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Iron wire phlebitis – a disease of underestimated significance. COVID-19 as a factor increasing the risk of Mondor's disease

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ABSTRACT

Mondor's Disease, also known as iron wire phlebitis, is a rare and self-limiting superficial vein thrombophlebitis that presents with a palpable cord-like induration beneath the skin. Others symptoms include: pain, swelling and redness of the affected area. It typically affects the vessels of the chest wall, less frequently the vessels of the penis or the upper limbs. The etiology of the disease is not fully understood, but it is known that it may be caused by local injuries or surgeries, and it may accompany cancer or infections. The diagnosis is based

in most cases on an anamnesis and physical examination, confirmed by ultrasound. There are approximately 500 cases of this disease described in the literature. Iron wire phlebitis is a disease of underappreciated importance, raising awareness of this condition can facilitate the MD' diagnosis and reduce unnecessary diagnostic procedures.

A 36-year-old female patient detects a lump during breast self-examination. The lesion was located in the upper outer quadrant of the right breast. The ultrasound revealed dilated venous vessel with thrombosis, which led to diagnose Mondor's Disease. In this case the cause of increased coagulation may be ablation or COVID-19 infection. It is necessary to find the etiological factors predisposing to the disease, and extending the diagnosis to exclude other rheumatological, hematological and neoplastic diseases. The patient received low-molecular-weight heparin, heparin ointment, painkillers and anti-inflammatory drugs. After one week treatment, the change wasn't palpable. Then, instead of LMWH, oral sulodexide was used for treatment.

Thanks to awareness of this disease, it was possible to made an appropriate, quickly diagnosis and implement treatment, as well as reduce unnecessary medical procedures. The early diagnosis of MD can help to identify serious causes (for example breast cancer) at an early stage which will allow to treatment previously undetected changes.

Keywords: thrombophlebitis, iron wire phlebitis, Mondor's disease, superficial thrombophlebitis of the Breast, COVID-19

INTRODUCTION

Mondor's Disease (MD), also known as iron wire phlebitis, is a rare and self-limiting superficial vein thrombophlebitis that presents with a palpable cord-like induration beneath the skin. [1]. Others symptoms include: pain, swelling and redness of the affected area. [2] It typically affects the vessels of the chest wall, less frequently the vessels of the penis or the upper limbs. The diagnosis is based in most cases on an anamnesis and physical examination, confirmed by ultrasound. The etiology of the disease is not fully understood, but it is known

that it may be caused by local injuries or surgeries. MD is generally considered self-limited and benign, but there is a potential link with serious underlying diseases— malignancy (breast cancer, vascular neoplasm, cutaneous metastasis of any type of cancer), hypercoagulable state or systemic vasculitis, so these patients should be carefully examined and followed-up. [1]

This condition was described in 1939, however, it is believed to have been depicted in 17th-century paintings by Rembrandt and Rubens. (Figure 1. and Figure 2.)

Until this day, only approximately 500 cases have been described in the literature. There is a possibility that it is more common than reported since the lesion is often nonpainful and self-resolving, so some patients do not seek medical attention. [1] The absence of clear diagnostic criteria and lack of needed awareness of physicians cause it to be underdiagnosed.

Differential diagnoses of Mondor’s disease include inflammatory breast cancer, mastitis, abscess, dilated duct (Table 1) and thrombophlebitis migrans, Buerger disease, Behcet disease and polyarteritis nodes [1,2]. Mondor’s disease of the breast is not commonly considered as a differential diagnosis for patients presenting with breast complaints. Majority of patients presenting to the Emergency Department with focal breast swelling alongside with non-specific inflammatory symptoms are commonly investigated and treated for mastitis or breast abscess. [3] Even though Mondor’s disease is an uncommon cause of chest pain, it is not considered a differential diagnosis due to lack of awareness of this condition. [4]

Table 1. Differential diagnoses of Mondor’s disease [1].

