Digital Gangrene in a Patient with Systemic Lupus Erythematosus and Systemic Sclerosis

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Nearly half of patients with systemic sclerosis (SSc) experience a digital ulcer, and many of these ulcers may progress to digital gangrene. Gangrene can stem from inadequate healing of digital ulcers or complications of comorbidities along with elevated C-reactive protein (CRP) levels.

A 49-year-old woman diagnosed with systemic lupus erythematosus (SLE) and an overlap with SSc since 2006 presented in December 2010 with a 1-day history of acute pain and discoloration of all her digits (Figure 1).

Her connective tissue disease course was characterized by sclerodactyly, gastrointestinal reflux, inflammatory arthritis, serositis, oral ulcers, Raynaud's phenomenon (RP), positive antinuclear antibody with titer 1:640 in a speckled pattern, rheumatoid factor, anti-Sm, and anti-RNP antibodies. She was treated since 2008 with stable doses of methotrexate and leflunomide. She was not known to have any risk factors for atherosclerosis such as diabetes mellitus, hypertension, or dyslipidemia, and she did not smoke.

Examination revealed sclerodactyly, facial telangiectasias, and scleroderma facial changes. There were no fea-

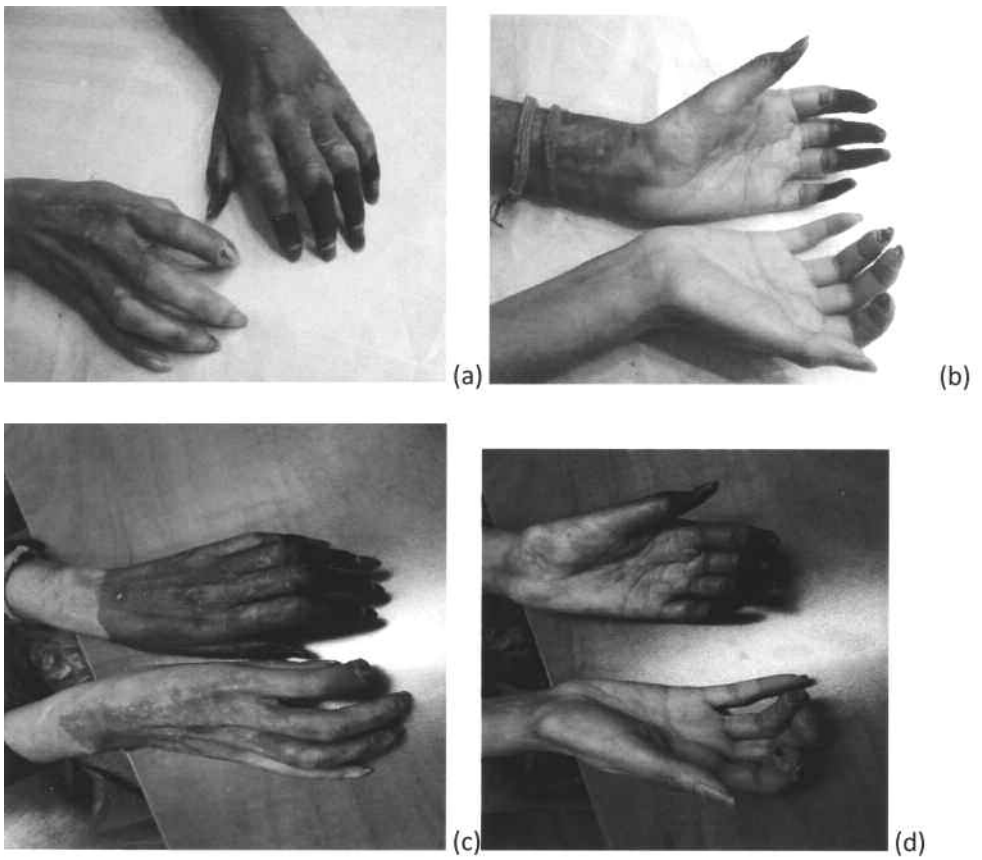

Figure 1. Dorsal and palmar views showing acute gangrene of all 5 digits on the right hand and chronic ulcers affecting the palmar aspect on the left hand (A, B). Panels (C) and (D) show both hands after 6 months of followup. Note the extensive skin desquamation on both hands.

tures of synovitis, malar rash, discoid lesions, oral ulcers, or pleural or pericardial rubs at this presentation. Cardiopulmonary examination was unremarkable. She had no vascular bruits and normal radial and ulnar pulses. There were no signs in the hands or fingers suggestive of vasculitis (Osler nodes, Janeway lesions, or splinter hemorrhages).

She was admitted to hospital with severe digital ischemia of hands and feet that presented abruptly and without warning over several days. There was no antecedent acceleration of her RP. Initial treatment was started with intravenous prostaglandin and oral daily prednisone 40 mg as her physicians investigated the cause of her presentation. She continued leflunomide 20 mg daily along with oral methotrexate 15 mg weekly.

