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Radiological Characteristics of Immunization Adenitis in the Axilla Following the Covid-19 Vaccine

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Abstract: It was aimed to investigate the ultrasonography (US) features of axillary COVID-19 immunization adenitis. Patients with axillary COVID-19 immunization adenitis detected between April 2021 and January 2022 were included. US features of the lymph nodes identified at the patient's initial US were all recorded. Radiological follow-up information and if exists pathology results were investigated. 104 immunization adenitis in the axilla following Covid-19 vaccine were detected. Only 18.3 percent had axillary pain or edema. Biopsy was recommended for 4 patients and follow-up was recommended for the other 100 patients. Core biopsy results were lymphoid tissue with focal micro-abscess formations, reactive lymphoid hyperplasia and plasma cell increase. All of the patients had a history of vaccination in the last 3 months. After immunization, initial US imaging was conducted mean 24-days later. The mean long and short axis were 22-mm and 13-mm, respectively. The mean long-short axes ratio was 2.2. The mean thickness of the cortex was 4.8-mm. The long and short axes of the lymph nodes in the first US and control examinations were compared statistically and they decreased in time. The hilum existed (96%). Elastography revealed soft features. The majority of the immunization adenitis are just enlarged benign-appearing lymph nodes. The majority were found during the extensive immunization campaign and were asymptomatic. Patients and their physicians should be aware of the vaccination and imaging evaluation of specific patient groups considering that these vaccinations will continue to be used for a while in the next years. ©2023 NTMS.

Keywords: Axillary Lymph Nodes; Covid-19; Lymphadenopathy; Vaccine.

1. Introduction

Millions of lives are saved annually thanks to vaccination, which is a success story in global health and development. In order to create immunity, vaccines act in conjunction with your body's natural defences. Your immune system reacts when you receive a vaccination [1,2]. Although immunizations are generally regarded as safe, the most frequent side effects are local adverse reactions, such as discomfort, swelling, and redness at the injection site. They often start a few hours after the injection and are usually neither severe or self-limited. Depending on the vaccine type, up to 80% of vaccine doses may cause local responses.[3] It is recognized that some vaccines can cause adenitis [4]. Instead of being an illness, it is the body's response to the vaccine; it is a sign of immunization [5]. Even though many vaccines cause immunization adenitis, the axilla

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is a significant location that warrants attention and caution, especially in some particular groups [6-8]. Actually, the axilla is an intersection. In addition to diseases of the lymph nodes themselves, it accepts lymphatic outflow of the breast, lungs, upper extremities, and the skin that covers these areas [9, 10]. It is therefore essential to determine the source of an abnormal finding in the axilla. In this study, we aim to demonstrate the radiological characteristics of patients with COVID-19 immunization adenitis.

2. Material and Methods

The study received approval from the non-interventional clinical research ethics committee at our university in a decision with the reference number E-10840098-722.02-4333. As a retrospective observational study, informed consent could not have been acquired.

2.1. Patients

Between April 2021 and January 2022 in the Radiology department axilla US findings were reviewed. Patients having COVID-19 immunization adenitis were. Patients who underwent evaluation between these dates and had previously been diagnosed with pathologically benign lymphadenitis or axillary involvement due to breast, lung or head and neck carcinoma were excluded from this study. The dimensions, shapes, thicknesses of the cortex, vascularity, and elastic stiffness of the lymph nodes identified at the patient's initial visit were all recorded using ultrasonography. Radiological follow-up information and if exists pathology results were investigated. Detailed clinical history and vaccination history of each patient were obtained before ultrasonography and recorded. A short wait, 1-month, and 3-month US control were recommended for patients with immunization adenitis.

2.2. Axilla Ultrasonography

As per institutional procedure, ultrasonography was performed by a high-frequency (12 MHz) linear transducer. The axilla was assessed in ultrasonography by comparison on both sides. Atypical lymph nodes were enlarged, round or those with a thickened cortex (greater than 3 mm), a flattened or missing hilum [11]. The patients with the diagnosis of immunization adenitis were advised to undergo follow-up or biopsy if an abnormal lymph node was found in the axilla and there was a history of vaccination given to the same arm during the previous three months.