	SYMPTOMS	SKIN CHANGES	PALPATORY FINDING	USG FINDING
MD	Mild, aching pain may be present initially; soreness	Often erythematous; may be raised or retracted	Linear, cord-like lesion adherent to the skin	Tubular anechogenic, beaded structure; thrombus distending the vein may be visible.
INFLAMMATORY BREAST CANCER	Nonpainful in spite of the alarming appearance on examination; progressive worsening	Possible skin retraction; Peau d’orange, erythema, crusting, blistering, or retraction of the nipple.	There may or may not be an underlying palpable mass, which may become adherent to the skin; fixed palpable ipsilateral axillary lymph nodes may be present	Hypoechogetic shadowing mass; skin thickening; pectoral muscle invasion; axillary involvement.
MASTITIS	Exquisite tenderness; fever	Erythematous skin; mild skin thickening.	Warm; indurated breast; nipple retraction may be present; nodal enlargement is common.	Ill-defined area with hyperechogenic, infiltrated and inflamed fat lobules, hypoechogetic areas in the glandular parenchyma; mild skin thickening; inflammatory axillary lymph nodes.
ABSCCESS	Exquisite tenderness; fever	Erythematous skin	Warm; rounded lesion; indurated breast; palpable fluctuance; nodal enlargement is common.	Hypoechogetic multiloculated collection with an hyperechogenic, vascular rim; acoustic enhancement due to fluid content; no vascularity within the collection; inflammatory axillary lymph nodes
DILATED DUCT	Often asymptomatic; pain or tenderness may be present	Often asymptomatic; nipple retraction may be present; nipple discharge may be present	Often asymptomatic; sometimes may present as a palpable mass	Distended (>2mm) anechogenic branching or tubular structures

In cases of breast MD, it is imperative for clinicians to correctly differentiate this condition from a breast cancer, which may be challenging—due to palpable finding and skin retraction, MD can resemble breast cancer on clinical exam. [1] It may lead to unnecessary biopsy, if physician is not familiar with clinical features of MD.[1] In some cases, the presence of Mondor's disease of the breast (MDB) led to the diagnosis of an underlying breast cancer. Thus, it raises the question of a possible association between breast cancer and MDB. That is the reason why regardless of the disease's etiology, it is recommended to carry out diagnostic examinations to exclude co-occurring breast cancer. [5, 6]

Superficial vein thrombosis can occur in COVID-19 patients. Available evidence suggest the presence of hypercoagulable state in COVID-19 patients and thrombophlebitis could be clinical manifestation due to tight interconnection between inflammation and hemostasis abnormalities. Clinicians should also be aware of rare forms of venous thrombosis such as Mondor's disease. [1]

The global healthcare systems are facing significant challenges posed by the COVID-19 pandemic. COVID-19 is a viral disease characterized by a wide range of symptoms, including fever, cough, difficulty breathing, and loss of taste and smell. It has been observed that infection with this virus can affect other systems, including the respiratory, neurological, cardiovascular, hematopoietic, gastrointestinal, and immune systems.

Studies have shown that infection with this virus increases the risk of both arterial and venous blood clots, due to excessive vascular and systemic inflammation, endothelial dysfunction, cytokine storm, hypoxia and immobilization [7, 8, 9]. Emerging data indicate that COVID-19 patients may exhibit a hypercoagulable state, and thrombophlebitis could manifest as a clinical symptom during infection or up after 30 days after disease.[10] COVID-19 disrupts the immune system and causes an abnormal and intensified inflammatory response, activates blood platelets, impairing functioning of blood vessels, causes increased production of blood clots, and the formation of fibrin, as evidenced by elevated levels of D-dimers, which leads to a lowering the level of anticoagulants. [1,7]

Increasing reports regarding venous thrombosis and thromboembolism caused by the coronavirus indicates the need for heightened awareness. It has been shown that this risk is increased even a year after recovering from COVID-19 [4] It is crucial to recognize that thrombophlebitis could be a potential clinical sign of COVID-19 or it can also be a result of a previous COVID infection. Hence, physicians should remain vigilant and have a heightened awareness of both common and less common cases of thrombosis in individuals, including Mondor's disease. [7, 11]



Figure 1. Peter Paul Rubens, „Samson and Delilah” and detail of Delilah, The National Gallery, London.



Figure 2. Rembrandt van Rijn „Bathsheba at Her Bath” and detail of Bathsheba’s breast, The Louvre, Paris.

