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Unilateral axillary lymphadenopathy following COVID-19 vaccination

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Abstract---Objectives: COVID-19 vaccine effects on the lymph nodes of the axillary lymph nodes were examined in this study by comparing the characteristics of the nodes before and after immunisation. Methods: More than twenty-five employees who took part in the company's immunisation campaign were considered for employment. Before vaccination, one week after the first dose, and one week after the second dose, the ipsilateral vaccinated arm was examined by axillary ultrasonography. The total number of visible nodes, the maximum diameter and cortical measures, and Bedi's categorization were recorded. The Mann–Whitney U test was used to compare the collected data and determine the differences between the two groups. As long as the statistical significance threshold was met, the variables were regarded to be of interest to researchers. Results: There was a statistically significant increase in the number of visible nodes, maximal diameter, cortical thickness, and Bedi's classification grade (p 0.001) between the three US examinations. In comparison to patients who had previously been infected with COVID-19, those who were naive to the virus had a greater lymph node response. Conclusions: This study found a statistically significant difference between the two doses of COVID-19 vaccine in terms of increasing all axillary lymph node characteristics.

Keywords---axillary ultrasound evaluations, COVID-19 vaccine, US examinations.

Introduction

SARS-CoV-2 pandemic containment and normalisation of social and economic activities will only be possible if vaccination campaigns are rolled out quickly and effectively over the world. As of July 27, 2021, the World Health Organization lists 292 candidate vaccines in clinical development, 184 in the pre-clinical phase and 108 in the clinical phase [1]. The World Health Organization (WHO) has approved the use of a number of COVID-19 vaccines (given Emergency Use Listing). As of the first week of December 2020, the first round of mass vaccinations had begun, with a total of 1.6 billion doses administered. Obesity, cardiovascular disease, pulmonary disease, and diabetes have all been linked to an increased risk of severe COVID-19, and vaccination is therefore suggested for those at higher risk. Preventive measures against COVID-19, such as mass vaccinations, have emerged as a crucial option.

Covishield or Covaxin were used in the initial phase to vaccinate health care personnel, including medical students, who were exposed to the virus. Serum Institute of India manufactures Covishield (adenovirus vectored ChAdOx1 nCoV-19 vaccine – AZD1222) under licence from Astra Zeneca, whereas Bharat Biotech manufactures Covaxin (inactivated SARS-CoV-2) vaccine Covaxin (BBV152) in conjunction with Indian Council of Medical Research [3]. The COVID-19 immunisation has been expanded to adults over 60 and those with comorbidities between the ages of 45 and 59, effective March 1, 2021. As a result, from April 1st, 2021, and May 1st, 2021, all Indians aged 45–59 and 18–44 will be able to acquire the vaccine [4]. They presented various immunisation plans and utilised a variety of vaccine development methodologies, such as messenger RNA (mRNA) and adenovirus vector-based vaccines. Some mild but widespread local and systemic reactions have been observed in both clinical trials and in the population-wide rollout of vaccines, including pain at the injection site, axillary lymph node enlargement, tiredness, headache, and fever; these reactions are most common in those receiving the second dose.

However, even though the MHRA stated that lymphadenopathy was an unusual but possible side effect of both vaccines, their widespread usage has led to the development of benign unilateral axillary lymphadenopathy. Unilateral axillary lymphadenopathy is associated with the COVID-19 vaccine because of the vaccine's ability to elicit a significant immunological response, even though this association is not brand new [5]. The axillary lymph node enlargement reaction, which has the potential to have a significant influence on breast imaging, is the subject of this research, which offers management advice for this side effect. This new diagnostic challenge and the current widespread use of COVID-19 vaccinations for the general population necessitated our study's focus on the effects of COVID-19 vaccination on unilateral axillary lymph nodes, comparing nodal basal features with their characteristics following the first and second vaccinations.

