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Case Report

COVID-19 Vaccine-Associated Lymphadenopathy Mimicking Regrowth of Axillary Lymph Node Metastasis of Lung Adenocarcinoma

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We encountered a woman with re-enlarged axillary lymph nodes during a computed tomography (CT) scan for surveillance of lung adenocarcinoma with axillary lymph node metastasis at the initial diagnosis that had shrunk with standard chemotherapy. We first suspected cancer recurrence and considered a change in the chemotherapeutic regimen. However, after careful history taking regarding the timing of her Coronavirus Disease 2019 (COVID-19) vaccination, and subsequent careful, close follow-up, radiological shrinkage suggested a strictly benign cause. Especially in lung cancer with a medical history of axillary lymph node involvement, clinicians should be aware that vaccine-associated lymphadenopathy can mimic cancer recurrence and sometimes prompt serious misjudgment regarding a current treatment course and strategy.

Key words: lung cancer, COVID-19 vaccination, axillary lymphadenopathy, case report

C oronavirus Disease 2019 (COVID-19) messenger RNA (mRNA) vaccine-associated axillary lymphadenopathy has become well known, especially in the field of breast and skin cancers [1], possibly because of the proximity of cancer distributions and vaccination sites. This phenomenon necessitates careful differential diagnosis from cancer recurrence in patients with breast and skin cancer. However, because lung cancer rarely spreads to the axillary lymph nodes (<1%) [2-3], even if axillary lymph node swelling does occur during the treatment course, accurate diagnosis should not be difficult.

However, some patients with lung cancer present with axillary lymph node metastases. Therefore, reemergence of axillary lymph node swelling in their

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treatment courses due to vaccine-associated axillary lymphadenopathy might be misdiagnosed as cancer recurrence if clinicians do not perform detailed and careful medical interviews about the timing of the patient's COVID-19 vaccination.

Here, we report a case of COVID-19 mRNA-1273 vaccine-associated axillary lymphadenopathy mimicking cancer recurrence in a patient with lung adenocarcinoma with axillary lymph node metastasis at the initial diagnosis that had shrunk with standard chemotherapy.

Case Presentation

In 2015, a 55-year-old woman with a performance status of 0 was diagnosed with left lower lobe lung ade-

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nocarcinoma with multiple lymph node metastases in the mediastinum, left upper clavicle, left neck, retroperitoneum, and left axilla (Fig. 1A). Combination therapy of cisplatin plus pemetrexed followed by continuous maintenance pemetrexed, the standard firstline treatment at the time, resulted in remission, including remission of the left axillary lymph node metastasis (Fig. 1B).

While the patient was receiving pemetrexed therapy beyond the oligo-recurrence of the primary site treated with local therapy (resection) in February 2019, a routine follow-up CT scan in July 2021 detected an unexpected aggregation of swollen lymph nodes in the left axilla. She was 61 years old. White blood cell count, LDH, and CRP were within normal range, and no inflammatory reaction or tumor marker elevation were apparent from the laboratory data and physical assessment. Some of the swollen lymph nodes corresponded to those that were positive at the initial presentation (Fig. 1C). Thus, despite the lack of progression at any other known disease sites (Fig. 2), we strongly suspected cancer recurrence in left axilla lymph node based on the imaging findings. When we shared this information and our plan to change the treatment regimen with the patient, she told us that she had received the COVID-19 mRNA-1273 vaccine in her left shoulder at a nearby mass vaccination site four days before the CT scan (Jul. 2021) and had experienced axillary pain after the vaccination.

Assuming the possibility of COVID-19 vaccine-associated lymphadenopathy mimicking regrowth of lung adenocarcinoma, we opted to wait three weeks and perform careful follow-up at that time based on the timing of the vaccine and the reexamination of the CT scan. Three weeks later (Aug. 2021), the relevant symptoms had abated, and CT showed gradual shrinkage of all left axillary lymph nodes (Fig. 1D) without any other abnormal findings suspicious of recurrence. After an additional six weeks of careful follow-up (Sep. 2021; nine weeks post-vaccination), we confirmed further shrinkage of the lymph nodes (Fig. 1E) and concluded that the incidental finding was unlikely to have been a cancer recurrence. We decided to continue the maintenance pemetrexed therapy.

Discussion

The physicians of patients with advanced lung can-

cer must perform careful ongoing follow-up to comprehend current disease status and provide appropriate treatment strategy adjustments when needed. This is just as true during the COVID pandemic as ever. As COVID-19 vaccination rates increase worldwide, incidences of vaccination-associated lymphadenopathy as high as 14% and 0.9% have been reported in the adult recipients of mRNA-1273- and BNT162b2-vaccines, respectively [4]. Other type of vaccines against H1N1 influenza, tuberculosis and human papilloma virus vaccine can also cause lymphadenopathy, although with lower incidences [5-7].

In one study, as many as half of the cancer patients who underwent FDG PET-CT shortly after COVID-19 mRNA vaccination showed FDG accumulation in the axillary lymph nodes, caused not by cancer recurrence but by the vaccination [8]. However, that study mostly enrolled patients with cancers other than lung cancer. In another study, vaccine-associated lymphadenopathy was documented in the lung cancer mass screening setting and in the initial diagnostic work-up for a solitary pulmonary nodule in an individual patient [9]. The present case is significantly different in that our lung cancer patient did originally have axillary lymph node metastasis, and she was under active surveillance for cancer recurrence.

For lung cancer patients with a history of axillary lymph node involvement like our case, it is vital to not commence inappropriate treatment strategies, including the immediate discontinuation of ongoing effective treatment, simply because of the reemergence of lymphadenopathy. In the COVID-19 era, clinicians should be aware of the possibility of vaccine-associated lymphadenopathy in addition to cancer recurrence. This case emphasizes the importance of clear and effective communication with patients about vaccination history. Further, patients with a history of axillary metastasis should be vaccinated on the side contralateral to the metastatic lesions and should avoid radiological cancer surveillance immediately after vaccination [10].

Conclusion

We encountered a case of COVID-19 vaccine-associated lymphadenopathy resembling regrowth of lung adenocarcinoma with axillary lymph node metastasis. This case highlights the clinical importance of accurate

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Fig. 1 Computed tomography of the left axillary lymph nodes over time. (A) At the initial presentation (Oct. 2015), (B) under remission with maintenance chemotherapy (Mar. 2021), (C) evident re-enlargement four days after administration of the COVID-19 vaccine (Jul. 2021), (D) three weeks later (Aug. 2021), and (E) after an additional six-week interval (Sep. 2021).



Fig. 2 Computed tomography of the primary lesion and mediastinal lymph nodes (A) at the initial presentation (Oct. 2015), and (B) at the time of evident re-enlargement after administration of the vaccine (Jul. 2021).

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diagnosis of axillary lymph node swelling that appears to reemerge during the treatment course through a detailed and careful history taking regarding the the patient's COVID-19 vaccination status and timing.

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