



OLGU SUNUMU / CASE REPORT

**B-mode and Doppler ultrasonography patterns of axillary and supraclavicular lymphadenopathy associated with mRNA COVID-19 vaccine**

mRNA COVID-19 aşısı ile ilişkili aksiller ve supraklaviküler lenfadenopatinin B-mod ve Doppler ultrasonografi paternleri

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**Abstract**

In this study, we present the ultrasound imaging features of lymph nodes arising in the regional lymph node chain after the first or second dose of the Pfizer-BioNTech COVID-19 vaccine. Ipsilateral lymphadenopathy adjacent to the vaccine injection site is an extremely rare but expected adverse reaction following COVID-19 vaccination. Although axillary lymphadenopathy is more common, cases of supraclavicular lymphadenopathy have also been reported after widespread vaccination against COVID-19. Ultrasonography examinations were performed on seven patients with no previous pathological conditions, who presented to our radiology department after receiving the Pfizer-BioNTech COVID-19 vaccine. Bilateral axillary, supraclavicular and subclavicular lymph node stations were explored. These patients typically present with enlarged hypoechoic lymph nodes with the loss of fatty hilum, asymmetric or diffuse cortical thickening, and increased hilar and cortical vascularization on the color doppler ultrasonography of the ipsilateral axillary and supraclavicular regions. Radiologists and clinicians should be aware of the ultrasonographic features of these lymph nodes and should inform the patient that these lymph nodes are often a self-limiting process. Thus, unnecessary axillary lymph node biopsies should be avoided, and patients should be treated conservatively.

**Keywords:** COVID-19, mRNA vaccine, supraclavicular, axiller, lymphadenopathy, ultrasonography

**Öz**

Bu çalışmada, Pfizer-BioNTech COVID-19 aşısının birinci veya ikinci dozundan sonra bölgesel lenf düğümü zincirinde ortaya çıkan lenf bezlerinin ultrason görüntüleme özelliklerini sunuyoruz. Aşı enjeksiyon bölgesine komşu ipsilateral lenfadenopati, COVID-19 aşısını takiben son derece nadir ancak beklenen bir advers reaksiyondur. Aksiller lenfadenopati daha yaygın olmasına rağmen, mevcut COVID-19'a karşı yaygın aşılama sonrasında supraklaviküler lenfadenopati vakaları da bildirilmiştir. Pfizer-BioNTech COVID-19 aşısı yapıldıktan sonra radyoloji bölümümüze başvuran, daha önce herhangi bir patolojik durumu olmayan yedi hastaya ultrasonografi incelemesi yapıldı. Bilateral aksiller, supraklaviküler ve subklaviküler lenf nodu istasyonları araştırıldı. Bu hastalar tipik olarak, ipsilateral aksiller ve supraklaviküler bölgelerde büyümüş hipoeoik lenf nodları ile birlikte yağ hilusu kaybı, asimetrik veya yaygın kortikal kalınlaşma ve renkli doppler ultrasonografisinde artmış hiler ve kortikal vaskülarizasyon ile başvurdular. Radyologlar ve klinisyenler bu lenf nodlarının ultrasonografik özelliklerinin farkında olmalı ve bu lenf nodlarının sıklıkla kendi kendini sınırlayan bir süreç olduğu konusunda hastayı iyi bilgilendirilmelidir. Bu nedenle gereksiz aksiller lenf nodu biyopsilerinden kaçınılmalı ve hastalar konservatif olarak tedavi edilmelidir.