Materials and Methods

Study design and study population

Patients who got the COVID-19 vaccine and underwent breast imaging at our hospital between December 30, 2020, and April 12, 2021, were included in our trial, which was approved by our institutional review board. Volunteers were those who had received the COVID-19 vaccine and had to wait three weeks between injections. Three axillary ultrasonography (US) examinations were done on volunteers who had received both doses of the vaccine in the same arm (ideally the non-dominant arm). Two weeks after the first dose of vaccination, the second axillary US exam (first follow-up) was performed, followed by one week after the second dosage (second follow-up) (second follow-up). The average follow-up time was 32 days, beginning with the initial US examination and concluding with the second follow-up after the final dose was administered. Age and gender were recorded, and all subjects were asked if they had previously been infected with COVID-19 [6]. Those patients who had cortical thickness larger than 3 millimetres following the second dosage had their lymphadenopathy reaction outcome evaluated using a prospective US follow-up examination. When patients' cortical thickness reached normal levels (3 mm), their follow-up period was over. There was no follow-up study until the return to baseline values.

Image acquisition and assessment

Axillary US tests of the vaccinated arm were performed using two separate broadband linear transducers with a band frequency of 8–13 MHz (Logic E9, GE Healthcare, and Aplio i800 series ultrasound system, Canon Medical Systems Corporation). Each patient's X-ray images were evaluated by two radiologists in order to minimise interobserver variability. The number of visible nodes, maximum measurements of long-axis size and cortical thickness, morphological Bedi's classification and colour Doppler evaluation were all nodal findings collected in our research. The cortical Bedi classification was used to evaluate lymph nodes morphologically as follows: Hyperechoic, no visible cortex or less than 1 mm thick; thin (less than 3 mm) hypoechoic cortex; thicker than 3 mm hypoechoic cortex; lobulated hypoechoic cortex; hypoechoic node with no hilum; and lobulated hypoechoic cortex are all types of hypoechoic cortex. Using the maximum values of each variable, as well as separate nodes if necessary (i.e., the cortical thickness and Bedi's classification might be obtained in one node, while the bigger diameter could be measured from a different node), these attributes were registered.

Statistical analysis

An EXCEL database was used to keep track of data collecting (Microsoft). Three US tests were used to collect data on the effects of the drug, one at the beginning, one after the first dose, and the second after the second. The statistical analysis was carried out using IBM SPSS Statistics version 21.0. In order to examine the progression of data obtained, two comparison analyses were conducted: baseline against first follow-up and the first follow-up versus the second follow-up. Paired-sample Quantitative continuous variables (number of nodes, long-axis size, and

cortical thickness) and ordinal variables (Bedi's classification and Doppler scale) were studied using Student's t-test and Wilcoxon rank-sum test. After identifying patients according on their prior history of COVID-19 disease, additional studies were carried out. The Mann–Whitney U test was used to see whether there were any differences in the data between the two groups. Cortical thickness results were compared amongst four radiologists using an analysis of variance (ANOVA) test as a quality control measure. As long as the statistical significance threshold was met, the variables were regarded to be of interest to researchers.

Results

Twenty-five people from our centre took part in this study. There were 125 participants at the beginning of the study. After the first dose, three volunteers and two patients failed to show up for follow-up US exams, both of which were scheduled after the second dose. As of this writing, there are 20 patients who have been recruited in the current trial. Patients in the study ranged in age from 20 to 60, on average, with a median age of 39. COVID-19 infection was detected in roughly five individuals (about 65 percent) of those who participated in the study (25 percent). The first and second US examinations, as well as the first and second global comparison analyses between the baseline and the first US follow-up, all indicated statistically significant increases in all variables, including quantitative and ordinal variables. There was a continuous increase in the number of total visible nodes, from 2.87 mean nodes at baseline to 4.46 mean nodes in the first follow-up and 6.56 mean nodes in the second. This is important to keep in mind when analysing the data. Cortical thickness also increased from a mean baseline value of 1.9 millimetres to 4.1 millimetres in the first control and to 5.2 millimetres in the final control.

