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Timing and Duration of Axillary Lymph Node Swelling After COVID-19 Vaccination: Japanese Case Report and Literature Review

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Abstract. *Background/Aim: COVID-19 vaccination is now performed in most of the world to limit the spread of the disease. The first mRNA vaccine was approved in clinical settings and has specific side effects including axillary lymph node swelling, which can be misdiagnosed as breast cancer metastasis. The timing of axillary lymph node swelling and its duration are unclear. Here, we present a Japanese case and review of the existing literature. Case Report: We report the case of a 67-year-old woman with breast calcification. She had regular follow ups in our hospital for this calcification and received ultrasonography of the breast and axilla at every visit. She visited 6 months before having her COVID-19 vaccination, and 7 days and 6 months after the first COVID-19 vaccination. She had a swollen axillary lymph node 7 days after the first vaccination, which although it was improved, remained for 6 months. Conclusion: Axillary lymph node swelling occurred 7 days after vaccination and remained up to 6 months after it.*

COVID-19 first occurred in Wuhan in December 2019 (1), and the pandemic continues to develop globally 2 years later. The new Omicron strain has been confirmed and a new wave of the pandemic is spreading. In Japan, "the 6th wave" has occurred in some prefectures. The Omicron strain can infect those who have received two COVID-19 vaccinations; therefore, the COVID-19 pandemic might continue in the near future.

COVID-19 vaccination started in the late 2020 in some countries and in Japan in early 2021. Medical staff were vaccinated first followed by elderly people, and then adults in the general public. Most Japanese have received two vaccinations. Currently, a third vaccination is being offered.

One of the COVID-19 vaccines available is an mRNA vaccine (2), which has been approved for the first time in a clinical setting, and in Japan only the mRNA COVID-19 vaccine was initially used. It has specific side effects, such as fatigue, fever, injection site swelling, and axillary lymph node swelling, which can be confusing for breast oncologists. Previous studies reported axillary lymph node swelling after vaccination; however, when the swelling occurs or is cleared remains unclear. We experienced a case who had received COVID-19 vaccination whose axillary lymph node situation was assessed by ultrasonography continuously during breast calcification follow up during the pandemic. Here, we report this case and provide a literature review about the influence of the COVID-19 vaccine on axillary lymph nodes.

Case Report

The patient was a 67-year-old woman, who came to our breast surgery clinic for a follow up of a mammogram calcification in December 2020. She had no abnormality by palpation, had punctate segmental calcification in her left upper outer mammogram (Figure 1), and ultrasonography showed no remarkable abnormalities: 8.4 mm and 7.5 mm axillary lymph nodes that were not suspicious for

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Key Words: COVID-19 vaccine, axillary lymph node swelling, time-course change.

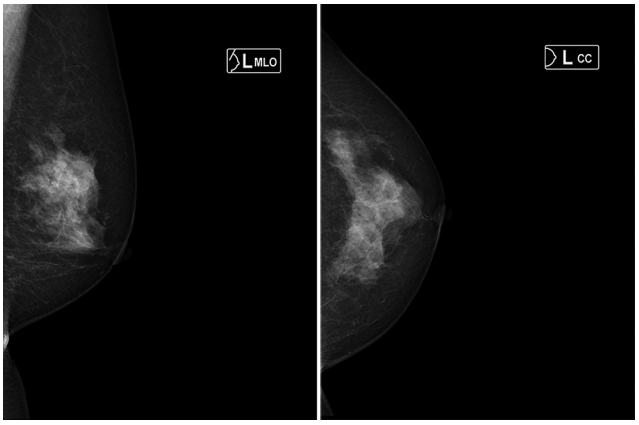

Figure 1. *Mammogram (December 2020) shows punctate segmental calcification in the left upper outer area.*

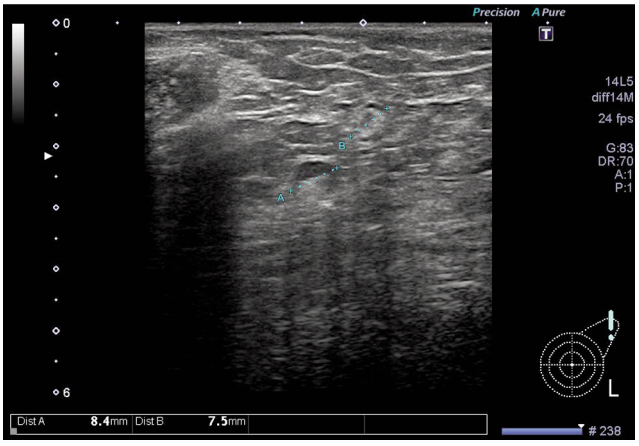

Figure 2. *Ultrasonography (December 2020) shows axillary lymph node lengths of 8.4 mm and 7.5 mm, which were not suspicious of malignancy.*

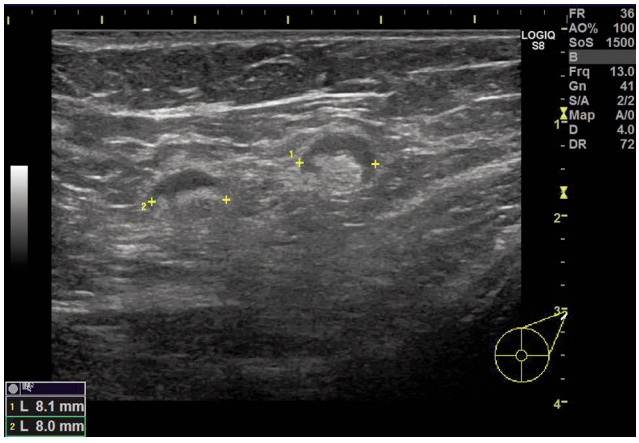

Figure 3. *Ultrasonography (June 2021) shows an axillary lymph node of 8.1 mm length with a thickened cortex caused by previous COVID-19 vaccination.*

