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Review Article

May-Thurner syndrome: a review

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ABSTRACT

May-Thurner syndrome (MTS) is an underdiagnosed entity and level of suspicious should be raised during evaluation of deep vein thrombosis (DVT) of the left lower limb, especially in women between the third and fifth decades of life. To correctly identify MTS, high clinical suspicion, and imaging studies such as phlebography, magnetic resonance imaging (MRI), computed tomography (CT), and intravascular ultrasound are required. In correct clinical context, CT/MRI venography can be used to facilitate early diagnosis and treatment that includes pharmaco-mechanical thrombolysis with angioplasty and stenting, both of which minimize late morbidity from post-thrombotic syndrome.

Keywords: MTS, Cockett syndrome, Iliac vein spur, Iliac vein compression, DVT, Recurrent thromboembolic disease

INTRODUCTION

Cockett syndrome is also known as MTS or iliac vein compression syndrome. In 1851, Virchow published his preliminary observations, although the pathophysiological process was not yet described with certainty. It was not until 1908 that McMurrich found spinous substance (spurs) in the common iliac vein and considered it a "congenital anomaly." May and Thurner in 1957, Cockett and Thomas in 1965 described the disease in detail.[1,2]

MTS has an estimated incidence between 18-49%, it is an anatomical condition resulting from extrinsic venous compression of left common iliac vein (LCIV) and less common right common iliac vein (RCIV) by right common iliac artery (RCIA) and fifth lumbar vertebra (L5), (Figure 1) which over time produces vascular remodeling that can develop DVT, chronic venous insufficiency/associated sequelae.[3-5] RCIA is considered to cause this partial obstruction by direct mechanical compression of LCIV also, intimal hyperplasia in LCIV due to shear stress on anterior, posterior walls of LCIV secondary to pulsation of overlying RCIA contributes to venous obstruction and subsequent thrombosis. [6]

An association of between 2-5% is estimated in patients with MTS and symptomatic venous disease of the lower limbs and 20% of patients who present thromboembolism, especially in those with recurrent thromboembolic disease, [7] this syndrome is usually diagnosed in patients with symptoms of chronic edema or DVT in the lower limbs. [8] There are certain physiological changes such as pregnancy, where compression of the inferior vena cava, both by the gravid uterus and the associated exaggerated lordosis, can exacerbate the compression associated with MTS, which can result in an increased risk of thrombosis in this population.[5]

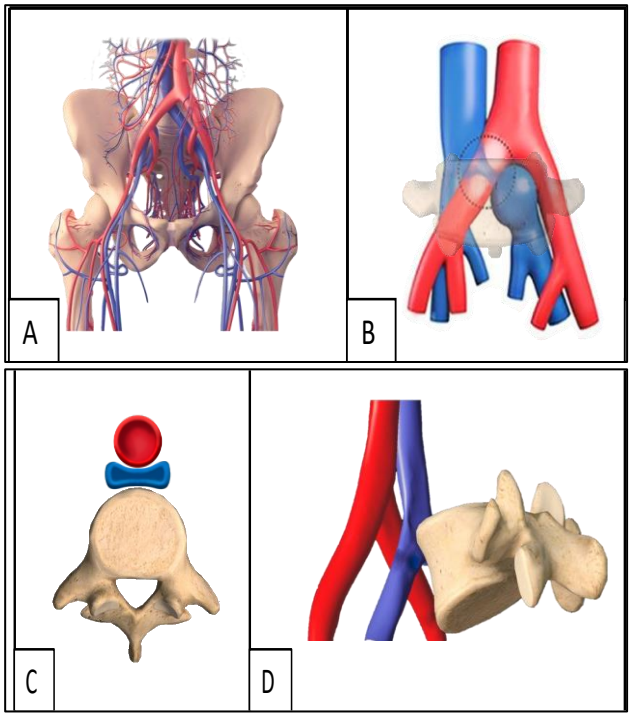

Figure 1 (A-D): Schematic representation of MTS. Anatomical distribution of the left iliac vein. The "compressive" position is observed as the LCIV is between the RCIA and the fifth lumbar vertebra.