**Anahtar kelimeler:** COVID-19, mRNA aşısı, supraklaviküler, aksiller, lenfadenopati, ultrasonografi

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## INTRODUCTION

Vaccination against coronavirus disease 2019 (COVID-19) is currently being implemented across the world<sup>1-4</sup>. In order to end the global crisis caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, an intensive vaccination campaign is being carried out across the world to achieve herd immunity<sup>1-5</sup>. It is important for clinicians to recognize possible adverse reactions associated with COVID-19 vaccines in order to distinguish expected temporary reactions following vaccination from true pathological processes. Several recently published articles have reported ipsilateral lymphadenopathy (LAP) on the vaccinated arm following vaccination with primarily mRNA vaccines (i.e., Pfizer-BioNTech and Moderna)<sup>1-4, 6,7</sup>. Most of the reported cases were axillary LAPs, with supraclavicular LAPs being less frequently observed<sup>1-4, 6,7</sup>. Data on the number, size, site, morphology and imaging characteristics of vaccine-associated LAPs are still limited.<sup>1</sup>In oncological patients, such abnormal findings may be mistaken for metastases, and a recent history of COVID-19 vaccination can provide relevant information to guide the differential diagnosis of enlarged lymph nodes<sup>8,9</sup>.

This paper presents the B-Mode ultrasonography (US) and color Doppler US (CDUS) findings of a case series with ipsilateral supraclavicular LAP and accompanying axillary LAP that developed after Pfizer-BioNTech vaccination.

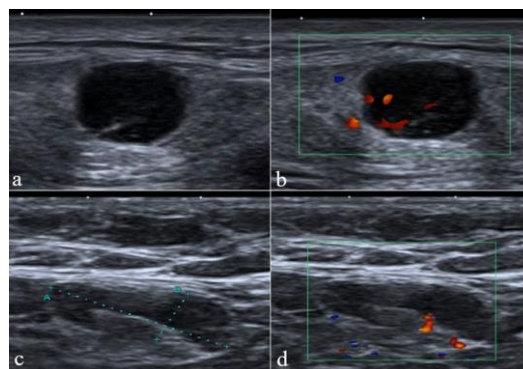
## CASES

B-mode US and CDUS were performed on seven volunteer patients with the complaints of fever and local pain, tenderness, redness and palpable swelling in the ipsilateral axilla or neck region after Pfizer-BioNTech vaccination, who had no previous pathological condition. US was performed using a Toshiba Aplio 500 (Aplio 500 Platinum, Canon Medical Systems Corporation, Japan SpA, Genoa, Italy) device with a high-resolution 14L5 MHz linear sequence transducer. Bilateral axillary, supraclavicular, subclavicular and cervical lymph node stations were examined. The presence of lymph nodes, their long and short axis diameters, shape, cortical echogenicity, cortical thickness, asymmetric cortical thickness, and presence of central fatty hilum, necrosis/cyst and poorly circumscribed capsules were evaluated with B-mode US. The blood flow pattern (hilar/cortical) was evaluated using CDUS. If

there was an abnormal lymph node in the axilla on the side of vaccination, US was performed on the breast of the same side to rule out a possible breast lesion. None of the patients had any other disease in their history. All patients with a previous history of cervical lymphadenopathy were excluded. After 4-6 weeks, follow-up US showed regression in the size, cortical thickness and vascularization of the LAPs. Informed consent was obtained from all cases.

### Case 1

A 30-year-old male patient presented with the complaints of palpable swelling in the left supraclavicular region and pain in the ipsilateral axillary region and arm on the left arm at three days after the first dose of Pfizer-BioNTech vaccine was administered through the left arm. He also described weakness and sweating. In the US examination, an 8x7-mm LAP with a round appearance, diffuse cortical thickening (6 mm), thin hilum, and cortical and hilar blood flow was observed in the supraclavicular area. An axillary LAP (maximum diameter 17.2x6.1 mm) with an ipsilateral preserved fatty hilum, increased diffuse cortical thickness (5 mm), and hilar blood flow was detected (Figure 1). No pathological lymph nodes were found in the contralateral axilla-supra/subclavicular area.



