Letter to the Editor

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Discrimination between Benign and Malignant Post-SARS-CoV-2 Vaccination Lymphadenopathy is Feasible

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Please also read an editorial by Jung Min Chang et al. on the topic on page 691.

I read with interest the article by Ashoor et al. [1] about three patients who developed axillary lymphadenopathy (ALP), also known as reactive axillary lymph nodes (ALNs). The patients were examined 5 days after the first dose of SARS-CoV-2 vaccination with the AstraZeneca vaccine (patient 1), 27 days after the AstraZeneca vaccine (patient 2), and 1 day after the second dose of the AstraZeneca vaccine (patient 3). All three patients developed ALP/ALN homolaterally to the injection site [1]. The study is interesting but raises concerns that need to be discussed.

I do not agree with the recommendation to administer the vaccine to the contralateral side in patients with previous breast carcinoma. Though ALP/ALN frequently occurs unilaterally and homolaterally to the injection site, cases of bilateral development have been described [2]. Patients may also receive the first and second injections at different sites. If the latency period between the two injections is short, bilateral ALP/ALN attributable to the vaccination can be observed. Furthermore, in rare cases, ALP/ALN may develop contralaterally to the injection site, as was reported in a 52-year-old male patient with lung cancer 12 days after the second dose of the Pfizer vaccine [3].

The morphology of lymph nodes after vaccination in patients with ALP/ALN may mimic lymphadenonopathy due to malignancy. Therefore, morphology should not be used to differentiate between malignancies and vaccination reactions. In some cases, they may be difficult or impossible to differentiate.

Although ALP/ALN is not rare, it is a frequent complication of all approved SARS-CoV-2 vaccines. In a retrospective study of 204 patients undergoing ^{18}F-fluorodeoxyglucose (FDG)-PET CT between January and March 2021, 36% of patients had ALP/ALN [4].

Other complications, such as fever, headache, chills, fatigue, arthralgia, or myalgia, may also occur in association with ALP/ALN after SARS-CoV-2 vaccination. These additional complications may help to distinguish between benign and malignant lymphadenopathy.

If ALP/ALN is associated with high fever, hemophagocytic lymphohistiocytosis should be considered [5]. This is a life-threatening hyperinflammatory syndrome that occurs at all ages because of persistent stimulation of lymphocytes and histiocytes [5].

If ALP/ALN occurs in patients with a history of breast cancer, routine ultrasound, CT, MRI or ^{18}F FDG-PET screening could be helpful prior to vaccination; these images could then be compared with post-vaccination images. If lymphadenopathy is absent prior to vaccination and present after, it can clearly be attributed to the vaccination and not to a relapse of the carcinoma [6].

Overall, the case series has some limitations that challenge the results and their interpretation. Patients with a history of breast or lung cancer or lymphoma should undergo axillary ultrasound prior to SARS-CoV-2 vaccination to assess if post-vaccination lymphadenopathy is attributable to the vaccination or to a relapse of the malignancy.

Conflicts of Interest

The author has no potential conflicts of interest to disclose.

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