Vasculopathies of Peripheral Arterial Disease: Uncommon Etiologies
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Peripheral arterial disease (PAD) or peripheral arterial occlusive disease broadly refers to any arterial occlusive disease other than aortic arch arteries, coronary and cerebral vasculature. However, since most lower extremities are the most commonly involved, the term PAD have been almost synonymously used for Lower extremity arterial disease (LEAD). It is assumed to be limb threatening rather than lifethreatening.

However, often digital gangrene is a sign of systemic diseases especially diabetes, vasculitis, infection or malignancy, a proper evaluation of which may be life saving. The intense physical, functional, psychological and social impact on a patient is massive and often depressing. As pointed in the article, the importance of evaluation of a specific cause for PAD is often overlooked. PAD is an emergency and timely evaluation and management can dramatically recuce the suffering and prevent morbidity.

Smoking, Hypertension, Diabetes, Obesity and hyperlipidemia are commonly associated with digital gangrene. Homocysteinemia and various thrombophilic states and vasculitides have also been associated with digital ischemia. Infections such as Infective endocarditis due to various organisms, Syphilis, Leprosy and rarely fungi have all been reported to cause digital gangrene.

Recent evidences have proven beyond doubt that, premature atherosclerosis is a complication of chronic inflammatory diseases such as Rheumatoid arthritis and Systemic lupus Erythematous. Further, atherosclerosis and atherosclerotic plaques the commonest cause for PAD is considered to be inflammatory and the link between atherosclerosis and other chronic inflammatory diseases has been elucidated. Premature atherosclerosis itself may be a “chronic arterial disease” in itself. It is found that similar to the pathogenesis of autoimmune disorders, in atherosclerosis there is endothelial dysfunction which can initiate a local inflammation and increased presentation of oxidised LDL perpetuating the chronic local inflammation. Thus the gap between atherosclerotic and non-atherosclerotic etiology for PAD has narrowed significantly.

However, vasculitis and thrombophilic states are distinct entities which can cause digital ischemia; the former by inflammatory infiltration into vessels causing stenosis and local occlusion and the latter by hypercoagulability. Vasculitis should be suspected in any patient presenting with digital ischemia who are young, has constitutional features, associated characteristic cutaneous rashes, neuropathies, renal involvement or an acute phase response. Similarly a young patient presenting with digital ischemia with notable lack of constitutional symptoms, family history of thrombosis, history of OCP use, recurrent abortions, idiopathic DVT, venous thrombosis at unusual sites, non infectious leg ulcers etc. should definitely be worked up for an underlying thrombophilic state.

Among the vasculitides causing digital ischemia, primary systemic vasculitis is an important cause. Medium vessel vasculitis such as Polyarteritis nodosa commonly presents with cutaneous necrotizing rashes and digital gangrene in upto 28 to 58%. However in the absence of mesenteric arterial involvement or neuropathies the diagnosis is difficult. Evaluation of HbsAg is often helpful. Thromboangiitis Obliterans (TAO) or Buerger’s disease can cause claudication and digital gangrene with ulcers in more than 70%. It is commonly associated with smoking. Cutaneous manifestations including palpable purpura and digital gangrene has been described in upto 30 -40 % of Wegener’s granulomatosis, Churg Strauss syndrome and 15 – 20 % of Microscopic polyangiitis. Cryoglobulinemic vasculitis is a close differential for ANCA positive vasculitis with digital ischemia. Evaluation of HCV status is mandatory. Digital ischemia has rarely been reported in large vessel vasculitis such as Takayasus’s arteritis and Giant cell arteritis. Behcet’s syndrome and Sarcoidosis also can rarely account for digital gangrene.

Systemic lupus erythematosus is far more common than primary systemic vasculitis and is probably the most common cause for vasculitis associated digital ischemia. Not only vasculitis, but Antiphospholipid antibodies, premature atherosclerosis all can contribute to PAD in SLE. In all cases of vasculitis associated digital ischemia, SLE must be ruled out. In our experience, SLE was the commonest cause of digital ischemia. Long standing seropositive rheumatoid arthritis causes vasculitis and consequent digital ischemia. Considering the frequency of RA, it should account for a significant proportion of vasculitic digital gangrene. In many cases a specific connective tissue disease or vasculitis cannot be identified and are labelled as undifferentiated connective tissue disorder. Scleroderma is commonly associated with Raynaud’s phenomenon and is a well known cause for digital ischemia. Almost equally important cause is antiphospholipid syndrome (APS). Often it presents with digital ischemia either as a single entity or in combination with other autoimmune disorders. The frequency of APS is actually higher than previously thought of following the advent of new ELISA incorporating B2 glycoprotein.

In this issue of the Journal an article by Tulankar et al Peripheral Arterial Disease: Vasculopathies of Uncommon Etiologies have given relevance to a topic that is often neglected in routine practice and the effort deserves appreciation. In younger individuals at least the differentiation between atherosclerotic and nonatherosclerotic groups may not be as significant as previously thought that atherosclerosis itself is turning out to be a chronic inflammatory disorder. It is quite surprising that in the study only 1 case of SLE has been noted. Malignancy is always to be kept in mind when dealing with a case of suspect vasculitis as exemplified by the patient who turned out to have myeloma. In the study the authors have noted upper limb PAD alone or associated with lower limb involvement to be a feature of nonatherosclerotic vasculopathy and isolated lower limb involvement to be a feature of atherosclerotic vasculopathy. This is a very relevant clinical tool to differentiate between the two study groups.

References