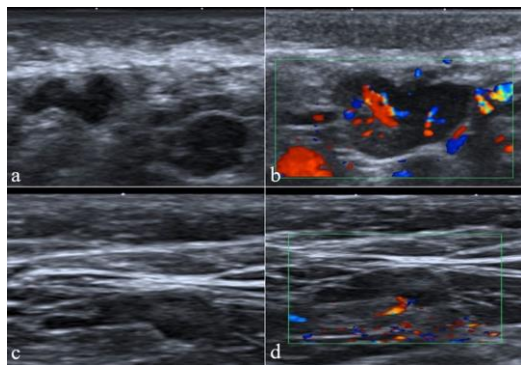
**Figure 1. US imaging of the left supraclavicular region of Case 1:**

a. A round, heterogeneous lymph node with an increased diffuse cortical thickness on B-Mode US and b. cortical and hilar blood flow on CDUS. US images of the left axillary region of the same case: c. A lymph node with an increased diffuse cortical thickness on B-Mode US and d. hilar blood flow on CDUS.

### Case 2

A 49-year-old female patient presented with headache, fever, and pain in the left armpit on the

seventh day after the first dose of Pfizer-BioNTech vaccination on the left arm. The US examination revealed two LAPs (dimensions, 16x8 mm and 9x5 mm) in the supraclavicular area, which had a partially selected fatty hilum, asymmetric cortical thickening, and significant cortical and hilar blood flow. There was an enlarged (15x13.5 mm) axillary LAP with an ipsilateral preserved fatty hilum and asymmetric cortical thickening (5 mm), with hilar blood flow on CDUS (Figure 2). No pathological lymph nodes were found in the lymph node stations contralateral to the injection site.



**Figure 2. US imaging of Case 2:**

a. Two supraclavicular lymph nodes on B-Mode US and b. a heterogeneous lymph node with an increased heterogeneous asymmetric focal cortical thickness and significant cortical and hilar blood flow on CDUS. Left axillary lymph node US images: c. increased heterogenous focal asymmetric cortical thickening on B-mode US and d. hilar blood flow on CDUS.

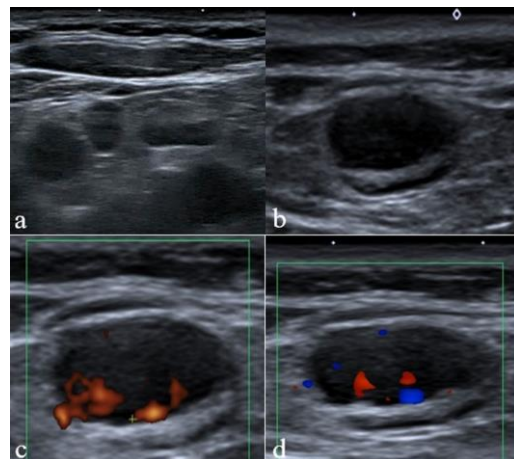
### Case 3

A 53-year-old female patient presented with weakness, sore throat, and pain in the left lower neck region on the fifth day after the first dose of Pfizer-BioNTech vaccination on the left arm. Multiple LAPs, the largest 11x9 mm in size, were detected in the ipsilateral supraclavicular region, with a round shape, focal cortical thickening (10 mm), and cortical and hilar blood flow (Figure 3). No pathological lymph nodes were found in the ipsilateral axilla or the contralateral axilla-supra/subclavicular area.

### Case 4

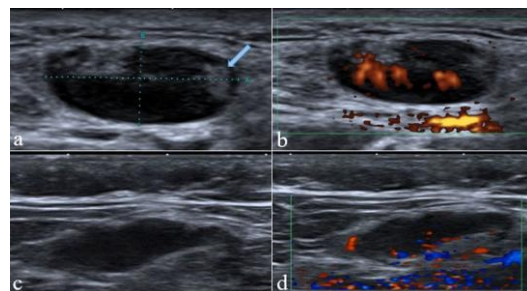
A 24-year-old female patient had the complaint of joint pain, fatigue, and pain on the left side of the neck on the fourth day after the second dose of Pfizer-BioNTech vaccination on the left arm. The US examination showed a hypoechoic LAP (17 x 6 mm) in the left supraclavicular region, with diffuse cortical

thickening (10 mm) and a thin hilum, increased cortical and hilar blood flow on CDUS, and a focal echogenic area in the cortex. An enlarged LAP (21x7.5 mm) with significant cortical and hilar blood flow, asymmetric cortical thickening (6 mm), and a preserved fatty hilum was detected in the ipsilateral axillary region on the side of vaccination (Figure 4). There was no pathological lymph node in the contralateral supra/subclavicular region and axilla.



