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Superficial Venous Thrombosis in Atypical Locations

ABSTRACT

KEY WORDS: superficial venous thrombosis, atypical location, Mondor disease, Trousseau's syndrome

Superficial venous thrombosis (SVT) is an inflammation of the venous wall with subsequent secondary thrombus formation. In the majority of cases, it affects the superficial venous system of the lower extremities. SVT which appears in functionally and structurally normal veins without varicose changes is a heterogeneous group of diseases in which different etiopathogenetic mechanisms are present with varying expressions of inflammatory and thrombotic processes. Trousseau's syndrome is a rare variant of venous thrombosis that is characterised by recurrent, migratory thrombosis in superficial veins and in uncommon sites, such as the upper extremities, trunk, and chest wall. Superficial migratory thrombophlebitis is associated with systemic diseases like hypertension, Buerger syndrome/thrombophlebitis obliterans, hypercoagulable conditions like protein C and S deficiencies, lupus anticoagulant, factor XII deficiency, systemic inflammatory diseases, Behcet disease and cancer. Mondor disease describes a syndrome of sclerosing superficial thrombophlebitis of the veins of the anterior thoracic wall. The most commonly involved vessel is the superior epigastric vein, producing a palpable cord in the inferior outer quadrant of the breast. It has often been linked to local trauma, including repetition injury or direct injury associated with surgery. In addition to the diagnosis of superficial venous thrombosis using ultrasound, more extensive diagnostic procedures in order to look for a systemic procoagulant state are often needed, since underlying diseases are important for the treatment of SVT in an atypical location.

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INTRODUCTION

Superficial venous thrombosis (SVT) is an inflammation of the venous wall with subsequent secondary thrombus formation. In the past, it was perceived as a benign and self-limited disease. However, recent observations showed that SVT, particularly in the lower limbs, can cause different complications, attributed mostly to deep venous thrombosis (DVT) and pulmonary embolism (PE). Therefore, SVT was recently accepted as a part of venous thromboembolic syndrome. In most cases, it affects the superficial venous system of the lower extremities. It mainly occurs in varicose veins as a consequence of damage to the vessel wall because of turbulent blood flow, stasis and chronically increased venous pressure, which provokes an increase in the systemic inflammatory response and promotes the process of coagulation.

SVT that appears in functionally and structurally normal veins without varicose changes is a heterogeneous group of diseases in which the inflammatory and thrombotic processes are differently expressed. It can appear as an isolated clinical manifestation or as a part of different clinical conditions.

Trousseau's syndrome and Mondor disease are two specific forms of SVT in atypical locations, which have specific etiopathogenetic, clinical, and prognostic characteristics.

TROUSSEAU'S SYNDROME

Trousseau's syndrome, also known as superficial migratory thrombophlebitis, is a rare variant of venous thrombosis, characterised by recurrent, migratory thrombosis in superficial veins in uncommon sites, such as the upper extremities, trunk, and chest wall. It is usually associated with systemic diseases like Buerger disease, hypercoagulable conditions like protein C and S deficiencies, lupus anticoagulant, factor XII deficiency, systemic inflammatory diseases, Behcet disease and cancer, most commonly gastrointestinal (including pancreatic and gastric), lung and urogenital cancers *(1)*. It most commonly occurs between the ages of 25 and 50 years, three times more frequently in males than females.

Cancer-associated SVT is distinctive and its pathogenesis is not well understood. Research has reported the spectrum of overlapping mechanisms, including mucins that have been produced by some adenocarcinomas that trigger thrombotic cascades, as well as highly procoagulant tissue factor positive microparticles that are produced by cancer cells and cysteine proteinase expressed by malignant cells, which directly induces the conversion of factor X to factor Xa. There are reports that tumor tissue hypoxia increases the expression of tissue factor and plasminogen activator inhibitor type 1 (PAI-1) that facilitate coagulation *(2)*.

Patients with superficial thrombophlebitis present with pain, erythema, and induration along the course of a superficial vein. Due to a thrombus within the affected vein, a nodular cord is often palpable. A fever might be present. Signs and symptoms of DVT and PE should be evaluated in high-risk patients, such as patients older than 60 years, those of male sex with the presence of bilateral SVTs, and absence of varicose veins.

The diagnosis of superficial migratory thrombophlebitis is based on clinical presentation and is confirmed by ultrasound investigation. An ultrasound investigation is especially indicated in patients with pain along the course of the superficial vein but who have no physical exam findings suggestive of thrombophlebitis, obese patients, patients with SVT of the great saphenous vein or small saphenous vein, as they have a higher risk for DVT, and patients with significant extremity swelling.

The diagnosis of migratory thrombophlebitis is essential, as it correlates with cancer and other systemic disorders, and it

can be the initial presentation of underlying occult malignancy. These patients should undergo evaluation for underlying malignancy and other systemic disorders at the time of superficial migratory thrombophlebitis diagnosis.

