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## Case Report

# Superficial thrombophlebitis in ipsilateral breast after COVID-19 vaccination ☆

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## ABSTRACT

On December 2020, the US Food and Drug Administration issued the first emergency use authorization for a vaccine for the prevention of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We report development of superficial thrombophlebitis in the ipsilateral breast of a 43-year-old female 7 days after receiving the first dose of the Pfizer-BioNTech COVID-19 vaccine. Given that this is the first case of superficial thrombophlebitis in the breast shortly after mRNA vaccination for COVID-19 reported to our knowledge, we suggest that this may be a rare vaccine-related event.

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## Background

The World Health Organization has approved 6 vaccines against coronavirus disease 2019 (COVID-19) and more than 11.5 billion doses have been administered globally [1,2]. The workhorse of the vaccination program of the world against COVID-19 is the mRNA COVID19 vaccine manufactured by Pfizer-BioNTech and Moderna with approximately 1.4 billion and 0.5 billion doses respectively, which have been administered worldwide [3]. As more doses are administered there is a higher propensity to identify rare vaccine-related adverse

events which have been reported including anaphylaxis, myocarditis and pericarditis, deep vein thrombosis and vaccine-induced immune thrombotic thrombocytopenia (VITT) [4–7]. Similar events have been consistently reported in SARS-CoV-2 infection, likely as the result of a thrombophilic state secondary to inflammation and activation of the host's coagulation system. This occurs through a series of interactions between macrophages, monocytes, endothelial cells, platelets, and lymphocytes [8].

Published data demonstrates high protective efficacy of the mRNA COVID-19 vaccines which mainly result in mild-to-moderate and short-lasting adverse effects, primarily after

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**Fig. 1 – 43-year-old woman with vertical and horizontal creases in the left breast. Physical examination of the left breast demonstrates linear indentations of the skin with associated discoloration.**

the second dose [9]. We discuss a patient who developed superficial thrombophlebitis of the breast after the first dose of Pfizer-BioNTech COVID-19 vaccine and presented to a breast clinic.

### Case presentation

A 43-year-old female presented to the breast clinic with a chief complaint of at least 3 new horizontal creases in her left breast, which developed 1 week after administration of the Pfizer-BioNTech COVID-19 vaccine intramuscularly in her left arm. Her past medical history was unremarkable, except for hypertension. She never had SARS-CoV-2 infection, previous thromboembolic events, and a personal or family history of thrombophilia. She was a nonsmoker, and her obstetric history included delivery of a now 9-year-old son through Cesarean section, without any complication. The patient had no history of malignancy or autoimmune disease and reported no other breast-related symptoms including nipple discharge, a focal lump or pain. She denied any recent trauma or allergic reactions, and her body mass index was 39.7 kg/m<sup>2</sup>. The only medication she took on daily basis was nifedipine, and she denied intake of exogenous estrogens or any contraceptive medications.

### Investigations

Inspection of the left breast demonstrated 3 linear creases in the left breast, 1 vertical in the lateral aspect and 2 horizontal in the superior and inferior aspects of the left breast. The creases were not painful or tender to touch and were associ-

ated with discoloration of the overlying skin (Fig. 1). Inspection of the right breast did not reveal any abnormality.