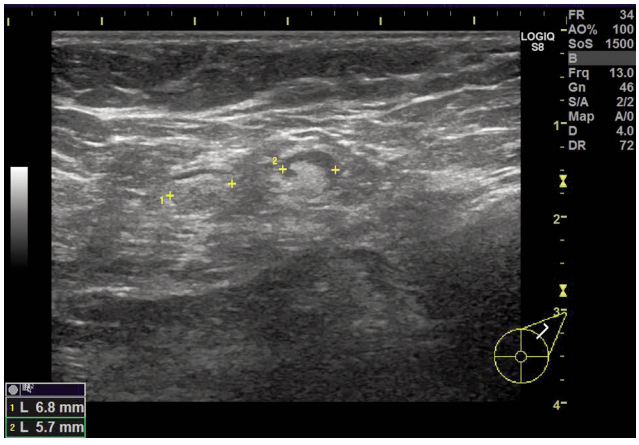

Figure 4. *Ultrasonography (December 2021) shows an axillary lymph node of 5.7 mm length with a cortex thinner than that observed in June 2021. The cortex was still slightly thick.*

malignancy (Figure 2). Because the calcification was slightly decreased compared with one year before, we decided to follow up after 6 months.

In June 2021, seven days after the 1st COVID-19 vaccination in her left upper arm, she came to our clinic again by chance. She had no abnormality by palpation, a mammogram was not performed, and ultrasonography showed an 8.0 mm axillary lymph node that had not changed from that observed in December 2020, and an 8.1 mm lymph node with a cortex that was thicker than that observed in December 2020 (Figure 3). We decided to follow up similar to the previous visit, because the swelling appeared to be related to simple inflammatory reactions as the lymph node structure was normal and not malignant. Furthermore, at this time in Japan, it was not established whether COVID-19 vaccination could cause axillary lymph node swelling.

In December 2021, the patient visited our clinic with regularity. She had no abnormality by palpation, the left calcification in the mammogram was slightly decreased compared with one year before, and ultrasonography showed the left axillary lymph node had a thinner cortex than in June 2021, although it was still thicker than normal (Figure 4), and a smaller lymph node (5.7 mm) than six months before. At this time, it was well known that COVID-19 vaccination could cause axillary lymph node swelling; therefore, the swollen lymph nodes were retrospectively considered to be related to the COVID-19 vaccination, which was administered in June 2021. We continued to follow up the patients because it was important to continue to check whether the lymph nodes were malignant and mammographic calcification did not change.

Written informed consent was obtained from the patient for the publication of this case report and any accompanying

images. This was a case report and therefore we did not require additional permission from our review board.

Discussion

The COVID-19 pandemic has presented an unusual situation. In the second half of 2021, there were some reports of axillary lymphadenopathy after COVID-19 vaccination, which became more common with time (3-5). Giogris *et al*. reported some patients with this symptom who previously had breast cancer (6). However, there had been few reports of axillary lymphadenopathy after vaccination. Igual-Rouilleault *et al*. reported some cases of axillary lymphadenopathy 8-13 days after the first vaccination, but the timing and duration of this symptom were still unclear. Our case underwent ultrasonography seven days after her first vaccination and lymph node swelling was diagnosed; therefore, our findings are of interest. Cocco *et al*. reported that most symptoms related to vaccination were improved by 30-45 days (7). In Israel, the COVID-19 vaccine was approved ahead of the rest of the world and Faermann *et al*. reported findings from a relatively large clinical study of lymphadenopathy caused by COVID-19 vaccination. They collected data of the axillary lymph node status who showed lymph node cortical thickening after the first COVID-19 vaccination or after the second one between January and March 2021 (8). They found that lymph node cortical thickness may occur after the first COVID-19 vaccination, and this thickness was found to be thinner 4-5 weeks after the second vaccination. In our case, it took about 6 months for the lymph node to return to its almost normal size, which is longer than the period observed by Faermann *et al*. The axillary lymph node status of our case was examined six months before COVID-19 vaccination, and seven days and six months after the first vaccination. Therefore, the consecutive follow-up of this case was very valuable regarding the timing and duration of lymph node swelling after COVID-19 vaccination. In our case, axillary lymph node swelling caused by COVID-19 vaccination occurred just seven days after the first vaccination and changes in cortex thickness were improved six months after vaccination, although the cortex remained slightly thicker than normal as a result of the vaccination.

Axillary lymph node status is very important when diagnosing cancer malignancy, especially in breast tumours assessed by MRI (9-11) and PET/CT (12-15) where swollen lymph nodes can be confused with breast cancer metastasis. Therefore, we should be careful when diagnosing these findings during the COVID-19 pandemic era.

Major limitations of this study were that only one patient was assessed, in one institute, and of one ethnic background (Japanese). The analysis of more cases should provide more insights. Furthermore, the generalisability of the findings should be confirmed in other ethnic groups.

Conclusion

The COVID-19 pandemic will continue to affect our lives for a while. During the pandemic, oncologists have to diagnose breast cancer and axillary lymph node metastasis without delay. Therefore, it is important to provide an appropriate follow up analysis of axillary lymph node swelling caused by COVID-19 vaccination.

Conflicts of Interest

The Authors report no conflicts of interest in relation to this study.

Authors' Contributions

Research design: Yoshimoto N; collection and analysis of data: Yoshimoto N, Yanagi A; all authors read and approved the final article.

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