Connective Tissue Disorders Associated with Vasculitis and Vaso-Occlusive Disease of the Hand

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KEYWORDS

• Scleroderma • Lupus • Buerger disease • Hand ischemia • Hand vasculitis

KEY POINTS

- Vasospastic symptoms are common with scleroderma, systemic lupus erythematosus, and Buerger disease.
- Recent success with botulinum toxin injections has provided new hope for patients wishing to avoid surgery.
- If a patient fails medical management, distal sympathectomies in conjunction with vascular reconstruction can help in preventing tissue loss and preserving hand function.

INTRODUCTION

Vasculitis is a secondary finding in many autoimmune disease processes, including rheumatoid arthritis, scleroderma, and thyroiditis. Certain forms of vasculitis have a predilection for upper extremity involvement, and over time can lead to debilitating changes to the hand. Many of these conditions are now managed with tumor necrosis factor α regulators, which can prevent the development of occlusive disease, tissue ischemia, and tissue loss. Unfortunately, several disease conditions are still recalcitrant to many medications and can result in ischemic changes within the hand, which may require operative intervention. This article briefly reviews the major connective tissue disorders associated with vasculitis and vaso-occlusive disease of the hand, and their surgical treatment.

VASOSPASTIC AND VASO-OCCLUSIVE DISEASE

The body maintains tight regulatory control over the peripheral vasculature. Autonomic control of vasoconstriction and vasodilatation allows for a balance of adequate nutritional flow and thermoregulatory control, and prevents blood loss in the setting of trauma. Dysfunction of vasoregulatory control can lead to vasospasm, defined as inappropriate tone of an artery or vein that results in impaired vasodilatation with increased physiologic demand, leading to tissue ischemia manifested as cold intolerance or tissue death. If vasospasm occurs in the setting of underlying occlusive disease, distal ulceration or gangrene can occur within the digits. Vasospastic disease can be classified as either primary or secondary; primary vasospasm exists independently without an identifiable cause,

The authors have nothing to disclose.

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Hand Clin 31 (2015) 63–73

http://dx.doi.org/10.1016/j.hcl.2014.09.006

0749-0712/15/$ – see front matter

whereas secondary vasospasm is the result of an existing disease such as systemic sclerosis.

Vaso-occlusive disease differs from vasospastic disease in that the pathogenic mechanism leading to signs and symptoms associated with ischemia are a result of thrombus formation and the remodeling of the intima of small vessels. Immune-mediated vessel remodeling can result from stimulation or destruction of cells within the vessels at multiple levels, such as the endothelial cell, smooth muscle cell, pericyte, or adventitial fibroblast.[1] Autoantibody formation and deposition along with complement activation may lead to inflammatory changes and vessel fibrosis.[2] Inflammatory thrombi may form in the presence of irritants such as tobacco; in such cases pathologic intravascular changes can result in thrombus formation in the absence of complement activation or disruption of the intima media or adventitia, as seen in Buerger disease.[3] Vaso-occlusive disease can also develop in the setting of repetitive trauma, leading to aneurysm formation, thrombus, and thromboemboli, as seen in cases of hypothenar hammer syndrome. Because vaso-occlusive disease of the hand can be present within a broad spectrum of underlying pathophysiologic conditions, a thorough history and physical examination is imperative in guiding treatment.

SCLERODERMA

The main features of this complex disease, also known as systemic sclerosis, include tissue fibrosis, changes in host vasculature, and the formation of autoantibodies directed at many different host proteins. The estimated prevalence of scleroderma is variable and ranges from 50 to 300 persons per 1 million.[4] There are 2 further classifications for scleroderma: limited cutaneous scleroderma and diffuse cutaneous scleroderma.[5] Limited scleroderma is usually confined to the hands, arms, and face, and often presents as isolated Raynaud phenomenon before development of tissue fibrosis. Also associated with limited cutaneous scleroderma is the presence of pulmonary fibrosis and anticentromere antibodies in up to 90% of patients.[1] Diffuse cutaneous scleroderma, a term often used synonymously with CREST syndrome (Calcinosis, Raynaud phenomenon, Esophageal dysmotility, Sclerodactyly, Telangiectasias), is a progressive disorder that affects a significant amount of skin and, commonly, 1 or more internal organs. Patients may also display features of other autoimmune conditions such as systemic lupus erythematosus (SLE; lupus), Sjögren disease, rheumatoid arthritis, or polymyositis.

Scleroderma can have functionally debilitating consequences in the upper extremity. Changes commonly associated with sclerosis of the hand include Raynaud phenomenon, arthropathy, and calcinosis.[6] Triggered by a cold stimulus or other environmental stressor, Raynaud phenomenon results in blanching, cyanosis, and reactive hyperemia. Raynaud phenomenon is due to unopposed vasoconstriction of the small vessels of the hand (**Fig. 1**). Histopathologic changes affecting the vessels are preceded by immune-mediated vascular injury, which affects essentially all vessels, including those in the hands. Damage is initiated by immune-mediated damage to the endothelium with generation of reactive oxygen species. Early stages of scleroderma are marked by perivascular invasion of mononuclear cells, release of inflammatory cytokines, and activation of smooth muscle cells, resulting in intimal hyperplasia and vasospasm ultimately leading to Raynaud phenomenon. Later stages of vascular disease include migration and activation of fibroblasts in the perivascular space leading to excessive collagen deposition, fibrosis, and rarefaction of capillaries.[7–11]

Raynaud phenomenon can precede other signs of systemic sclerosis by several years. Intimal hyperplasia and later fibrosis of the vessels lead to progressively worsened ischemia distal to the level of disease, with resulting ulceration and gangrenous changes. Common locations for ulceration include the fingertip and over the proximal interphalangeal (PIP) and metacarpophalangeal (MP) joints (**Fig. 2**). Ulceration of the fingertip can be related to both ischemia and calcinosis. Wounds over joints, specifically the PIP joint, can result from flexion contracture and sclerosis of the skin (**Figs. 3** and **4**). Nonhealing wounds over joints can lead to osteomyelitis or septic arthritis.

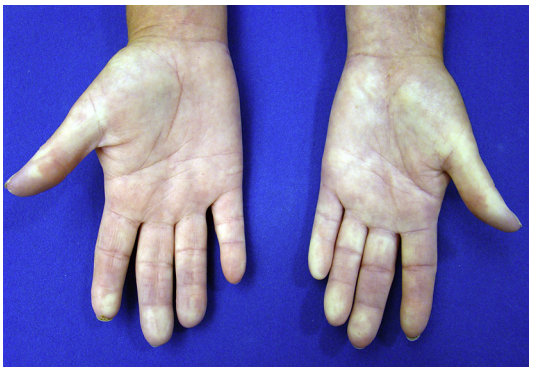

Fig. 1. A 50-year-old woman with limited scleroderma displaying the appearance of Raynaud phenomenon. In addition, one can see evidence of cutaneous involvement throughout the hand.