Received: 25 May 2022 | Revised: 20 June 2022 | Accepted: 6 July 2022

DOI: 10.1002/cia2.12270

Journal of Cutaneous Immunology and Allergy

WILEY

CORRESPONDENCE

# Development of severe fingertip ulcers, pulmonary hypertension, and scleroderma renal crisis in a patient with systemic sclerosis and anti-PL12 antibodies

A 50-year-old Japanese woman received prednisolone treatment (2.5 mg/2 days) for systemic sclerosis (SSc) and interstitial pneumonia for approximately 15 years. She suddenly developed severe pain, cold sensation, and digital cyanosis and was treated with intravenous alprostadil (10 μg/day). Two days later, she presented with acute exacerbations of hepatic (aspartate aminotransferase, 4400 IU/L; alanine aminotransferase, 1997 IU/L), renal (creatinine, 2.14 mg/dl), and respiratory (blood oxygen saturation, 77% on room air) functions. Upon admission to the hospital, she presented with increased blood pressure (160/80 mmHg), and within a week developed severe gangrene in the second-to-fifth fingertips of the right hand and the second and fourth fingertips of the left hand (Figure 1A). A modified Rodnan skin score of 2, Raynaud's phenomenon, and nailfold bleeding were observed. Scleroderma was noted only in the extremities and was confirmed by histopathological examination of the forearm lesions. The patient tested positive for anti-nuclear (40×, cytoplasmic), aminoacyl-tRNA synthetase (ARS, 170 index), and PL-12 antibodies,[1] but tested negative for anti-topoisomerase 1, centromere, RNA polymerase III, ribonucleoprotein, cardiolipin, anti-cardiolipin β2-glycoprotein I complex, lupus anticoagulant, and myeloperoxidase antineutrophil cytoplasmic antibodies. The findings from lung perfusion scintigraphy were normal. Computed tomography showed mild interstitial pneumonia. The trans-tricuspid pressure gradient (assessed by echocardiography), mean pulmonary arterial pressure, and levels of N-terminal prohormone of brain natriuretic peptide all showed marked elevation to 65 mmHg (normal, <35 mmHg), 50 mmHg (<25 mmHg), and 62,991 pg/ml, respectively. The patient was diagnosed with limited cutaneous-type SSc with anti-PL12 antibodies, acute heart failure, and congestive liver failure, owing to scleroderma renal crisis (SRC) and pulmonary arterial hypertension (PAH). The cardiac, renal, and hepatic functions of the patient improved after 5 days of treatment with continuous hemodiafiltration and a combination of an angiotensin-converting enzyme inhibitor and a Ca-channel antagonist. Endothelin receptor antagonist, phosphodiesterase-type 5 inhibitor, and selective prostacyclin receptor agonist were systemically administered (Figure 1B), and absolute ethanol and a sucrose povidone-iodine ointment were topically applied on the gangrenous fingertips. Seven months later, re-epithelialization in the fingertips was observed (Figure 1C).

Anti-synthetase syndrome is often associated with the development of specific clinical symptoms, such as Raynaud's phenomenon, mechanic's hands, polyarthritis, interstitial pneumonia, and myositis.[2] Anti-ARS antibodies, including anti-PL12 antibodies, are typically specific to polymyositis/dermatomyositis.

The frequency of SSc in patients positive for anti-ARS antibodies is relatively low (3.6%).[2] A few cases of SSc with anti-PL12 antibodies have been reported. However, there are no reported cases of this condition with digital gangrene, PAH, and SRC. Generally, SRC or PAH develops in SSc patients with anti-RNA polymerase III or anti-centromere antibodies, respectively.[3,4] Therapeutic agents for PAH are often effective for the concurrent treatment of digital ulcers and gangrene in patients with SSc.[5] In this case, we prevented the progression of gangrene and achieved cure through a combination treatment with multiple anti-PAH agents. This approach may be useful for the treatment of patients with SSc who develop refractory digital ulcers and/or gangrene.