2.3. Statistical Analysis

The statistical analysis was carried out using SPSS 22.0 software. Counts and percentages were used to report categorical data, whereas the mean and standard deviation were used to display continuous variables. The distribution of the data was confirmed using the one-sample Kolmogorov-Smirnov test. When a normal distribution could not be determined, log transformation was used. Descriptive statistics were employed. The Wilcoxon test was used to assess the short and long axes and long-short axes ratio that was captured in the initial and subsequent US exams. Every analysis was two-sided, and a statistically significant level of significance was set at 0.05.

3. Results

On the specified dates, 1934 superficial tissue US was performed in the Department of Radiology. Axilla assessment was performed in 230 of these. Among them 104 had immunization adenitis in the axilla following Covid-19 vaccine (101 females (97%), 3 males (3%); mean±standard deviation (SD), 37±9 year-old) were involved. Only 19 patients (18.3 percent) of those we questioned in the first US reported experiencing axillary pain or edema. Among those recommended biopsies, 1 patient did not accept the biopsy and did not come to the controls. It was reported as the results of 3 patients who underwent core biopsy were lymphoid tissue with focal micro-abscess formations, reactive lymphoid hyperplasia and plasma cell increase. The months in which the patients were examined initially are given in Figure 1.

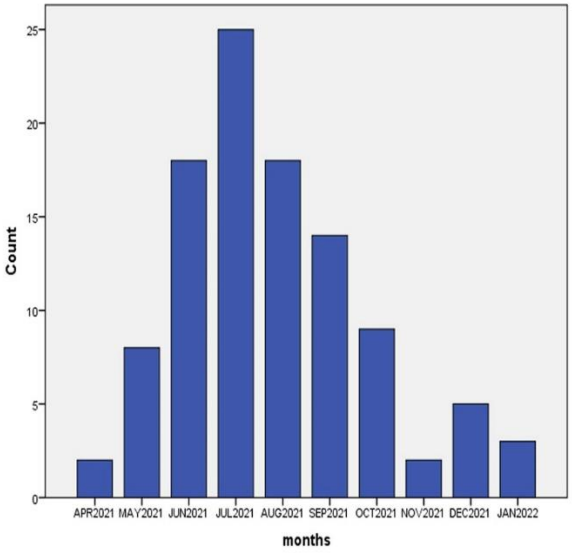

Figure 1: The months in which the patients were detected.

All of the patients had a history of vaccination in the last 3 months. After immunization, US imaging was conducted Mean±SD, 24±29-days later (between 1 and 160-day). Biopsy was recommended for 4 patients and follow-up was recommended for the other 100 patients. After an average of 90±56 days (15-212), 31 of them came to the first control and 10 of them came to the second control after an average of 191±31 days (137-225). 51 patients were called and invited to the US for control, but they chose not to come because they had no complaints.

The lymph node was located on the left in 87 patients (84%), bilateral in 14 patients (13.5%), and on the right in 3 patients (2.5%). In 90 patients, the lymph node arose on the same side as the vaccinated arm (86.5%), while it appeared bilaterally in 14 patients (13.5%).