**Figure 3. US imaging of Case 3:**

a. Multiple round-shaped lymph nodes in the left supraclavicular area, b. a heterogeneous hypoechoic lymph node with an increased focal cortical thickness on B-Mode US, and c and d. cortical and hilar blood flow on CDUS.



**Figure 4. US imaging of the left supraclavicular region of Case 4:**

a. A heterogeneous lymph node with an increased diffuse cortical thickness and focal echogenic focus (arrow) on B-Mode US and b. significant cortical and hilar blood flow on CDUS. US images of the left axillary region of the same patient: c. Increased focal cortical thickness on B-Mode US and d. cortical and hilar blood flow on CDUS.

### Case 5

A US examination was performed on a 50-year-old female patient who presented with the complaint of

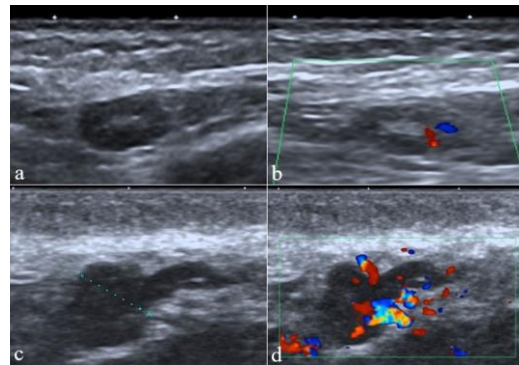
pain in the left armpit at 10 days after the first dose of Pfizer-BioNTech vaccination on the left arm. The patient also stated that she began to experience fatigue and headache after the injection. In the left supraclavicular region, there was a lymph node (8.5x5 mm) with diffuse cortical thickening and significant cortical and hilar blood flow on CDUS. In the ipsilateral axillary area, there was an enlarged LAP (32x9 mm) with asymmetric cortical thickening (5mm), a preserved fatty hilum, significant hilar and cortical blood flow on CDUS examination (Figure 5). No pathological lymph node was detected in the contralateral axilla-supra/subclavicular area.

### Case 6

A 34-year-old male patient presenting with the complaints of fever, myalgia, and ipsilateral armpit and lower neck pain at eight days after the second dose of Pfizer-BioNTech vaccination on the left arm. The US examination revealed a hypoechoic LAP (8x3 mm) in the left supraclavicular region with diffuse cortical thickening and a hardly distinguished hilum, and hilar blood flow on CDUS. As well as an enlarged LAP (16x4 mm) in the ipsilateral axillary region with asymmetric cortical thickening (3mm), a preserved fatty hilum, and hilar blood flow on CDUS (Figure 6). No pathological lymph node was observed in the contralateral axilla-supra/subclavicular area.

