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CASE BASED REVIEW

# Rituximab for refractory digital infarcts and ulcers in systemic sclerosis

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**Abstract** Systemic sclerosis is an uncommon connective tissue disease characterised by excessive deposition of collagen and vasculopathy which affects the skin and multiple internal organs. It is associated with autoimmunity, inflammation, vasculopathy and fibrosis. Managing Raynaud's phenonemon, digital infarcts and ulcers in systemic sclerosis patients is often a challenge particularly among rheumatologists. We report a case of systemic sclerosis patient with refractory digital infarcts and ulcers responded successfully with rituximab.

**Keywords** Digital ulcers · Infarcts · Rituximab · Systemic sclerosis

Dear Editor,

Systemic sclerosis (SSc)-related vasculopathy is manifested by Raynaud's phenomenon (RP) and digital ulcers (DUs) resulting functional impairment with a significant impact on the patient's quality of life physically and psychologically [1]. We believe this case is an interesting case of SSc patient with refractory digital infarcts and ulcers responded successfully to rituximab.

In May 2007, a 32-year-old nonsmoker gentleman presented with 4-year history of SSc to our unit. He had RP, skin sclerosis with blackish discoloration at left index and middle fingertips associated with painful paraesthesia and dysphagia. He denied any history of fever and trauma. Despite the medications given (nifedipine, prednisolone 5 mg bid, aspirin, penicillamine and cilostazol) and careful protection from cold, joint deformity and ischemic necrosis were noted over the distal interphalangeal and proximal interphalangeal joint of both hands particularly left index and middle fingers.

Investigations showed elevation of C-reactive protein (CRP) (3.4 mg/dL), ESR (24 mm/h) and autoantibody screening tests were positive for anti-nuclear antibody (ANA 1:160), anti-Scl 70 antibody (28.30 U/ml and negative serology for antiphospholipid syndrome. Nailfold capillary microscopy revealed predominant giant capillaries with few ramified capillaries and avascular area compatible with active scleroderma pattern. Video pharyngoesophagography demonstrated oropharyngeal dysphagia, and echocardiography was normal. Chest X-ray showed bilateral increased lung marking without cardiomegaly, and lung function test observed impaired diffusion lung capacity (14.82 ml/min/mmHg, 48.3 % predicted). SSc with pulmonary, oesophageal and digital gangrene was impressed. Hence, pulse cyclophosphamide 600 mg was administered intravenously on top of his previous medication.

In 2011, although his respiratory and oesophageal symptoms improved, his RP deteriorated with recurrent, progressive worsening infected digital gangrene, digital soft tissue loss with bone resorption at both hands despite multiple cycles of pulse cyclophosphamide and optimal treatment for ischemic DUs. In Feb 2012, digital gangrene with pus formation noted at his fingers especially the right middle, ring and little fingers with elevated CRP level (1.2 mg/dL) (Fig. 1a). Subsequently, first cycle of rituximab (500 mg on days 1 and 15) was commenced. By October 2012, he received second cycle of rituximab and CRP level was 0.9 mg/dL. Six months later, the digital wounds improved and CRP level reduced to 0.5 mg/dL. Third cycle of rituximab was administered in April 2013. In early December 2013, Fig. 1b shows completely healed digital infarcts and ulcer with CRP level 0.2 mg/dL.

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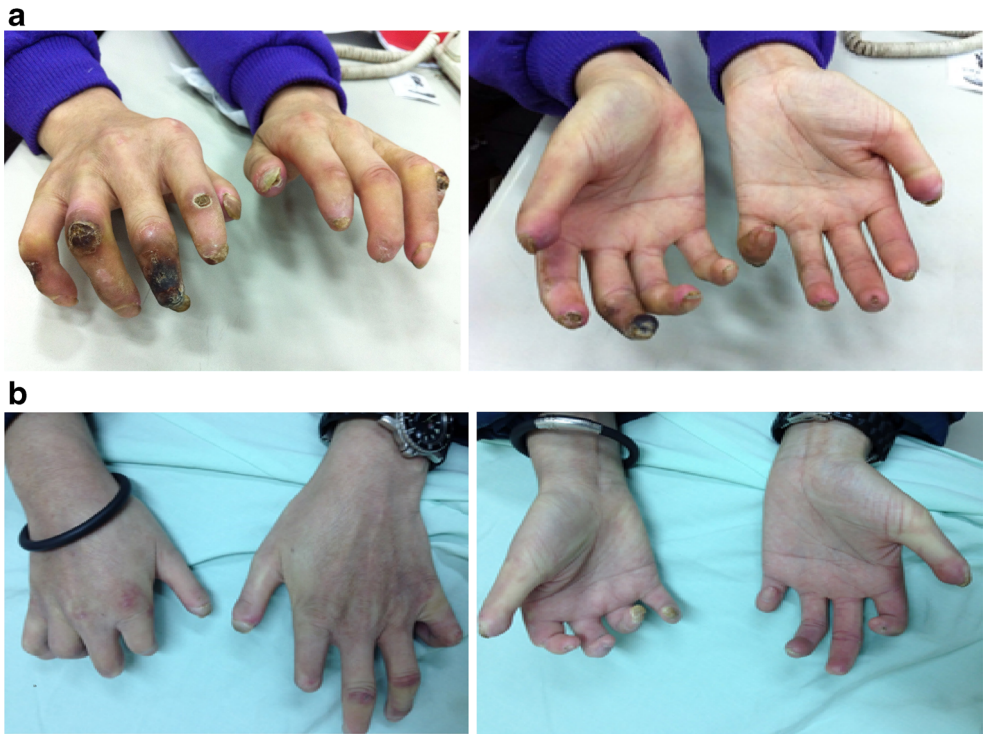


**Fig. 1** **a** Images showing digital gangrene with pus formation noted at patient's fingers especially the right middle, ring and little fingers. **b** Images showing completely healed digital infarcts and ulcer with CRP level 0.2 mg/dL

SSc has a heterogeneous clinical course and the pathogenesis is complex. Patients with SSc show evidence of autoimmunity and inflammation, vasculopathy and fibrosis [2]. RP occurs in almost all of patients with SSc, and DUs are the most serious complications of RP [3]. DUs can appear on the tips of the fingers or over the bony prominences frequently related to repetitive trauma of contractured joints. Usually, DUs heal slowly owing to the avascular, atrophic nature of the tissue overlying the ulcer sites, and 14–29 % evolves to infection, gangrene or osteomyelitis and even autoamputation [4]. Besides nonpharmacologic treatment, pharmacological treatment for SSc-related DUs includes dihydropyridine-type calcium antagonists, prostacyclin analogues and endothelin receptor blockers, but often found limited effectiveness.

Fujimoto M et al. [5] and Kraaij MD et al. [6] documented that the presence of B cells hyperactivity in SSc. Furthermore, Smith VP et al. [7] reported the efficacy of B cell depletion therapy by rituximab, a chimeric monoclonal antibody, in reducing total skin score among SSc patients. With regard to our case, despite commencing cyclophosphamide for the pulmonary symptoms and extensive poor healing DUs, recurrent refractory digital infarcts and ulcers persisted. Nevertheless, there was markedly improvement in the digital infarcts and ulcers as well as CRP levels observed in our patient after rituximab therapy. Hence, we believe rituximab may be a therapeutic option in SSc patients with refractory digital infarcts and ulcers.

**Disclosures** None

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