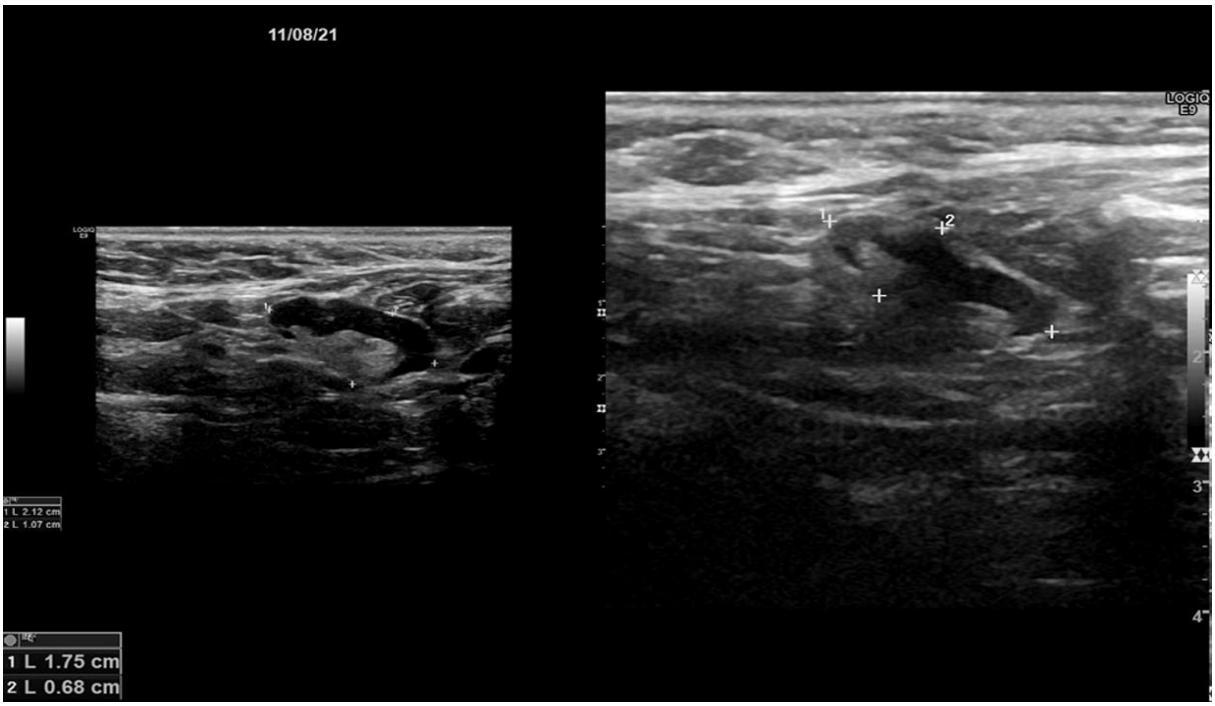

Figure 5: An oval, thick cortex, enlarged lymph node is observed in a 37-year-old female patient who was vaccinated against COVID-19 (left). In the first US control, it is noteworthy that its size has decreased, its cortex has become thinner and its hilum has become prominent (right).

Table 1: The dimensions of the lymph nodes in the first US and control examinations.

	Long Axis (Mean±SD)	**Short Axis (Mean±SD)**	**Long-Short Axes Ratio (Mean±SD)**
Initial US	22±6 mm	13±11 mm	2.2±0.6
First control	18±3 mm	10±4 mm	2.4±0.7
Second control	17±3 mm	9±4 mm	2.6±1.3
Comparison of the initial US and the first control (p value)	0.004*	0.045*	0.012*
Comparison of the initial US and the second control (p value)	0.010*	0.077	0.210
Comparison of the first and the second controls (p value)	0.223	0.069	0.184

The Wilcoxon test was used. *Statistically significant.

In the initial ultrasonography, the mean long and short axis of the lymph nodes were 22±6-mm (8-49) and 13±11-mm (4-58) respectively. The mean long-short axes ratio was 2,2±0.6 (0.3-4.0). 100 (96%) of the lymph nodes were oval and 4 (4%) round. The mean thickness of the cortex and SD was 4.8±1.9-mm (2-13.8 mm). The long and short axes of the lymph nodes in the first US and control examinations were compared statistically and significant difference existed between the initial US and the others (Table 1, Figures 2-5).

The hilum was missing or flattened in 4 lymph nodes (4%), while in others do exist (96%). While the expression of hilar blood supply for 18 lymph nodes was included in the report, the anarchic blood supply was not mentioned in any of them. Elastography information was available for only 20 lymph nodes. Elastography revealed soft features in 19 lymph nodes (95%), and a stiff elastic score for only one lymph node (5%). All but one patient had received the mRNA vaccine.

4. Discussion

The majority of the lymph nodes in our study population with COVID-19 immunization adenitis are oval-shaped, benign-appearing, have a distinct hilum, normal hilar vascularity, are soft on elastography, with normal long-short axes ratio, and only have increased dimensions. 99 percent of cases were due to mRNA vaccination. The bulk was found during the extensive immunization campaign that took place between June and October of 2021 and was asymptomatic.

An oval or lobulated shape, as well as a smooth, clearly defined edge, are characteristics of a healthy axillary lymph node. The cortex should be uniformly thin, measuring 3 mm or less, and mildly hypoechoic [12].

Normal, non-metastatic lymph nodes have long-short axes ratio greater than 1.6 [13].

