWT NHS Trust

**Mr. Nirbhaibir Singh**<sup>#</sup>, RWT NHS Trust

**Mr. Brian Isgar**<sup>@</sup>, RWT NHS Trust

**Mr. Tapan Sircar**<sup>@</sup>, RWT NHS Trust

**Dr. Dharamjeet Kaur,**

**Dr. Bal Jaskaran Singh**<sup>#</sup> Pennine Acute NHS Trust

<sup>\*</sup>Specialty Doctor, <sup>#</sup>Clinical Fellow, <sup>@</sup>Consultant

<sup>#</sup>Corresponding Author: Mr. Nirbhaibir Singh, E-mail: [nirbhaibir.singh@nhs.net](mailto:nirbhaibir.singh@nhs.net)

### **Abstract**

With the ongoing mass vaccination program we are receiving reasonable number of patients with unilateral axillary lymphadenopathy on the vaccination site and it is sometimes bring about lots of puzzle in our mind specially with the background history of breast cancer and the history of vaccine in the same side as it may mimic metastasis. We are presenting the case to inform that it is very natural to get unilateral axillary lymphadenopathy due to strong immune response from Covid 19 vaccine. So it is extremely important for clinicians as well as the radiologists to ask about the recent history of COVID -19 vaccination when the presentation is with unilateral axillary lymphadenopathy.

**Keywords:** COVID -19, axillary lymphadenopathy, vaccination.

### **Background**

In this era of covid -19 pandemic mass vaccinations is the only way to control spread of the disease. But this vaccination derive is leading to increased number of patients being referred to breast clinic with complains of pain and swelling in axillary region. Mostly the swelling is unilateral and on the same side as the vaccination injection site. It is important that the clinicians and breast radiologists should be aware of vaccine induced reactive lymphadenopathy so as to reduce the need for unnecessary lymph node biopsies. Ours is the case report of a 45 F patient who presented to fast track breast clinic with pain and swelling in left axillary region three weeks after getting covid-19 vaccine in the same arm.

### **Case Presentation**

45 f presented to fast track breast clinic with complains of pain and swelling in upper outer quadrant of the left breast and the axillary region. There was no significant personal medical history or any family history of breast or ovarian cancer. On clinical examination there was no worrying abnormality noted in the breast apart from slight benign breast changes in the upper outer quadrant of the breast. But there was some tender cord like thickening present in the breast which was most likely to be inflamed lymphatic channels. After further questioning we noticed that she had injection of Pfizer-bioNTec covid -19 vaccine in the same arm about 3 weeks ago.

## Investigations

After clinical evaluation, she underwent radiological assessment with bilateral mammogram and left axillary ultra sound scan. Mammographic examination did not reveal any significant focal or suspicious features in either breast; however two prominent dense axillary lymph nodes were noted within the left axillary tissue. Ultra sound scan of the left axilla demonstrated two prominent axillary lymph nodes as seen mammographically both of which had retained their fatty hilar tissue however displayed a cortical thickening up to 6.23mm. Given the recent history of covid -19 vaccination the lymph nodes were felt to be most likely reactive in nature.

## Differential Diagnosis

Given the age group and gender of the patient although it is imperative to exclude malignant conditions but benign aetiologies like reactive lymphadenopathy post viral illness or after vaccination were also considered.

## Outcome and Follow-up

Upon confirming recent ipsilateral COVID-19 vaccination status in the patient, our local MDT recommended repeat targeted ultrasound of the affected axilla just before they are scheduled to have their second dose of covid -19 vaccine, which in UK is after 12 week intervals from first dose, to ensure resolution.

If the abnormal adenopathy persists on follow-up imaging, then as per local protocol patient would be re discussed in local Breast MDT regarding further management planning.

