A Rare Case of Systemic Sclerosis with Bilateral Digital Ischemic Vasculopathy Hyperpigmentation and Internal Organ Involvement

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Abstract

Background: A connective tissue disorder, systemic sclerosis, is characterized by fibrosis, auto antibody production, fibro proliferative stenosis, thickened and fibrotic response. 250 cases in a million is the estimated prevalence of the disease and it is more common in women than in men.

It is categorized into two subgroups which are described as systemic and localized. Systemic sclerosis differs from localized type because it is accompanied by Raynaud’s phenomenon, digital ulcers and internal organ involvement. Normal collagen type I and III are thought to be deposited excessively at various tissues by immunologically over-activated fibroblasts. Clinical diagnosis is mainly based on the presence of skin thickening and variable involvement of internal organs.

Rarely found in collagen diseases, digital gangrene, including systemic sclerosis, however it is often misdiagnosed as aggravated digital ulcers related to Raynaud’s phenomenon, especially in case of scleroderma-spectrum disorder. Dysfunction of vascular beds throughout the body cause many clinical complications of systemic sclerosis. Cutaneous and mucosal telangiectasias, digital ulcers and tissue ischemia are a result of the involvement of microvasculature. In the case of involvement of medium sized blood vessels, manifestation includes digital loss, renal crisis, gangrene and pulmonary arterial hypertension. Occlusive vasculopathy, while a well-recognized feature of the disease, less is known about the occurrence and consequences of frank vascular inflammation.

Our aim is to report a classical case of diffuse type of Systemic Sclerosis so that early evaluation and attention to the presence of digital ulcers with internal organ involvement could improve our ability to diagnose SS patients early.

Case Report

Our patient was a, 35-year-old, Asian woman, who presented with a 4-year history of progressively evolving skin pigmentation over her entire body, which had become accentuated over her trunk and extremities. Hyperpigmentation was associated with intense itching throughout the body. Another presenting feature was ulcers on finger tips and over the extensor aspects of her hands. Few of the finger tips were reabsorbed and the whole process evolved over the past 4 years. Our patient reported the presence of Raynaud’s phenomenon during winter season that had started occurring about 4 years prior to the skin changes of the hands. The problem started with Raynaud’s phenomenon and bilateral hand swelling long before ulceration developed. She also complained of appetite loss resulting in an unintentional weight loss of 10 kg in 1.5 years. Weight loss was also associated with dry cough and gradual development of shortness of breath. There was no family history of a similar skin condition or history of chemical exposure in this case.

A physical examination revealed a generalized hyperpigmentation and skin thickening over the trunk and extremities. Additionally, there was sclerosis of her distal fingers with pitted scars and digital reabsorption. Telangiectasia and calcinosis were absent in this patient (Figure 1).

Laboratory investigations revealed normal white blood cell count, urea, creatinine, electrolytes and blood sugar. Her C reactive protein was positive, ESR was normal. Patient was anti HCV positive and her liver function tests were slightly deranged. Anti topoisomerase I Antibodies and anti CENP antibodies were positive. To find out the
systemic involvement, we performed barium swallow to investigate the lower esophagus sphincter functioning, and it was unremarkable. High resolution CT chest was also performed which revealed patch ground glass haze in bilateral lower lobes along with multiple fibrotic bands in apico-posterior segment of left upper lobes with calcified granuloma suggesting chronic inflammation with pulmonary fibrosis (Figure 2). Echocardiography was also done which showed mild mitral regurgitation with good systolic function and Grade I dystolic dysfunction.

Figure 1: (a) Fingertip digital ulcer, multiple extensor (dorsal) digital ulcers, critical digital ischemia. (b) Clinical presentation. Widespread hyperpigmentation over the trunk and lower extremities with discrete erythematous indurated plaques over lower abdomen.

Figure 2: HRCT Chest revealed bilateral ground glass haze in bilateral lobes with fibrotic band with calcified granuloma in left apico posterior lobe suggesting fibrosis and chronic inflammation.

CT angiography bilateral upper limb revealed thinning of whole arterial trunk walls on left side with poor distal run off. Total obliteration of radial artery from bifurcation level showed no collateral formation (Figure 3). On right side, there was hypertrophy of whole arterial trunk due to increased flow and collateral formation, may be due to compensatory mechanism. A dedicated multidisciplinary approach was taken to her treatment; digital ulcers were infected and very painful, so antibiotic and strong analgesics were prescribed and patient was sent to dermatology department for proper wound care. Further, the patient was referred to pulmonologist for the treatment of pulmonary fibrosis and to medical department for the treatment of hepatitis C.