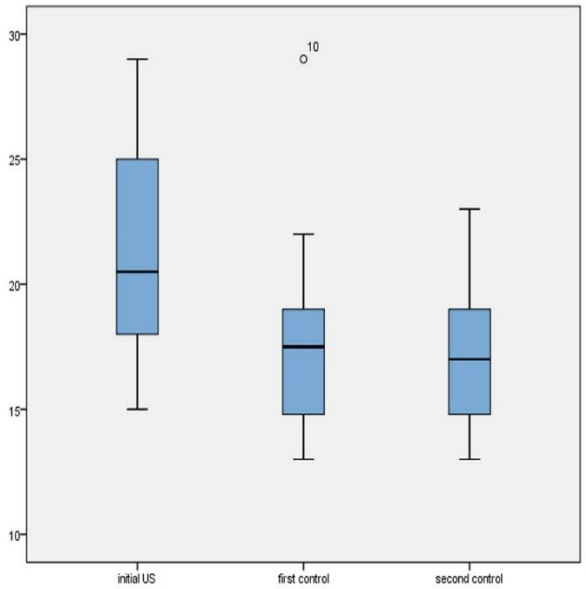

Figure 2: The long axis of the lymph nodes in the first US and control examinations.

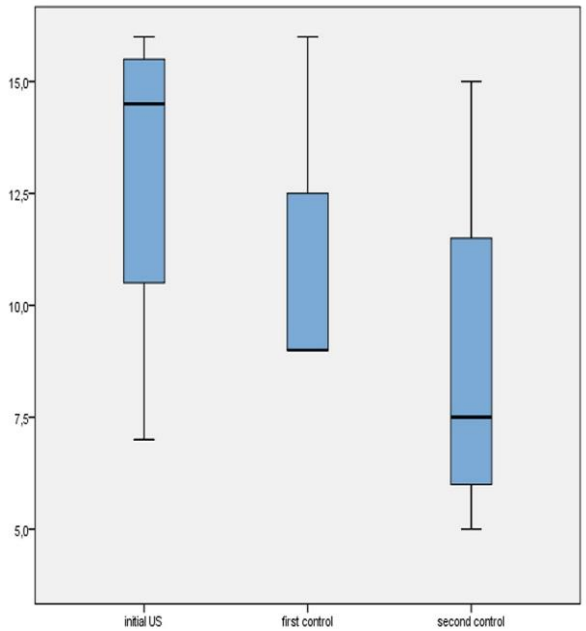

Figure 3: The short axis of the lymph nodes in the first US and control examinations.

A common although the minor effect of the COVID-19 vaccine is unilateral axillary lymphadenopathy. The European Society of Breast Imaging (EUSOBI) offers the following suggestions with the aim of standardizing management and cut back on unnecessary invasive and further imaging procedures: (a) Patients with a history of breast carcinoma should receive vaccination in the thigh or opposite arm; (b) Before breast imaging, vaccination history should have been obtained; (c) Breast imaging examinations should be performed preferably before or at least 12 weeks after immunization procedure; (d) Regardless of vaccination status, follow standard imaging protocols for patients with recently identified breast carcinoma; (e) in cases of axillary lymphadenopathy that is symptomatic or unrelated to vaccination, thoroughly image the other axilla and breasts to rule out carcinoma; (f) in cases of axillary lymphadenopathy on the side that was spared from vaccination, follow standard work-up; (g) Depending on the clinical situation, lymphadenopathy on the same side with the vaccination within 12-week-of vaccination can be considered benign or probably-benign in patients without a history of breast carcinoma and no suspect radiologic results; (h) in patients without a history of breast carcinoma , the immunization adenitis in conjunction with a suspicious breast finding necessitates the standard work-up, including biopsy when appropriate; (i) In individuals with a history of breast carcinoma , notify and treat the immunization adenitis taking into account the amount of time since vaccination and overall risk of nodal metastatic disease; (j) a multidisciplinary team should handle difficult or unclear situations[14].

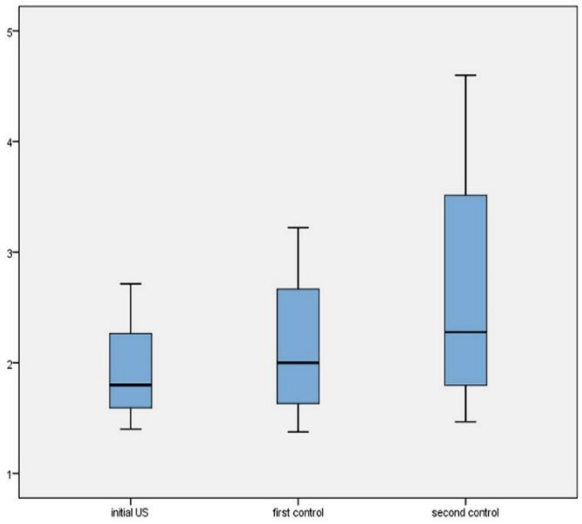

Figure 4: The mean long-short axes ratio of the lymph nodes in the first US and control examinations.