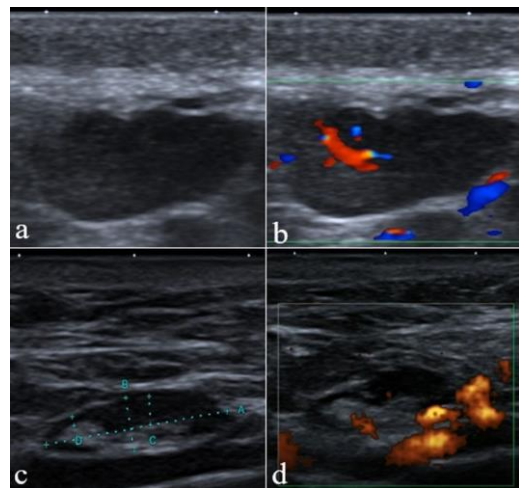
### Case 7

US was performed in a 43-year-old female patient with the complaints of left armpit pain that started after three days following the injection of the second dose of Pfizer-BioNTech vaccine into the left arm. She also described weakness, joint-shoulder pain, and mild fever. In the US examination, there was a 15x8-mm LAP in the left supraclavicular area with diffuse cortical thickening, a thin echogenic hilum, and significant hilar/cortical blood flow. In addition, the ipsilateral axillary region was observed to have a LAP with a maximum diameter of 20x14 mm with a preserved fatty hilum, diffuse cortical thickening, and hilar blood flow (Figure 7). There was no pathological lymph node in the contralateral axilla-supra/subclavicular area.



**Figure 5. US imaging of the left supraclavicular region of Case 5:**

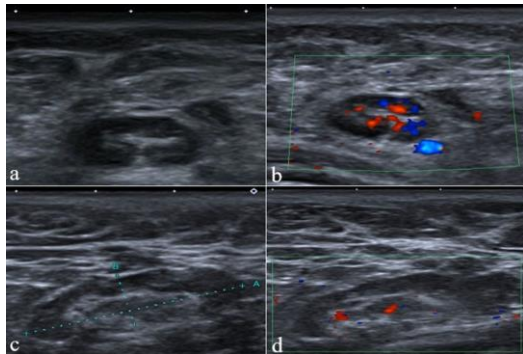
a. A heterogeneous lymph node with an increased diffuse cortical thickness on B-Mode US and b. hilar blood flow on CDUS. US images of the left axillary region of the same patient: c. increased asymmetric focal thickness on B-Mode US and d. significant cortical and hilar blood flow on CDUS.



**Figure 6. US imaging of the left supraclavicular region of Case 6:**

a. A heterogeneous lymph node with an increased diffuse cortical thickness and no hilum on B-Mode US and b. hilar blood flow on CDUS. US imaging of the left axillary region of the same patient: c. A heterogeneous lymph node with an increased focal cortical thickness on B-Mode US and d. hilar blood flow on CDUS.





**Figure 7.** US imaging of the left supraclavicular region of Case 7

a. A heterogeneous lymph node with an increased diffuse cortical thickness on B-Mode US and b. significant cortical and hilar blood flow on CDUS. US imaging of the left axillary region of the same patient: c. A heterogeneous lymph node with an increased diffuse cortical thickness on B-Mode US and d. hilar blood flow on CDUS.

## DISCUSSION

This case report presents seven patients that developed ipsilateral supraclavicular reactive LAP accompanied by axillary LAP in some after the administration of the Pfizer-BioNTech vaccine against COVID-19.

While the mRNA COVID-19 vaccine is being widely administered around the world, numerous local and systemic reactions are encountered, often after the second dose<sup>3, 10</sup>. Vaccine-induced adenopathy occurs secondary to local immune response activation in the ipsilateral axillary and/or supraclavicular regions<sup>3, 10</sup>. Reactive axillary LAP formation has been rarely reported after other vaccines, such as Bacillus Calmette-Guerin, influenza and human papilloma vaccines, but it is a very common reaction after the COVID-19 vaccine (7). A previous study on the Pfizer-BioNTech COVID-19 vaccine reported the rate of ipsilateral axillary and supraclavicular LAP as 0.3%<sup>11</sup>. In recently published articles, the incidence of LAP in the supraclavicular and axillary regions was determined to be much higher after the COVID-19 vaccine<sup>1-4</sup>. According to the Centers for Disease Control and Prevention, axillary LAP can be seen at a rate of more than 11% after the first dose and up to 16% after the second dose<sup>12</sup>.