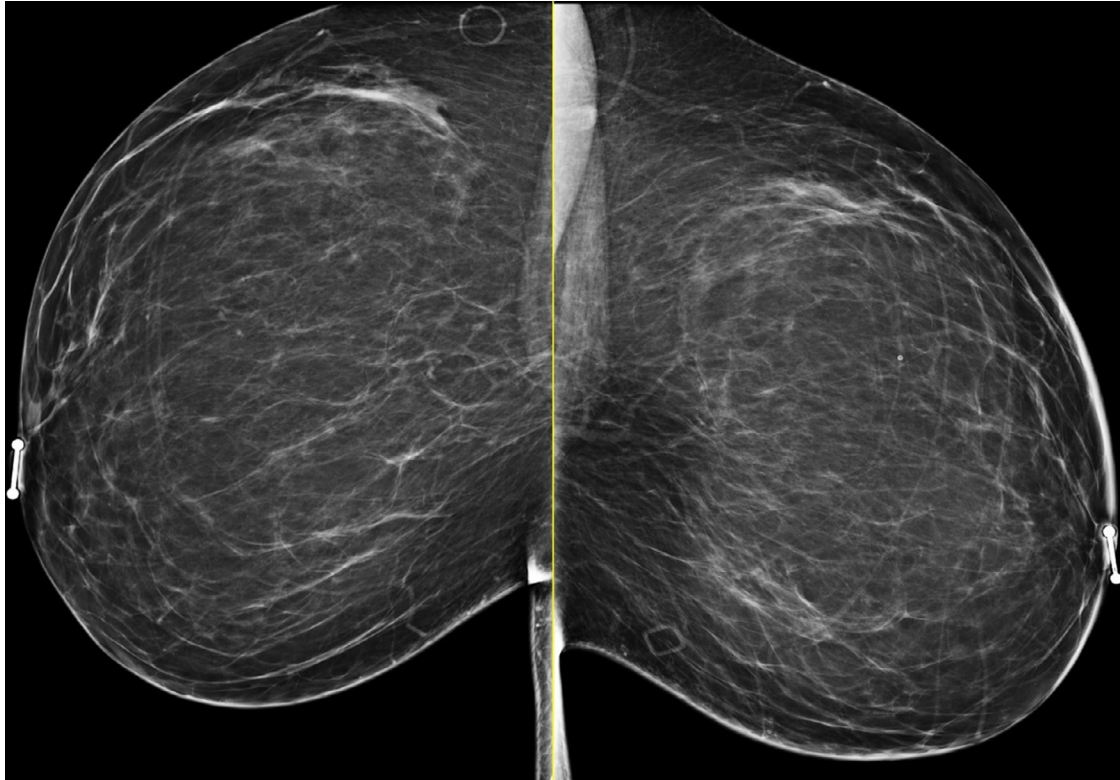
Bilateral diagnostic mammograms, including 2D and 3D digital tomosynthesis, showed fatty breasts with no abnormalities (Fig. 2).

The subsequent diagnostic targeted ultrasound of the left breast corresponding to the sites of the creases showed thrombosed superficial veins with absent flow and loss of compressibility (Fig. 3). The left axillary vein was examined, which was proven to be patent with no evidence of deep vein thrombosis. Targeted ultrasound of the left axilla showed no evidence of lymphadenopathy. Therefore, the left breast was assigned a BIRADS-2 category.

Following completion of the breast exam, the patient was instructed to go to the emergency room for a comprehensive examination. Vital signs in the emergency room were: blood pressure of 140/97, heart rate of 84, respiratory rate of 18, temperature of 37°C, and a pulse oximetry reading of 100% on room air, and were considered noncontributory to the patient's clinical concern. The patient weighed 108 kg, with a height of 165 cm, with a calculated BMI of 39.7 kg/m<sup>2</sup>. No laboratory data was obtained. The patient was seen and examined by an emergency physician and was subsequently discharged with a diagnosis of superficial thrombophlebitis.

### Differential diagnosis

Given the initial presentation of acute development of linear creases in the breast shortly after a vaccination event, the most likely diagnosis was superficial thrombophlebitis (Mondor's disease). Breast cancer, lymphoma, and deep vein thrombosis are other clinical considerations which need be considered given distinct management algorithm. Mammograms and sonographic evaluation demonstrate no suspicious find-



**Fig. 2 – 43-year-old woman with vertical and horizontal creases in the left breast. Mediolateral oblique mammograms show fatty breasts with no abnormalities.**

ing to suggest breast cancer or lymphoma and ruled out other considerations. Lack of pitting edema, no history of injury to axillary lymph nodes, no travel to endemic areas where a parasite that may cause filariasis is prevalent, and absence of subcutaneous edema and skin thickening on sonographic evaluation makes consideration of painless lymphedema of the breast an unlikely etiology [10]. Furthermore, sonographic evaluation demonstrated superficial thrombophlebitis corresponding to the sites of the creases.