## Discussion

There is a wide range of conditions which can result in unilateral axillary lymphadenopathy and these include both benign and malignant conditions. Common benign causes include benign reactive hyperplasia, inflammatory arthritides, and infectious etiologies [1, 2]. Among malignant causes, the majority of cases are due to lymphoma

or metastatic breast cancer [1-3]. While it is imperative to exclude malignancy, most cases of isolated axillary lymphadenopathy (e.g., lymphadenopathy without concurrent abnormality within the breast parenchyma, and with no known diagnosis to explain the lymphadenopathy) are due to benign causes [1-3]. As we understand that axillary lymph nodes drain upper limb and thoracic wall along with breast tissue; therefore, inflammation, trauma, or local infection in these areas can potentially result in unilateral axillary lymphadenopathy [4]. Lymphadenopathy after recent vaccination is a well established entity and has been reported following anthrax, Bacille Calmette-Guerin (BCG), and smallpox vaccination [5]. In some cases, recent vaccination history was overlooked leading to the misdiagnosis of malignancy. For example, in 1968 Hartsock concluded that 9 of 20 cases of post-vaccine lymphadenitis, related to recent inoculation with the smallpox vaccine, were misdiagnosed as malignant lymphoma. In 1990, Newfield et al. reported a case of initially misdiagnosed unilateral axillary lymph node enlargement in a 50-year-old woman who received the BCG vaccine two months earlier [6]. More recently, unilateral adenopathy has been reported in adults receiving the human papilloma virus (HPV) vaccine in the ipsilateral deltoid muscle [7]. Reactive unilateral axillary lymph nodes have also been demonstrated following vaccination in the ipsilateral upper extremity with the influenza vaccine, including the H1N1 influenza A virus vaccine, as evidenced by unilateral increased fluorodeoxyglucose (FDG) uptake on Positron Emission Tomography – Computed Tomography (PET/CT), which resolved on short-term follow-up PET/CT [8,9,10]. It is well documented that any vaccination in upper extremity can induce reactive lymphadenopathy in same side axilla; however it is seen more commonly after a vaccine that produce a very strong immune response, including the most recently FDA approved Moderna and Pfizer-BioNTech COVID-19 vaccines. As Per the Centers for Disease Control and Prevention (CDC), amongst recipients of the Moderna COVID-19 vaccine, axillary adenopathy ipsilateral to the vaccination arm was the second most frequently reported local reaction,

with 11.6% of recipients experiencing this after Dose 1 and 16.0% of recipients experiencing this after Dose 2 in the 18–64 year age group. In contrast, the CDC did not report data for axillary adenopathy occurring in recipients after receiving the Pfizer-BioNTech COVID-19 vaccine, but rather noted that reports of adenopathy were imbalanced between the vaccine group (64) and the placebo group (6), concluding that adenopathy was plausibly related to the vaccine[11]. Additionally, of those recipients who received the Pfizer-BioNTech COVID-19 vaccine, adenopathy was reported within 2–4 days after vaccination, similar to those recipients of the Moderna COVID-19 vaccine; however, the average duration of adenopathy was approximately 10 days, compared to an average duration of 1–2 days with the Moderna COVID-19 vaccine [11]. In our case, the time between receiving the Pfizer-BioNTech COVID-19 vaccination and detection of unilateral axillary adenopathy was about 15 days, which is longer than the average duration of 10 days reported by the CDC in recipients of the Pfizer-BioNTech Covid-19 vaccine. Nishi Mehta et al in their case series reported median time of 8 days to develop unilateral axillary lymphadenopathy after Pfizer-BioNTech COVID-19 vaccine and 13 days after Moderna vaccine[12]. With the recent FDA-approval and rollout of the Pfizer-BioNTech and Moderna COVID-19 vaccines, it is imperative for clinicians to recognize recent ipsilateral COVID-19 vaccination history as a potential differential diagnosis for unilateral axillary adenopathy. Patients may either present for diagnostic imaging for palpable unilateral axillary adenopathy or it may be discovered incidentally during routine or screening breast imaging. Recognizing this as a potential differential diagnosis is crucial to being able to provide appropriate follow-up recommendations. This would in turn decrease the number of false-positive axillary lymph node biopsy recommendations, thus minimizing patient harm and cost.

### **Learning points/take home messages 3-5 bullet points**

Recognising this potential side effect of covid -19 vaccination would in turn decrease the number of false-positive axillary lymph node biopsy recommendations, thus minimizing patient harm and cost.

Patients with known breast malignancy should ideally be vaccinated in the contra lateral arm, so as to avoid confusion and to reduce unnecessary referrals and interventions.

Hospitals should formulate local protocols to manage reactive lymphadenopathy post covid -19 vaccination.

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