DIAGNOSIS

MTS commonly affects women in their third to fifth decades of life, though is not confined to this group. The commonest presentation of these patients is that of venous hypertension. Patients may present with acute episodic (activity related) heaviness and swelling of left lower limb or venous claudication which is relieved with rest and leg elevation. This progresses to chronic venous insufficiency presenting with features of varicose veins, leg pigmentation or venous ulcers. A high degree of suspicion must be maintained to investigate these patients for iliac vein compression.[9,10] Sometimes, the first presentation may be that of deep venous thrombosis (DVT) with painful left lower limb swelling. There may be no precipitating cause, or the disease may first present during or after pregnancy.[11,12] A history of recent use of oral contraceptive pills may be present.[13]

Different studies have been carried out to develop and standardize the anatomical criteria in relation to the diagnosis of MTS, currently we do not have accurate diagnostic criteria, and at the moment there are no multicenter randomized clinical trials designed to evaluate and correlate the degree of stenosis with intravascular pathology that is clinically relevant, which can certainly inadvertently lead to overdiagnosis, with risk of exposure to potentially unnecessary invasive procedures and interventions.[14] In fact, it has been described that different primary and secondary signs of compression can be demonstrated in healthy patients. In a study carried out by Van Vuuren et al. In 2018, 80% of healthy patients participating in the study had at least 2 radiographic signs of compression by phlebography.[15] However, phlebography of the lower extremities and femoral vein catheterization are considered the gold standard for the diagnosis of MTS (Figure 2). Traditional treatment methods are surgical revascularization mainly including femoral-femoral venous bypass (Palma-Dale surgery), EPTFE artificial vascular graft, iliac vein angioplasty, ringed artificial vascular graft/ venous stent. Most traditional open surgery procedures have resulted in greater trauma, more complications, and a lower rate of vascular patency in the postoperative years, so they have been gradually replaced by endovascular procedures.[17]

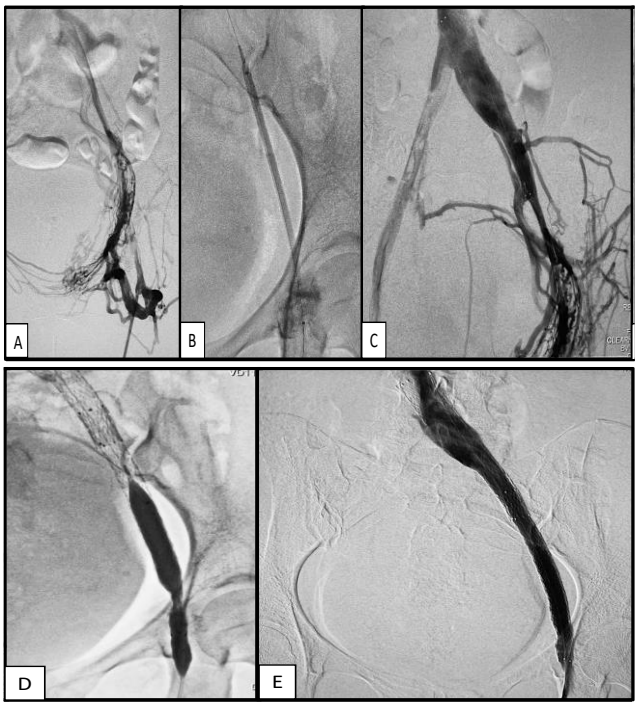

Figure 2 (A-E): Diagnostic and therapeutic phlebography of the left lower extremity. Collateral venous network and decreased passage of contrast medium can be seen in the left iliac vein. Balloon angioplasty in the left iliac vein. Post-angioplasty control, with placement of the first stent where the contrast medium can be seen passing through. Placement of second stent and angioplasty with adequate flow of contrast medium.