Discussion

Systemic sclerosis is an autoimmune connective tissue disease wherein antibodies target veins and connective tissue bringing about fibrosis and vasculopathy including different organ systems. Characterization into diffuse cutaneous types relies upon the degree of skin thickening, with the former affecting areas close to the elbows or knees, and the other being constrained to the face and distal extremities [6]. The illness starts with Raynaud’s Phenomenon. It is notable that behind Raynaud’s Phenomenon, there often hides Systemic Sclerosis and along these lines, a careful internal organ investigation is required. Moreover advanced ulcers are already present in those patients who as of now show asymptomatic or subclinical oesophageal or lung inclusion. Reabsorption of the terminal phalanges, short and hook like fingers on account of acrolysis ulcers on fingertips are common in patients with systemic sclerosis [7].

Connective tissue disorder characterizations were revisited in 2003, the mid 1980 American College of Rheumatology (ACR) criteria for System Sclerosis does not include sensitivity for early systemic sclerosis and limited information about cutaneous type. New classification criterion for System Sclerosis was developed by the joint efforts of ACR and European League Against Rheumatism (EULAR). It was concluded that skin thickening of the fingers extending proximal to the metacarpophalangeal joints is adequate for the patient to be diagnosed as System Sclerosis. If that is absent, seven additional features were applied; each with varying degree of importance. Telangiectasia, fingertip lesions, unusual nailfold capillaries, thickening of the fingers, interstitial lung disease or pulmonary arteria hypertension, Raynaud’s phenomenon and systemic sclerosis related antibodies. Every single chosen case was grouped on the basis of expert opinions [8].

Various autoantibodies, for example, anti-centromere, anti-topoisomerase I, anti-RNA polymerase III and anti-U3 (fibrillarin) antibodies were demonstrated to be of extraordinary symptomatic and prognostic factors in patients with systemic sclerosis. This investigation underpins the connection between autoantibody titers, systemic involvement and microvascular changes in systemic sclerosis patients [9].

Literature describes various cutaneous pigmentary alterations in System Sclerosis including diffuse, generalized hyperpigmentation with accentuation in sun-exposed areas, combined hyper and hypopigmentation in areas of sclerosis and a vitiligo-like depigmentation with perifollicular hyperpigmentation [3]. In our described case generalized hyperpigmentation was evident more pronounced in extremities and truncal area.

Skin thickening is one of the early organ involvements of systemic sclerosis and greatly affects life quality and daily living in patients with System Sclerosis [10]. It is commonly acknowledged that skin thickness
will in general increment in early diffuse of System Sclerosis and become reduced in late diffuse System Sclerosis, in spite of the fact that the time of peak involvement is mostly between 12–18 months after the beginning of skin thickening. “Early” diffuse System Sclerosis is regularly characterized as the time of rapidly increasing induration (“thickening”) of the skin. The modified Rodnan skin score (mRSS) is a score of skin thickness and is utilized as an essential or secondary result measure in clinical trials of systemic sclerosis [11].

Occlusive vasculopathy is a well-recognized feature of System Sclerosis. In the current pathogenic model of System Sclerosis, a vascular injury without any known cause leads to endothelial damage apoptosis and initiates a series of changes which leads to System Sclerosis vasculopathy. In vascular scleroderma, vascular changes occur up to capillary level. The change most studied in literature is the nailbed level. Changes in the nail fold capillaries are one of the earliest sign of System Sclerosis [5]. In System Sclerosis, microvascular involvement also occur but limited to digital artery and possibly induced by cold and vascular contraction due to Raynaud’s phenomenon. In recent studies, it was found that middle sized vessels distal from elbow or knee can also be involved in System Sclerosis and other spectrum of the disorder. New less invasive vascular imaging tools such as MR angiography and CT angiography have recently been introduced and used as digital screening tools for use in clinical trials of systemic sclerosis. CTA upper limb was done which revealed thinning and diminution of flow in whole left upper arm arterial trunk, however on right side vessels showed unique feature demonstrated as hypertrophy and collateral formation of whole arterial trunk which goes in line with peripheral arterial disease or may be due to compensatory mechanism.

Conclusion

Systemic Sclerosis is a systemic disease which causes significant radiographic and clinical changes in skin, blood vessels and internal body structures. Rheumatologists must be aware of these changes since digital ulcers and skin thickening are especially important for the early and accurate diagnosis and management. Multidisciplinary approach is of utmost importance since this is a multi-dimensional disease affecting all organs of the body.

References