In our clinical practice, whether there were axilla complaints or not, we used a similar approach to patients with abnormal axillary lymph nodes who had received the mRNA COVID vaccine during the previous three months: We advised physical examination, follow-up, US control after a month, and physical evaluation. On the first visit, we recommended a biopsy for a few lymph nodes that were highly suspicious due to size or an obliterated hilum, or an extremely thick cortex. We advised control in the third month after the initial control at the conclusion of the first month. On imaging, the majority of patients were unintentionally discovered. Most people had no complaints. Only 3 patients in our study received a biopsy, and the results were benign. Upon follow-up, the lymph nodes shrunk.

As much as 16 percent of patients who received the COVID-19 vaccine reported having axillary swelling afterward.[15] In a study, 750 patients who received at least one dose of the COVID-19 vaccine within 90 days of either screening or diagnostic mammograms were retrospectively analyzed. It was discovered that 23 (3%) of these patients had axillary adenopathy on mammography, and only 2 of these patients had symptoms.[16] The difference between a rate of 3 percent and 16% is significant. The authors have already mentioned some limitations in this study, such as small sample size, being a single center study.[16] An important limitation is related to mammography. Because mammography shows the lateral axilla well, lymph nodes in the deeper part may not be evaluated with mammography. However, US can show abnormal lymph nodes in the entire axilla[8]. In another study with US, reporting 23 women with COVID-19 immunization adenitis, only 13% of patients had swelling in the axilla[11]. According to their definition, 87 percent of cases were unintentionally found in women who had no symptoms. 18.3% of complaints were documented in our US study, which took place during the rigorous vaccination period, and it was noticed that other individuals had no symptoms. These variations can be connected to the vaccine campaign's time frame. Being aware of the effects of COVID vaccines, we have closely followed the recommendations of EUSOBI and the Society of Breast Imaging (SBI) in our own unit, as well as creating a scheme similar to our pre-COVID axilla management. The median time after the vaccine in patients with adenopathy is significantly shorter at 10 days compared with 18 days in patients without adenopathy[16, 17]. In our study, the mean time after the vaccine is an average of 24 days (1-160 days). The dimensions were statistically considerably reduced in the patients who could be examined after an average of 90 days. After that, there was no discernible difference in the evaluation, which took an average of 191 days. Currently, the SBI advises a BIRADS category 0 initial assignment to allow for additional evaluation of the ipsilateral breast, consideration of a follow-up examination 4–12 weeks after the second dose (BI-RADS 3), and consideration of lymph node sampling to rule out carcinoma if axillary adenopathy persists[11]. When we examined the time frame in which the cases were registered, we discovered that it matched the increase in mRNA immunization (https://ourworldindata.org/covid-vaccinations?country=TUR). Its subsequent decline might be attributed to a heightened awareness of vaccination side effects in particular. Another possibility is that the number of people who are asymptomatic may decline at specific times if there is a gap between repeat immunizations.

5. Conclusions

In conclusion, the immunization adenitis associated with COVID-19 is largely radiologically benign and only significantly enlarged. Patients are typically asymptomatic, and mRNA vaccinations cause axillary lymph node enlargement. Patients and their physicians should be aware of the vaccination and imaging evaluation of specific patient groups considering that these vaccinations will continue to be used for a while in the next years.

Limitations of the Study

The sample size and retrospective methodology of this study were limitations. Additionally, we did not calculate the proportion of patients who underwent various imaging tests at our facilities or comparison between patients who had and did not have immunization.

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Conflict of Interests

The authors declare that there is no potential conflict of interest for the research, authorship, and/or publication of this article. All authors read and approved the final manuscript.

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Author Contributions

AE and MD: design of the study, sample collection, data collection and/or processing, writing the original manuscript.

Ethical Approval

Ethics committee approval was obtained for the study from the Istanbul Medipol University Clinical Research Ethics Committee with the decision dated 02/09/2021 and numbered E-10840098-772.02-4333.

Data sharing statement, Consent to participate and Informed Statement

Waived due to retrospective design.

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