A complete blood count revealed normocytic anemia of 87 gm/l but normal white cell and platelet count. Liver function tests, serum creatinine, and urinalysis were unremarkable. She had an erythrocyte sedimentation rate of 75 mm/h and negative antiphospholipid antibodies and negative screening for hypercoagulation as well as cryoglobulin; serum complement C3 and C4 levels were within normal limits. An angiogram of the upper extremities did not reveal a structural etiology for her digital ischemia. An echocardiogram indicated no source for embolization. Despite therapeutic efforts, she progressed to dry gangrene in all digits in her right hand, and chronic digital volar ulcers at her fingertips in the left hand.

She had an improvement in her pain and transitioned to oral vasodilator therapy with irbesartan and a nitroglycerin patch at the time of her discharge. Over the next 6 months, prednisone was tapered to 10 mg. Her pain continued to diminish, and there were no new digital events as her gangrene progressed to clear demarcation.

Overlap of SSc and SLE is well described in the literature[1]. Sometimes this occurs within the context of mixed connective tissue disease (MCTD), as may be the case here. RP is a manifestation of all these conditions, occurring in 40% of patients with SLE, 96% of patients with SSc[2], and 99% of patients with MCTD[3]. The RNP and Sm antigens are both contained within the spliceosome complex, and sera reactive with 1 antigen frequently have additional serologic reactivity with the other. Anti-RNP has been observed in patients with SLE because of the cross-reactivity between the 2 conditions; the presence of anti-Sm has been excluded in the Sharp criteria for MCTD. This patient's disease is best characterized as an overlap syndrome. Our rationale for labeling her condition as SSc/SLE overlap is explained by the presence of oral ulcers and the anti-Sm positivity[3,4,5,6,7].

Nearly half of patients with SSc experience a digital ulcer during their disease course and 30% of these ulcers may progress to some degree of digital gangrene. The incidence of digital gangrene increases with greater duration of digital ulcers, suggesting that inadequate healing heralds further adverse digital sequelae and warrants aggressive treatment and monitoring[8]. On the other hand, digital gangrene can also be a complication of longstanding SLE with RP and elevated levels of CRP[9].

Interestingly, this case presented in a very dramatic and unexpected fashion, without concurrent acceleration of RP. Such digital gangrene has been reported in SSc as well as in SLE in conjunction with vasculitis or antiphospholipid antibody syndrome. Digital ulcers are frequent and often appear at the initial presentation in patients with MCTD. Digital gangrene appears to be a rare occurrence in MCTD.

Our case represents a digital sequela from SSc-related endothelial dysfunction, as there were no signs of active SLE or vasculitis. Angiographic and pathologic studies of SSc-associated RP further indicate that the vascular disease is characterized by progressive obliteration of affected arteries with defective angiogenesis and vasculogenesis, resulting in inadequate collateral circulation[10]. Endothelial dysfunction, vascular smooth muscle cell activation, and intimal hyperplasia are hallmark features of SSc vasculopathy[10].

It is critical for clinicians to have heightened awareness of the distinction between digital necrosis stemming from SLE in contrast to that seen with SSc, because management differs. SLE-related digital ischemia often necessitates the prompt initiation of corticosteroids, whereas SSc-related digital ischemia requires aggressive vasodilator therapy[9]. There may be a role for anticoagulation in some cases. Acute gangrene that fails to respond to potent vasodilators has a wide differential diagnosis of potential causes. Autoimmune disease may underlie many of these cases through a variety of mechanisms. Correct diagnosis of the autoimmune condition, along with accurate identification of the scleroderma spectrum of disorder (including MCTD) is helpful in guiding the management of digital ischemia.

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Omair MA, Bookman A, Mittoo S. Digital gangrene in a patient with systemic lupus erythematosus and systemic sclerosis. J Rheumatol 2012;39:1895-7. Degrees for the first author should be given as Mohammed A. Omair, MBBS, SF Rheum. We regret the error.

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Incidence of Spondyloarthropathy in Patients with Crohn's Disease: A Population-based Study

R. Shivashankar, E.V. Loftus Jr, W.J. Tremaine, T. Bongartz, W.S. Harmsen, A.R. Zinsmeister, E.L. Matteson. Incidence of spondyloarthropathy in patients with Crohn's disease: A population-based study. J Rheumatol 2012;39:2148-52. Table 2 should appear as follows. We regret the error.

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Table 2. Clinical characteristics of spondyloarthritis (SpA) in 311 patients with Crohn's disease (CD) from a population-based cohort of Olmsted County residents.

SpA Feature	Features Present Prior to CD, n	Features Appearing After CD, n
Psoriasis	5	9
Urethritis/cervicitis	1	0
Buttock pain	1	6
Plantar fasciitis	4	12
Achilles tendonitis	4	4
Sacroiliitis	0	5
Uveitis	2	10
Oligoarthritis	3	9
Polyarthritis	3	7
Inflammatory back pain (see Discussion)	0	2