CASE REPORT

A 37-years old woman detects a lump during breast self-examination. The lesion was located in the upper outer quadrant of the right breast. The change was painful. There was swelling, skin retraction and redness of the affected area. The lump appeared suddenly. The patient presented to the doctor and underwent a breast ultrasound. The ultrasound revealed a longitudinal thickening extending radially towards the areola, with no blood flow detected on Colour Doppler. The observed change was not affected by pressure. This description corresponds to a dilated venous vessel with thrombosis. [Figure 3]. Possible causes of thrombosis were investigated in this young patient. She had a recent history of COVID-19 infection less than a month ago and underwent a heart ablation procedure about 2 months ago due to arrhythmia. These factors can potentially increase the risk of thrombosis.

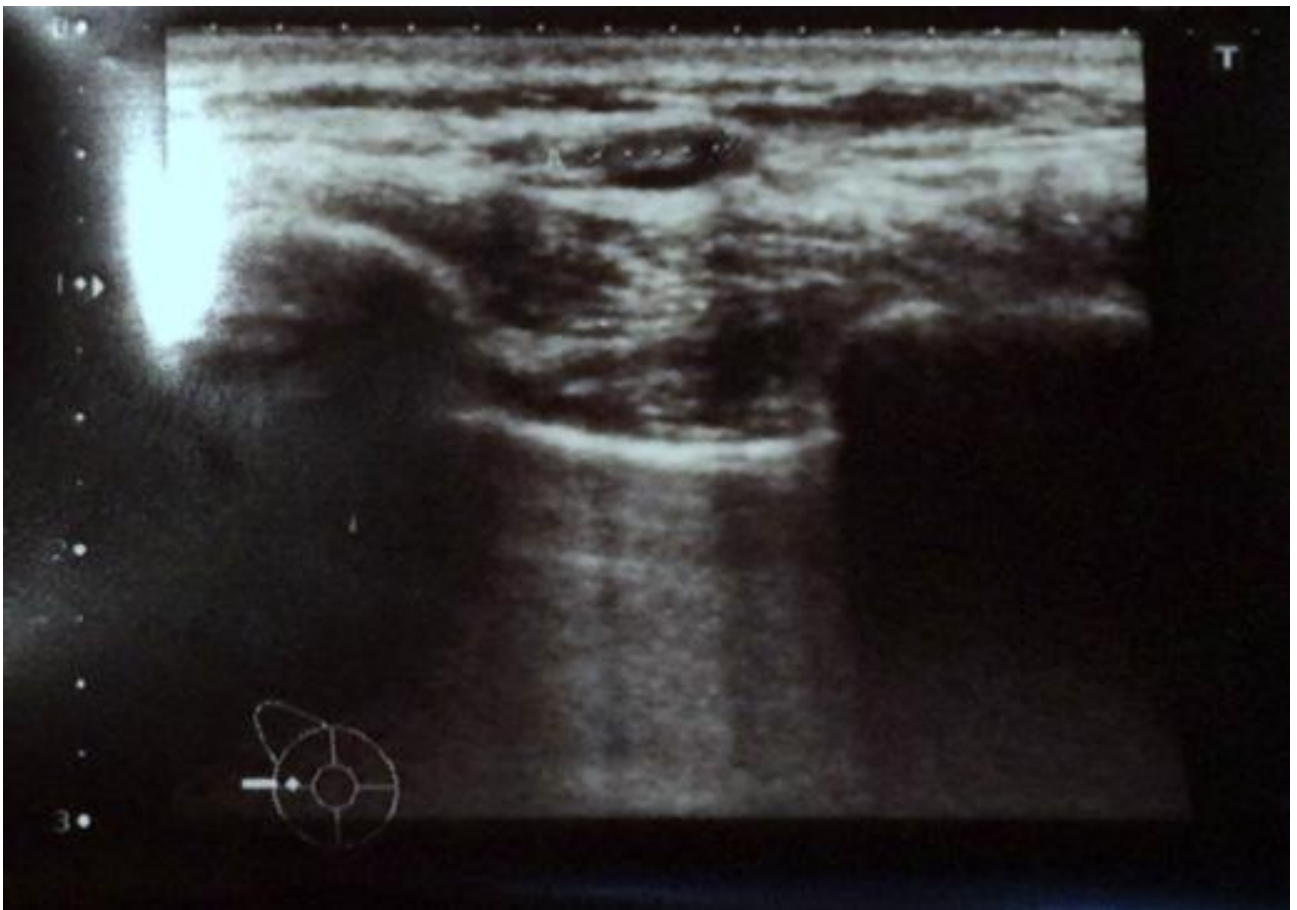


Figure 3. Ultrasonography of the right breast. The longitudinal change corresponds to a dilated venous vessel with thrombosis.