According to the literature, supraclavicular LAP following the COVID-19 vaccine predominantly affects women and usually occurs within the first 10-15 days (up to 24 days) after the administration of the

vaccine. Although some lymph nodes remain enlarged for up to six weeks, they often regress within a month<sup>1, 7</sup>. The literature contains young and otherwise healthy cases with solitary and multiple axillary, supraclavicular and subclavicular lymph nodes detected on the ipsilateral side in the US examination performed after both the first and second doses of the Pfizer-BioNTech vaccine. No pathological cervical lymph node has been reported<sup>6, 7</sup>. In the current case series, a single ipsilateral supraclavicular-axillary LAP was detected in six cases, and there was more than one ipsilateral supraclavicular LAP in one patient.

In the literature, it has been reported that LAPs observed after vaccination have imaging features that mimic nodal metastases, with hypoechoic appearance, round or oval shapes, a preserved fatty hilum, and increased (> 3 mm) diffuse or asymmetric cortical thickening on US. It has been shown that vascular signal increases locally in both hilar and cortical regions<sup>7</sup>. In the current case series, the findings were similar, but an area showing increased focal cortical echogenicity was detected in one of our cases. Cortical thickening and increased vascularity were confirmed to be the main imaging features in US and CDUS.

Cortex thickening in the lymph nodes, hyperechogenicity in the perinodal adipose tissue, poorly demarcated borders, loss of a normal fatty hilum, and increased lymph node size have been described after COVID-19 vaccination<sup>6</sup>. Sonographic findings vary in cases of supraclavicular LAP reported following the COVID-19 vaccine, but most show an increase in size and a thickened cortex with or without the loss of a normal fatty hilum<sup>13-15</sup>. The sonographic findings of axillary LAPs after the COVID-19 vaccine have similar features, but supraclavicular LAPs tend to have a thicker cortex and less preserved fatty hilum, and a more rounded appearance<sup>6</sup>. We observed similar findings were observed in our case series. While there was only a single axillary lymph node in most cases, supraclavicular lymph nodes tended to present as multiple nodes.

LAP after COVID-19 vaccine may be confusing for physicians since the differential diagnosis of unilateral axillary or supraclavicular LAPs is broad, including inflammation, infection, and malignancies, such as metastatic lymph nodes and lymphoma. Therefore, in patients undergoing malignancy investigation or follow-up, imaging should be performed either

before vaccination or should be postponed for at least four to six weeks after the administration of the COVID-19 vaccine unless the patient has an urgent clinical indication<sup>1</sup>.

Radiologists should be familiar with the sonographic findings of LAPs in order not to interpret reactive LAPs as pathological in patients with a recent COVID-19 vaccine history<sup>6</sup>. In patients with axillary and supraclavicular LAPs, if there is a recent history of COVID-19 vaccination, knowing that this is most probably a self-limiting immune reaction can reassure patients and prevent unnecessary lymph node aspiration or biopsy procedures<sup>6</sup>. In the management of these patients, conservative approaches, such as observation for at least six weeks or follow-up of lymph nodes for a short time with US are recommended<sup>1, 13</sup>.

In conclusion, mRNA vaccines can lead to the formation of pathological lymph nodes that are indistinguishable from metastatic masses on US. The B-mode and CDUS characteristics of reactive LAPs can clearly mimic those of metastatic lymph nodes, making the differential diagnosis difficult. Radiologists having knowledge of the imaging findings of axillary and supraclavicular lymph nodes after mRNA-COVID-19 vaccination can help prevent potentially unnecessary lymph node biopsy recommendations.

**Yazar Katkıları:** Çalışma konsepti/Tasarımı: VK, HK; Veri toplama: VK, HK, AD; Veri analizi ve yorumlama: AT, HK; Yazı taslağı: VK, HK; İçeriğin eleştirel incelenmesi: AT, AD; Son onay ve sorumluluk: VK, HK, AT, AD; Teknik ve malzeme desteği: VK, HK; Süpervizyon: AT, HK; Fon sağlama (mevcut ise): yok.

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**Ethical Approval:** The patient's written informed consent was obtained for the publication of the case report (clinical details and images).

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