

# Supraclavicular Lymphadenopathy after COVID-19 vaccination

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Abbreviation	
COVID-19	Coronavirus Disease of 2019
CDC	Center for Disease Control
FDA	Food & Drug Administration

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The Coronavirus Disease of 2019 (COVID-19) pandemic has impacted the lives of everyone, driving the need for mass vaccinations since February 2020. Rapid medical advances have brought about vaccination options for the world, helping to ameliorate the devastating effects of this pandemic. As of August 2021, the Center for Disease Control (CDC) has approved vaccinations for children 12 years of age and older. As further developments are made, the age requirement will eventually include younger children, and it is critical to understand the potential side effects of the vaccinations. These side effects, such as malignant appearing lymphadenopathy, may lead to potential invasive diagnostic measures.

This case report presents two pediatric cases of supraclavicular lymphadenopathy following COVID-19 vaccinations. These cases highlight the need to develop assessment guidelines to help prevent potentially harmful diagnostic procedures in the pediatric population.

In general practice, less than 1% of lymphadenopathies are malignant, with that number being 0.4% in patients under 40 years of age. In referral centers, the percentage of malignant cases rises to 17% and 40-60% in patients presenting with related symptoms. However, the location of lymphadenopathy brings about different prevalence rates with the supraclavicular region having the highest risk, 90% in those older than 40 and 25% in those younger. (Mohseni). Generally, it is standard practice to biopsy true supraclavicular nodes in the absence of known infectious causes. On the contrary, recent COVID vaccination may be an indication for watchful waiting of enlarged supraclavicular lymph nodes as we describe below.

We present two cases of patients who presented with supraclavicular lymphadenopathy within weeks after receiving COVID-19 vaccination. The patients underwent biopsies for the suspicion of a malignancy and both biopsies showed reactive lymph nodes without evidence of malignancy. Of note, the vaccine was given on the same side as the lymphadenopathy was recognized. We highlight these cases to discuss the possibility that the COVID-19 vaccines could potentially trigger an inflammatory response, resulting in lymphadenopathy which can be mistaken for a malignancy.

The first patient, a 16-year-old male presented for left supraclavicular adenopathy. The patient had noticed the mass two days prior to the visit and notably 2 weeks after his first dose of the COVID-19 vaccine. The patient did not present with any additional symptoms and denied any fever, night sweats, unexplained weight loss or other notable lymph nodes. The patient denied any travel or potential close COVID-19 contacts.

At the time of presentation, the lymph node was approximately 1 cm in size and was freely movable, non-matted, “rubbery,” singular lymph node in the left supraclavicular region. Due to the location, a surgical excision was performed. The pathology report showed a final diagnosis of reactive follicular hyperplasia and focal increased Epstein-Barr virus positive cells. The EBV positive cells are of uncertain significance and a diagnostic evaluation showed a serum negative EBV PCR. EBER in situ hybridization on the collected specimen are suggestive of a prior infection and the EBV IgG was positive in this patient.

The second patient, a 13-year-old male presented with left supraclavicular adenopathy. The patient had noticed the mass a few weeks prior and noted that it was transiently painful, but the pain had since subsided. There were no other systemic complaints. The COVID vaccination was given approximately 2 weeks prior to the appearance of the supraclavicular lump. The lump was an approximately 1 cm, freely moveable soft, non-matted, nontender, singular lymph node in the left supraclavicular region. Due to the location of the lymph node and suspicion of malignancy, the node was surgically removed. The pathology showed florid, reactive follicular hyperplasia with foci of follicular lysis, increased immunoblasts, and progressive transformation of germinal centers. (See images 1-4)

During the COVID-19 pandemic, the Food and Drug Administration (FDA) has approved multiple vaccinations to combat the viral outbreak. This case report presents two separate but remarkably similar cases of supraclavicular adenopathy that arose within 2 weeks post-COVID-19 vaccination. Lymphadenopathies corresponding with inflammation inducing vaccinations have been previously cited in the literature and are uncommon but potential side effects. There is literature supporting significant unilateral cervical and supraclavicular lymphadenopathy following human papilloma virus vaccination [1]. Furthermore, it has been reported that bacille Calmette-Guerin (BCG) lymphadenitis is the most common complication of the tuberculosis vaccine and has been found to either regress on its own, or become large and suppurative [2]. With the current and extensive vaccination efforts to combat COVID-19, it is increasingly important to recognize and understand possible complications and how to effectively diagnose without resulting in additional medical procedures.

There have been numerous publications about ipsilateral axillary lymphadenopathy and management strategies [3], [4], [5], [6]. In one publication by Mehta et. al, there were 4 reported cases of unilateral axillary lymphadenopathy in female patients ranging from ages 42 to 59. Our case discussion presents a unique situation due to the location of lymphadenopathy and age of the patients. The supraclavicular location of lymphadenopathy is less commonly reported than the axillary finding, and it is especially interesting that two cases presented similarly in a short time frame. As the FDA continues to expand the qualifying age group for vaccination, it is exceedingly important to develop an algorithm for potential similar cases. The need for routine chest radiographs as well as procedures requiring surgery and anesthesia it should be addressed in this setting. It can be suggested that in the absence of “B-symptoms” such as fever, night sweats and weight loss, the lymphadenopathy is to be closely monitored for changes that would increase the suspicion of malignancy. While there is always a risk-reward balance when it comes to testing for malignancy, especially with invasive or radiation-exposure modalities, the novelty of this virus and its vaccinations emphasizes a need for additional guidelines. It is critical to identify and delineate risk factors that would lead the clinician to aggressively pursue a biopsy as opposed to observation.

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