Given the characteristic image on examination, the ultrasound findings, and the predisposing factors, the diagnosis of Mondor's Disease was made. However, the patient was kept under observation with increased oncological vigilance. The diagnostic workup was expanded to exclude other possible causes that could increase the risk of thrombosis, including hematological and rheumatological disorders.

The patient was initially treated with LMWH (subcutaneously) for 10 days, along with heparin ointment, painkillers, and anti-inflammatory drugs. After one week of treatment, no palpable improvement was noted. Therefore, LMWH was replaced with oral sulodexide for further treatment.

During this time, a mammogram was performed, which did not reveal any suspicious oncological changes. A follow-up ultrasound was conducted, showing regression of the observed changes. Due to the observed improvement in the patient's condition and the increased accuracy of the initial diagnosis, a decision was made to forgo a biopsy. However, the patient continues to be monitored and observed closely.

CONCLUSION

Mondor's Disease, also known as iron wire phlebitis, is a rare and self-limiting condition characterized by superficial vein thrombophlebitis. The distinct appearance of "iron wire-like" changes in the affected vessels was initially described around 1850, but the disease was officially identified and named after Henri Mondor, a French surgeon, who reported cases in 1939. It is speculated that the symptoms of Mondor's Disease might have been noticed much earlier by renowned artists known for their precise depiction of the human body. Paintings like Rubens' "Samson and Delilah" and Rembrandt's "Bathsheba at Her Bath" show distorted venous vessels characteristic of the condition. [1, 12]

Despite the limited number of reported cases, there is suspicion that Mondor's Disease occurs more frequently, but not all patients seek medical help as the condition can be painless and may resolve spontaneously within 4-8 weeks. [13, 14] Moreover, the awareness among medical professionals about this condition is limited. It is crucial to disseminate information about this disease because, although generally considered self-limited and benign, it can sometimes be a symptom of underlying diseases. Cases have been described where Mondor's

Disease was associated with other serious conditions such as breast cancer, vascular neoplasms, cutaneous metastasis of various cancers, hypercoagulable states, or systemic vasculitis. The connection between Mondor's disease and breast cancer is not fully understood, but it should increase oncological vigilance, especially in patients at risk of breast cancer. Furthermore, Mondor's disease is a rare cause of chest pain and is not considered a differential diagnosis of chest pain due to lack of awareness about it. It should therefore be recalled that Mondor's disease may also be one of the causes of chest pain and should be considered in the differential diagnosis.

Educating physicians and patients about this rare disease can improve its recognition and understanding of potential risks, expedite diagnosis, prevent complications, and identify potential links to other serious conditions. [13,15,16]

Thrombophlebitis of the breast appears to be analogous to inflammation of blood vessels in other parts of the body.[17] However, Mondor's Disease should receive greater attention from physicians due to the need to differentiate it from breast cancer or to suspect its association with other systemic diseases. Although only a few cases linking COVID-19 and Mondor's Disease have been described so far, available evidence suggests the presence of a hypercoagulable state in COVID-19 patients, and thrombophlebitis could be a clinical manifestation due to the close interconnection between inflammation and hemostasis abnormalities. Therefore, a history of COVID-19 infection is essential information in the differential diagnosis. [18, 19, 20] This is particularly significant for clinicians who, besides making an accurate diagnosis of this condition, provide psychological comfort to the patient and avoid subjecting them to unnecessary and risky investigations. [21] Creating awareness of this condition through this case report would help to reduce unnecessary investigations and valuable time spent and would help identify a serious underlying cause, especially early stage carcinoma of the breast.

FOOTNOTES

Author's contribution

Conceptualization, K.T. J. W-S.; writing—original draft preparation, K.T. J. W-S. A.H.; writing—review and editing, ; visualization A.H.; translation, K.T.

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Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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