The treatment goal is to relieve local symptoms and prevent the propagation of the thrombus. Supportive care includes an elevation of the affected extremity, nonsteroidal anti-inflammatory drugs, warm or cold compress, compression stockings, and increased ambulation.

In patients with superficial thrombo-p-hlebitis involving a vein segment of size segment smaller than 5 cm and a thrombus site remote from the saphenofemoral junction and saphenopopli-teal junction and no medical risk factors for venous thromboembolism, supportive care is indicated. These patients are followed up in seven to ten days or sooner if symptoms progress, and if there is no clinical improvement in symptoms, an ultrasound duplex is performed to rule out DVT.

Anticoagulation in therapeutic dosage is indicated in patients with the propagation of clots and also in high-risk patients with thrombus longer than 5 cm and within 5 cm from the saphenofemoral junction or saphenopopliteal junction and in patients with concomitant DVT and PE. In patients with SVTs longer than 5 cm and more than 5 cm distant from the saphenofemoral or saphenopopliteal junction, subcutaneous fondaparinux 2.5 mg daily or low-molecular-weight heparin in prophylactic dosage for 45 days is suggested *(3)*.

In patients with DVT and PE, longer--duration anticoagulation is the recommended course. In patients with Buerger disease, the clinician should strongly recommend smoking cessation. If present, underlying systemic or cancer disease should be properly treated.

The prognosis for migratory thrombophlebitis depends on the cause. For malignancies, the prognosis is poor. For benign disorders, the prognosis is good, but residual post-phlebitic syndrome is an issue and should be prevented by using compressive stockings.

MONDOR DISEASE

Mondor disease classically describes a syndrome of sclerosing superficial thrombophlebitis of the veins of the anterior thoracic wall veins. The most commonly involved vessel is the superior epigastric vein, producing a palpable cord in the inferior outer quadrant of the breast or superficial penile veins *(4)*. There are less than 400 reported cases of Mondor disease in medical literature *(5)*. Women are three times more likely to be affected than men. While cases are present in all ages, most are observed among patients between 30 and 60 years of age.

It is a rare clinical entity with a poorly understood etiology. Inciting factors such as direct trauma from tight clothing, surgery, or underlying system diseases such as breast cancer or hypercoagulable states have been described as causes for the resulting sclerosing thrombophlebitis of the affected superficial veins. A recent literature review by Amano et al. revealed that 45% of cases are idiopathic, 20% iatrogenic, 22% traumatic, and 5% related to breast cancer *(6)*.

The disease presents with a sudden onset of mild discomfort with a palpable cord in the affected area. Penile lesions may involve a history of excessive sexual activity, trauma, or abstinence. Anterior chest lesions may include a history of recent mammoplasty, oncologic surgery with either sentinel lymph node biopsy, axillary dissection or core needle biopsy, or another injury such as weightlifting.

The diagnosis of Mondor disease is based on clinical investigation. With so few cases represented in medical literature, there is no consensus on its evaluation or management. In patients with a classic history and no other systemic complaints

and otherwise regular physical exam, it is reasonable to proceed without a laboratory, radiographic, or other invasive testing for diagnosis. In those patients with signs or symptoms suggestive of under-lying pathology, further evaluation with either a mammography of the breast or ultrasound of the breast or penis is needed *(7)*. In cases where the clinical picture is not definitive, ultrasound is considered the first line in the imaging evaluation of Mondor disease. Mammography may be inconclusive, or it may reveal a linear density in the breast in patients with super-ficial thrombophlebitis. MRI and other advanced imaging techniques are generally not indicated in the evaluation of Mondor disease.

Supportive care and expectant management are sufficient in most cases of Mondor disease. Warm compresses, nonsteroidal anti-inflammatory medications, and abstinence from irritating clothing or activities are first-line therapies. Most lesions will resolve with the cessation of discomfort and dissolution of the palpable cord. Treatment with low-molecular-weight heparin or acetylsalicylic acid has been reported in some case series; however, this is not recommended in patients without an underlying hypercoagulable state inciting superficial thrombophlebitis and associated Mondor cord.

Migratory thrombophlebitis can be resistant to anticoagulation treatment in cancer patients, resulting in the progression of thrombus and recurrent PE. There are reports in patients with malignancy and migratory thrombophlebitis that surgical removal of cancer results in cancer cure as well as improves phlebitis symptoms and reduces thrombotic events.

Mondor disease is usually a self-limited condition that resolves in six to eight weeks. In cases where the situation is secondary to a hypercoagulable state, the prognosis is directly linked to the inciting condition.

CONCLUSIONS

SVT which appears in functionally and structurally normal veins at atypical locations is a heterogeneous group of diseases with heterogeneous and poorly understood etiopathogenetic mechanisms. Severe systemic diseases, including various types of cancers should be considered as underlying clinical conditions that might trigger coagulation. In addition to diagnosing SVT by using ultrasound, more extensive diagnostic procedures in order to look for a systemic procoagulant state are often needed since underlying diseases are important for the treatment of SVT in atypical locations.

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