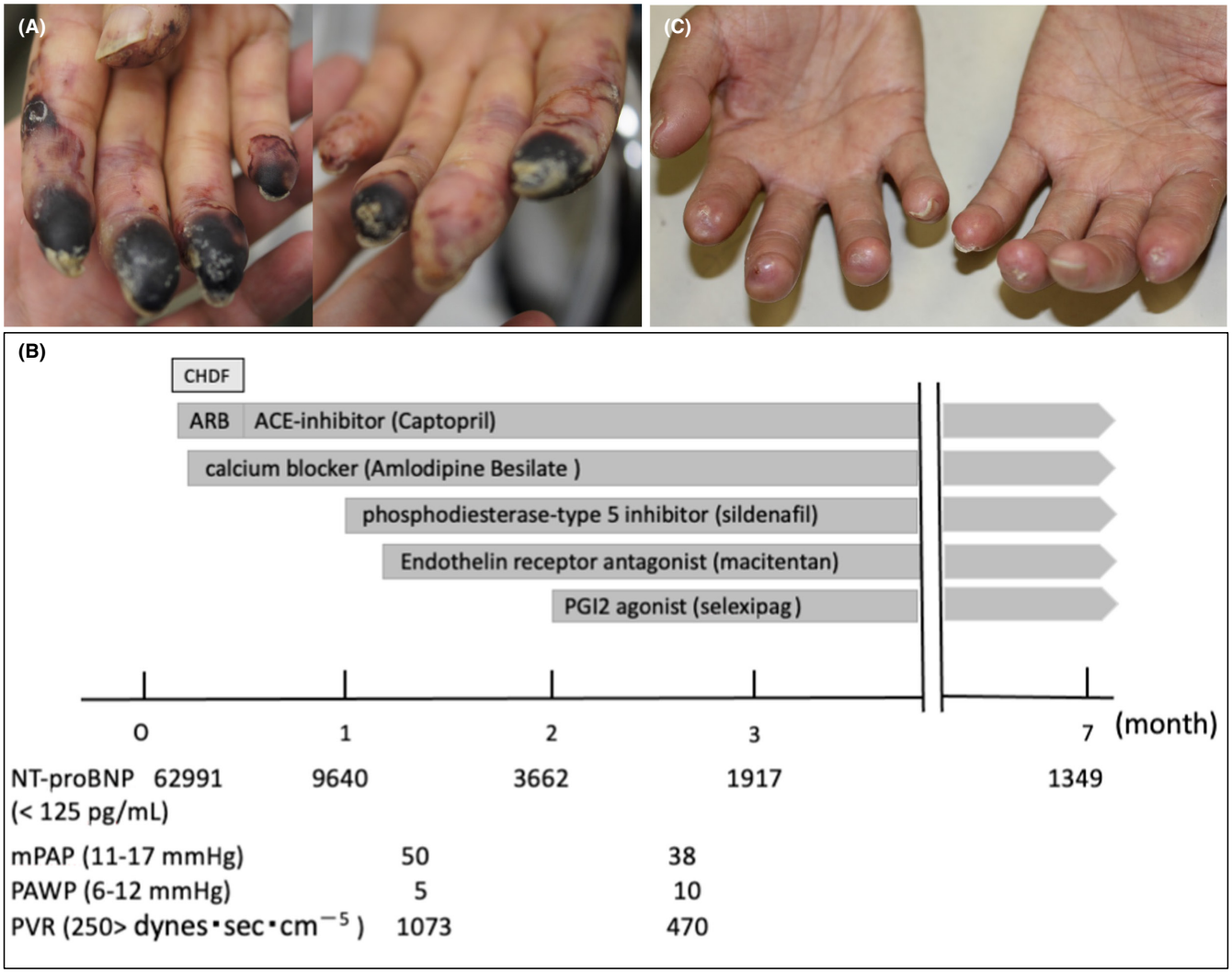


FIGURE 1 (A) Clinical findings at first visit. Severe gangrene was observed on the fingertips of both hands. (B) Time course of treatment and laboratory results. The parentheses indicate normal values. ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CHDF, continuous hemodiafiltration; mPAP, mean pulmonary arterial pressure; NT-proBNP, N-terminal pro-brain natriuretic peptide; PAWP, pulmonary artery wedge pressure; PVR, pulmonary vascular resistance. (C) Seven months after treatment, the gangrene had disappeared, and re-epithelialization was observed in all fingertips

## DECLARATION SECTION

Approval of the research protocol: N/A.

Informed consent: Acquired.

Registry and the Registration No. of the study/trial: N/A.

Animal Studies: N/A.

## KEYWORDS

anti-PL12 antibodies, systemic sclerosis

## CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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