Ultrasound

Ultrasound is an important tool for the diagnosis of DVT, especially in special situations such as pregnancy, however it cannot definitively determine the presence of MTS since although it can provide useful and non-invasive information, it may not show the exact point of compression. Secondary signs of MTS include stenosis of the iliofemoral vessels, turbulence in blood flow, presence of extensive collateral vessels as well as evidence of venous insufficiency. In pregnant or postpartum patients, the presence of a gravid or enlarged uterus may cause a lack of visualization of vascular structures. Different studies have documented that the common iliac vein may not be visualized or inadequately visualized in almost 50% of patients, and the external iliac vein may not be visualized or inadequately visualized in up to 20% of patients, even with experienced sonographers.[17,18] Doppler ultrasound is adequate and sensitive for the diagnosis of DVT and evaluation of varicose veins and venous incompetence, however, is less adequate to study the pelvic veins, especially the ilio-caval region. If the ultrasound can visualize the proximal CIV, it may demonstrate the lack or reduction of phasic variations of blood flow distal to the stenosis and turbulence (color mosaic) at the site of stenosis. The opposite side serves as a control. Venous collaterals, an important component of the diagnostic findings are poorly identified by ultrasound.[10]

Intra-vascular ultrasound (IVUS)

In the past decade, IVUS has steadily found increasing use in the diagnosis and management of MTS. During the interventional procedure, IVUS can help in documenting and localizing the cause of iliac venous obstruction-spurs and intimal lesions from chronic adherent thrombus. It can also show the dynamic compression by the overlying artery (Figure 3).

In addition to helping in re-canalizing the chronic occlusion, it can assess response of MT lesion to angioplasty and stent placement and presence of residual thrombus thus aiding in continuation of lysis.[10] IVUS can detect intraluminal and mural changes quite clearly compared to standard venography. However, the procedure is minimally invasive and inappropriate as a screening test.[19,20]

Magnetic resonance

MRI with magnetic resonance venography (MRV) is a useful tool for the diagnosis of DVT in pregnant patients with suspected DVT with negative ultrasound, as well as to help delineate the anatomic relationships necessary for the diagnosis of MTS. MRI is considered safe, with no conclusive evidence of harmful effects, as it does not use ionizing radiation and poses no risk unless the patient has some type of metal object implanted.[5]

Venography

CT venography has a high sensitivity and specificity to detect MTS. It has other advantages including its ability to rule out extrinsic compressions like lymphadenopathy and hematoma, identify acute DVT, and outline collateral pathways. CT also eliminates the need for technical expertise. It has limitations in pregnancy due to radiation dose and can overestimate the degree of compression in dehydrated patients.[21]

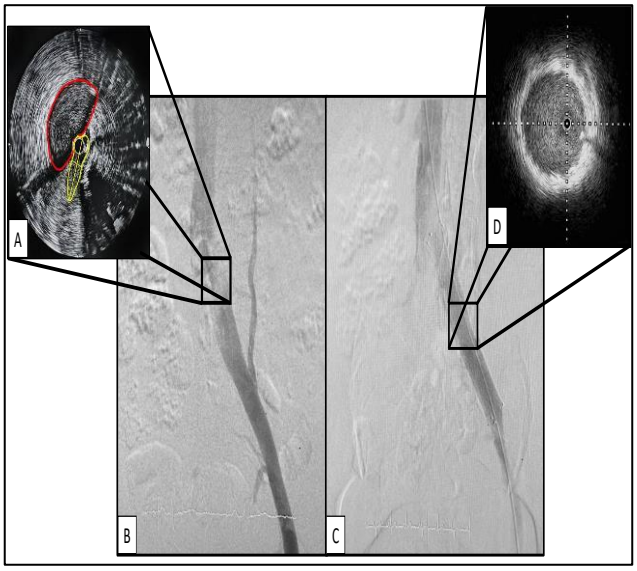

Figure 3 (A-D): IVUS in MTS. IVUS where it is seen in red (artery) compressing the vein (yellow). Inadequate passage of contrast medium was observed through the compression area in the left iliac vein. Control phlebography after venous stent placement. IVUS at stent placement site.