### Treatment

The patient was treated conservatively and was recommended to take over the counter nonsteroidal anti-inflammatory drugs as needed.

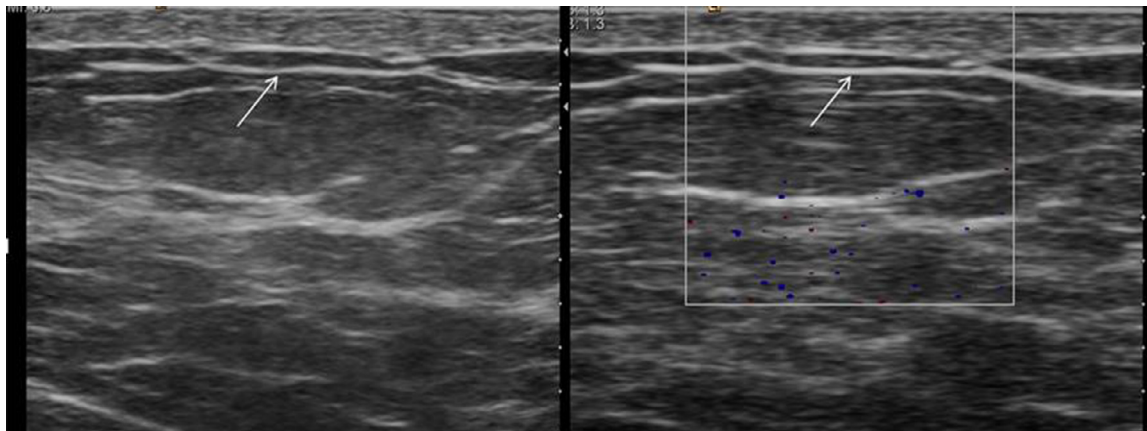
### Outcome and follow-up

The patient was recommended to follow-up with hematology for assessment of possible underlying thrombophilia; however, no hematology appointments were available at the time of this submission. Linear creases of the breast corresponding to the site of superficial thrombophlebitis resolved over a few weeks after the initial postvaccination. The patient elected not to complete the second dose of the COVID-19 vaccine.

### Discussion

We present a case of superficial thrombophlebitis (Mondor's disease) of the ipsilateral breast that occurred 7 days after intramuscular administration of the Pfizer-BioNTech COVID-19 vaccine. Mondor's disease is characterized by thrombophlebitis of the superficial veins of the breast and the anterior chest wall and may present clinically as a palpable cord; or a mass usually associated with pain [11]. It most commonly occurs in the lower extremities (great saphenous vein: 60%–80%, small saphenous vein: 10–20% and rarely occurs at the other sites (10%–20%) [12,13]. Although the most common etiology is idiopathic, breast cancer, trauma, hormone therapy and thrombophilic conditions have been determined to be the causative factors of Mondor's disease in some cases [14]. Even though the diagnosis is made clinically, if ultrasound is performed it demonstrates thrombophlebitis of the superficial veins.