There were also significant differences with p values less than or equal to 0.001 when looking at statistical analysis of ordinal variables (the grade of Bedi's classification). Specifically, the percentage of suspicious Bedi's classification grades (types 3, 4, 5, and 6) between the three US controls was as follows: 2 percent at baseline vs 67 percent at the first US control and 89 percent at the last scan control. Patients with and without prior COVID-19 infection had a greater axillary lymph node reactivity after receiving the COVID-19 vaccine, as did those who had been previously infected with SARS-CoV-2. Both groups did not have any statistically significant differences in any of the characteristics tested in a basic US evaluation. There was a greater cortical thickness (mean 2.77 mm vs. 2.98 mm) and a higher Bedi's categorization grade in the non-infected group than in the previously infected group (61.6 percent of grade 2) at the first follow-up. In the second follow-up, statistically significant differences were found, with a greater number of lymph nodes (mean 5.9 vs 6.17), a greater cortical thickness (mean 5.78 mm vs 2.59 mm), and a higher grade of Bedi's classification (53.1 percent of grade 3 vs 29.6 percent of grade 2), in the group that had not previously passed the infection. There were no significant changes in diameter measurements throughout the research.

Discussion

Small case studies of hyperplastic lymph nodes following injection of COVID-19 have been published in the literature, as have attempts to explain the effects of COVID-19 vaccination on locoregional lymph nodes using US inspection. In contrast, there is a dearth of data on the progressive imaging of axillary nodes in COVID-19 vaccinated patients. Before and after immunisation, nodal morphology and hyperplastic reaction in recipients were studied in this study, which is the first prospective study to examine nodal features before and after vaccination. All of these vaccines have been linked to an increased risk of axillary lymphadenopathy, but until the introduction of the COVID-19 vaccine, immunizations were thought to be an extremely rare cause of this benign reactive lymphadenopathy. High doses of the COVID-19 vaccination have been linked to increased rates of patients developing lymph node hyperplasia on the injected arm [8].

All of the volunteers who received vaccinations in our study were employees of our medical centre. It was mostly women that made up the majority of the sample, with a mean age of between 20 and 60 years old, as a result of the higher percentage of female employees. A total of 5 of the 20 patients studied had been previously infected with COVID-19, accounting for around 25% of the whole sample, which is lower than the 40% of healthcare workers in our nation who have been infected at this time. There are around three nodes visible in individuals without pathological conditions, with a mean diameter and cortical thickness that are classified as grade 1 by Bedi and Doppler signal evaluations, respectively, according to our data. Because US evaluations lack information on normal nodal imaging, these variables' values could be used as standard lymph node sonography criteria to ensure correct assessment and to discriminate between normal and abnormal results..

Since the maximal cortical thickness is easier to compare, we used it as a statistical control to examine the differences between four radiologists in their clinical care. A more comprehensive follow-up scan in the United States was chosen due to the vaccine's cumulative effect on nodal response, which showed more obvious changes in this most recent scan. Those who had not previously been infected with SARS-CoV-2 were compared to patients who had, even though both groups had the same nodal US features at baseline examination, showed a more substantial axillary lymph node response to vaccination. Is there any way to explain this seemingly contradictory reaction? Antigen-presenting cells (APCs) may have already presented spike proteins to previously exposed patients during the infectious phase, therefore a second clonal proliferation at the same location may not be as important as originally thought. It's also possible that cellular proliferation processes (which we equate with lymph node size) occur closer to the injection time, as do systemic symptoms, as evidenced by studies of cell infiltration following mRNA vaccination, in which the level of cell infiltration at injection sites appears to be at its highest 24 hours after vaccination. For these findings to be confirmed, lymph node responses will need to be monitored on a more frequent and serial basis.

More than half of the patients who experienced lymphadenopathy following the second immunisation had their cortical levels return to normal within a month. More research is needed to establish how long it takes to reach baseline values in the cortex [10]. Our work has a number of drawbacks, including a limited sample size, a focus on a single mRNA vaccination, and no US assessment of additional nodal sites (i.e., subclavian, submandibular). Because the study focused on health care workers rather than the general population, there is an inherent bias in reporting nodal changes in the elderly because the imaging scans were performed on two separate US machines. Unfortunately, there is a lack of long-term follow-up data.

Conclusion

As a result, among individuals who had never received a coronavirus vaccine before, both doses of the COVID-19 vaccine significantly increased all axillary lymph node parameters, providing fresh insights into prior studies of local adverse effects. This study may aid in identifying subgroups of patients that require close monitoring and maybe generating clinical guidelines for use in the management of US axillary lymphadenopathy following the COVID19 immunisation. But greater investigation is needed to comprehend and unravel the mechanisms at play.

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