TREATMENT

The results of ATTRACT trial suggested that catheter directed thrombolysis was not superior to systemic anticoagulation in patients with acute lower limb DVT.[22] However, in the subgroup of DVT patients with MTS, clearing the thrombus load and establishing an outflow still forms the cornerstone of management.[23] Patients who are eligible for thrombolysis should be strongly considered for pharmaco-mechanical thrombolysis for maximal thrombus clearance and assessment of underlying iliac stenosis, followed by angioplasty and stenting of the underlying stenotic lesion (Figure 4). Isolated catheter directed thrombolysis or mechanical thrombectomy can be chosen based on individual patient factors, expertise and availability of the devices. Newer techniques such as rheolytic thrombectomy with Angiojet (Boston Scientific, USA) or rotational thrombectomy (Cleaner-XT, Argon medical, USA) are additional options.[10] Minimally invasive techniques, now in combination with localized fibrinolytic therapy, have become the standard of care for MTS, even for limb-threatening diseases. Current Society for Vascular

Surgery guidelines recommend the use of endovascular therapy for primary treatment. Compared with anticoagulation alone, catheter-directed therapy is associated with a significant reduction in long-term complications associated with PTS (up to 90% develop PTS with anticoagulation alone, compared to less than 10% with endovascular therapy).[24] Compared to balloon angioplasty or thrombectomy alone, and especially compared to anticoagulation alone, long-term venous patency rates associated with stenting are higher, with a lower risk of re-thrombosis, more complete resolution of thrombus, and lower risk for PTS, with reduced PTS severity.[5,25]

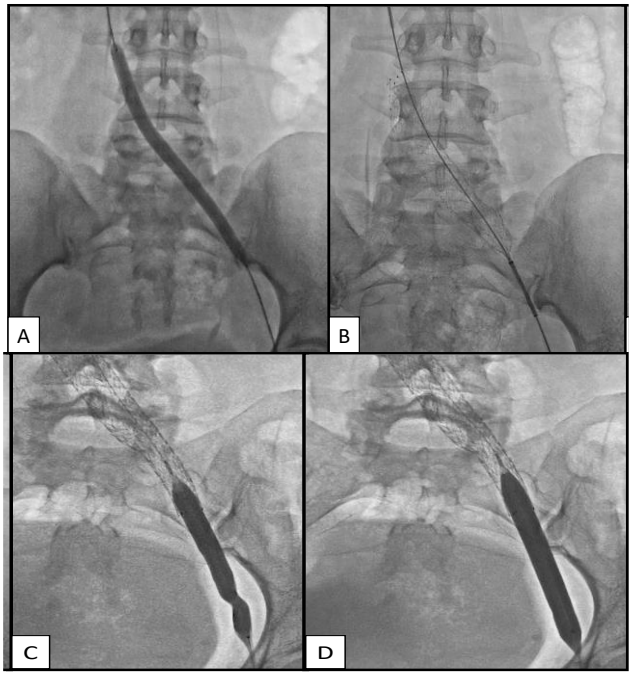

Figure 4 (A-D): Angioplasty and stenting in MTS. A narrow area is observed in the angioplasty process. Stent placement. Final angioplasty in which the area of narrowness is overcome.

The results of angioplasty alone are traditionally below par when compared with stenting, irrespective of the post angioplasty result.[24] At this point, an IVUS can help assess the response to plain balloon angioplasty and confirm the landing zones for the stent if required. Self-expanding, stainless-steel stents (Wallstent, Boston scientific, USA) are preferred, because of their higher radial force, long length and flexibility. As a principle, balloon mounted stents should be avoided as they can be deformed by the arterial pulsation.[10]