The current reporting rate for venous thrombotic events is 0.075 per 1 million of people vaccinated from COVID-19 [15]. For example a similar case was previously reported of idiopathic ipsilateral external jugular vein thrombophlebitis that manifested 2 days after a 55-year-old female received her second dose of the Pfizer-BioNTech COVID-19 vaccine [16]. Likewise, deep vein thrombosis involving the peroneal vein was reported in a 66-year-old female 1 day after the second dose of the Pfizer-BioNTech COVID-19 vaccine [6]. At



**Fig. 3 – 43-year-old woman with vertical and horizontal creases in the left breast. Sagittal ultrasound shows mildly dilated superficial tubular structure with echogenic intraluminal thrombus (arrow) (A). Color Doppler analysis shows lack of flow in the tubular structure (arrow) (B) consistent with thrombophlebitis.**

least 1 risk factor for development of thrombophlebitis was identified in our patient: obesity (body mass index of 39.7 kg/m<sup>2</sup>). Otherwise, all 3 patients are middle-aged females who were asymptomatic prior to vaccination, without known underlying thrombophilia and developed ipsilateral superficial thrombophlebitis or deep vein thrombosis within less than a week following mRNA vaccination for COVID-19. It is difficult to ascertain whether venous thrombotic events are more common following either the first or the second mRNA vaccination for COVID-19, as published reports do not demonstrate any apparent preponderance. As the cause of thrombophlebitis is unknown, other underlying thromboembolic conditions cannot be ruled out as a part of overall clinical picture.

To our knowledge, this is the first reported case of superficial thrombophlebitis in the breast presenting as an adverse event post Pfizer-BioNTech COVID-19 vaccination. Ipsilateral presentation of thrombophlebitis after mRNA vaccination for COVID-19 may be a sequel of acute inflammation as intense immunological response is evoked by the first vaccination dose and could be the trigger for such a thrombotic event. It is conceivable that pathogenesis of this event may be thrombotic, and this patient might have had a more serious adverse event following the second dose of mRNA COVID-19 vaccine such as previously reported cases of deep vein thrombosis, or cerebral venous sinus thrombosis [17,18]. However, it is almost unfeasible to affirm vaccination as the cause of thrombophlebitis. It is plausible that thrombophlebitis may be just a coincidental occurrence, given that over 1.4 billion Pfizer-BioNTech COVID-19 vaccine doses have been administered worldwide with a paucity of similar reports within the literature, which may be due to underreporting [3].

There is still much we do not know about thrombotic phenomenon potentially linked to a COVID-19 vaccination, as it is difficult to gather data especially regarding rare nonfatal events. Therefore, patients and physicians are to be vigilant regarding suspected new, unexpected, or serious adverse events which occur shortly after vaccination event, especially in the setting of massive vaccination with new vaccines. These findings have important public health implica-

tions, albeit carry limited clinical utility given that treatment of superficial thrombophlebitis is supportive.

### Limitations

This case report has several limitations. Although, this case is the first to our knowledge of superficial thrombophlebitis after the first dose of Pfizer-BioNTech COVID-19 vaccine, it is possible that real-world prevalence of such an event after mRNA COVID-19 vaccination may be underreported. Second, limited laboratory investigations were performed on this patient; hence, it is difficult to ascertain the pathophysiologic mechanism underlying this event.

### Conclusions

In conclusion, although the initial case of ipsilateral superficial thrombophlebitis after Pfizer-BioNTech COVID-19 vaccination may not necessarily represent a serious adverse event on its own, as the medical management is supportive. Our case illustrates that this event occurred in a young and relatively healthy female following the first dose of mRNA COVID-19 vaccine. Even though a cause-effect relationship cannot be ascertained and the association between the vaccine and the development of ipsilateral thrombophlebitis may be a mere coincidental occurrence. It is possible that this patient might have developed a more serious adverse event after vaccination with a second dose of mRNA vaccine for COVID-19. Therefore, this clinical scenario presents us an opportunity to do additional screening for occult events prior to second dose vaccine administration especially to the young females who may be potentially high-risk individuals with possible outcome of a serious or even a fatal cardiovascular event. This case report does not alter vaccination recommendations against COVID-19.

## Patient consent

We report that proper written consent from patient was obtained, and patient gave consent for material about her to be included in the publication. Patient saw the photos which are to be included in the publication and read text of the article submitted for publication. She is legally entitled to give her own consent. Patient understood that she would not receive any financial benefit from publication of the article.

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