Prophylactic IVC filter placement prior to clot removal is not recommended.[26,27] Some authors suggest use of IVC filters in the presence of large volume or free floating IVC thrombus, resistance or contraindication for anticoagulation or history of recurrent pulmonary embolism. If needed, an IVC filter is placed through the contralateral femoral access or jugular venous access. However, the incidence of pulmonary embolism is very low in MTS due to the protective effect of venous stenosis.[28]

DISCUSSION

The estimated prevalence of MTS in the general population is 14%-32%. It is however implicated in only 2%-5% of cases of lower limb DVT.[21] Risk factors for MTS include female sex, multiparty, scoliosis, oral contraceptive use, cumulative radiation, and hypercoagulable disorders.[12,29,30] Development of this syndrome occurs in 3 stages: asymptomatic left CIV compression, formation of a venous spur, and finally left lower extremity DVT. Most patients with MTS never develop DVT.[31]

MTS is an underrecognized etiology contributing to thromboembolic disease in pregnant and postpartum patients. Secondary to physiologic compression by the gravid uterus and exaggerated lordosis, underlying MTS can enhance and hasten thromboembolic events, particularly with increasing gestational age. It is yet unknown as to what degree of compression results in clinically significant disease. Therefore, the diagnosis of MTS as the causative etiology for venous disease in pregnant patients can be challenging, if not impossible, and requires maintenance of high suspicion. Failure to recognize MTS can lead to significant undertreatment, resulting in long-term morbidity.[5] CT, MRI, venography or intravascular ultrasound demonstrate flattening of the iliac vein beneath the artery. Importantly, this anatomy can be found incidentally in asymptomatic patients. It is thought that MTS confers an anatomic predisposition to DVT; vein compression results in endothelial damage and subsequent deposition of elastin and collagen spurs lead to sluggish venous flow. When these at-risk individuals enter a hypercoagulable state such as pregnancy, they often develop DVTs.[4,8]

The diagnosis of MTS is made by imaging. Imaging modalities used to diagnose MTS include Doppler USG, plethysmography, CT venography, MR venography, and conventional venography. Contrast venography is considered the gold standard modality for MTS.[18,31]

In a study conducted in China by Hai-Lei Li et al found a high prevalence in asymptomatic patients of radiological signs of compression in the left iliac vein using tomography where 47% of the sample studied had more than 50% degree of compression in LCIV, thus suggesting that LCIV is a common phenomenon that may not have a clinical correlation, they also found an inverse relationship between the degree of compression of the iliac vein and the body mass index.[20]

The findings of compression on LCIV by tomography are not necessarily related to the clinical presentation of the patients, so it is essential to integrate the clinical history, physical examination with the imaging findings. Many

authors address to this as May-Thurner anatomy and do not associate it with any hemodynamic component. [32] Though many people may harbor this anatomy, only a few people become symptomatic.[10]

May-Thurner anatomy only requires intervention when symptomatic. The mainstay of management of MTS is the removal of the clot with pharmaco-chemical thrombolysis and mechanical thrombectomy to prevent post-thrombotic syndrome.[33] MTS patients presenting with chronic venous insufficiency (recurrent edema, dermal changes, and superficial venous reflux) will also benefit from angioplasty and stenting.[10]

Catheter-directed thrombolysis with anticoagulation in iliofemoral DVT is superior to anticoagulation alone. Anticoagulation on its own is insufficient to manage MTS with DVT.[34] Unfractionated heparin has an increased risk of bleeding due to heparin-induced thrombocytopenia, so it is less preferred to LMWH and fonda-parinux. Factor Xa inhibitors, particularly rivaroxaban, have been shown to be safe in the management of iliofemoral vein thrombosis.[35]

CONCLUSION

Tomographic findings of compression greater than or equal to 50% of LVIC in asymptomatic patients tend to be mostly recognized and therefore the current prevalence is variable. Treatment is currently directed toward symptomatic patients in whom it is necessary to make a timely diagnosis in order to provide them with pharmaco-mechanical thrombolysis with angioplasty and stent placement, which minimizes the late morbidity of post-thrombotic syndrome.

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