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CASE REPORT
ΕΝΔΙΑΦΕΡΟΥΣΑ ΠΕΡΙΠΤΩΣΗ

Digital ischemic in patient with systemic sclerosis

A 49-year-old man was admitted to the hospital due to pain in the fingers for one year before admission. He also had shortness of breath, precipitating with activity and getting better when taking a rest. Patient fulfilled the American College of Rheumatology classification criteria for systemic sclerosis. He also had systemic involvement including interstitial lung disease and Raynaud's phenomenon with digital ischemia. We had to uplift the challenging issue in management of digital ischemia. We provided the initial treatment using standard treatment and heparinization. Necrotic lesion was improved but he was readmitted for worsening ischemic stroke after discharged with warfarin, and thereafter, amputation was performed. In conclusion, we reveal that the diagnosis of systemic sclerosis and identification of its complication should involve a comprehensive investigation, and the management of digital ischemia should prioritize non-invasive method, as currently no established recommendation regarding management of digital ulcers in Raynaud's.

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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2023, 40(6):851–855

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Ισχαιμία δακτύλων σε ασθενή με σκληρόδερμα

Περίληψη στο τέλος του άρθρου

Key words

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Systemic sclerosis remains a serious health issue. The global prevalence of systemic sclerosis has been reported to range between 15.1 and 20.5 cases per 100,000 populatio.[1] Of those, the survival rate ranges between 61% and 86%.[2] Systemic sclerosis has a wide variety of clinical presentation, one of the factors contributing to the challenge of diagnosis issue of this disease and requiring multidisciplinary management. The clinical manifestations of systemic sclerosis may involve several organs, including skin, gastrointestinal tract, nervous system, musculoskeletal system, heart, renal, and vascular system.[3] Of them, vascular manifestation, in the form of Raynaud's phenomenon with digital ischemia, is a serious issue due to this affected population had high risk of amputation.[4]

Digital ischemia is one of the critical complications in patients with systemic sclerosis. The prevalence of digital ischemia among patients with systemic sclerosis is predicted at approximately 30%. Moreover, out of them, 9.2–20.4% patients were treated with amputation.[4] This ironic circumstance had made patients have significant disability and low quality of life.[5] The management of digital ischemia in patients with systemic sclerosis remained debatable. Studies had reported that the management of digital ischemia was divided into the non-invasive and the invasive approach. In non-invasive approach, the treatment modality using pharmacological approach such as calcium channel blockers, phosphodiesterase type 5 inhibitors, angiotensin II receptor blockers, alpha blockers, selective serotonin reuptake inhibitor, and prostacyclin analogues has been widely applied.[6,7] However, in the case of pharmacological failure and if digital necrosis has occurred, digital amputation might be considered as the appropriate management method.[8] In the present study, we reported a case of systemic sclerosis with digital ischemia and provided the management with heparinization and amputation. Our case report conformed with the checklist of CARE (CAse REporting) statement.[9,10]

CASE PRESENTATION

A 49-year-old man was admitted to our hospital due to pain in the finger for five days before admission. The symptom worsened and his fingers had discoloration in the last two days before admis-

sion (fig. 1A). In the past, he also had complained about pain in the fingers for one year. Initially, he was treated with standard care and heparinization followed by the administration of warfarin, and improvement in the fingers was achieved (fig. 1B). Two weeks after discharge, he was readmitted for worsening of digital ischemia (fig. 2A), and amputation was performed (fig. 2B). In addition, he also had shortness of breath for one year before admission. The symptom worsened when he was active and got better when he took a rest. In physical examination, we found that he had cardiomegaly and pain with necrotic fingers (finger II, III, and IV of the right hand), as well as Raynaud's phenomenon. Oxygen saturation was not detected on the affected fingers.

In laboratory examination, we found that he had positive antinuclear antibodies (ANA) test and anti-double stranded deoxyribonucleic acid (anti-dsDNA), immunoglobulin G (IgG) and immunoglobulin M (IgM). Moreover, we also found elevated levels of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Further examination of ANA profile revealed that he had positive anti-scleroderma antibody (Scl-70). In chest high-resolution computed tomography (HRCT) it was found that he had cylindrical bronchial dilatation with tram-track sign and signet ring sign. Interlobular septa thickening with pulmonary fibrosis and ground-glass opacification were also found. Body plethysmography revealed that forced vital capacity was 3,660 and 1,790 for prediction and actual, respectively. Forced expiratory volume in the first second for prediction and actual was 2,990 and 1,230, respectively. Total lung capacity was 6,430 and 2,650 for prediction and actual,

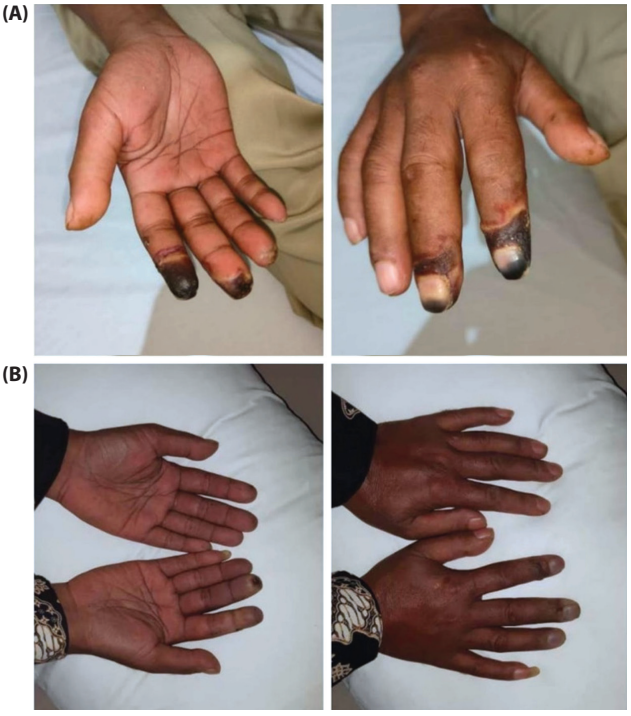

Figure 1. Clinical feature of digital ischemia in our patient on the first admission. **(A)** Before heparinization. **(B)** After heparinization.

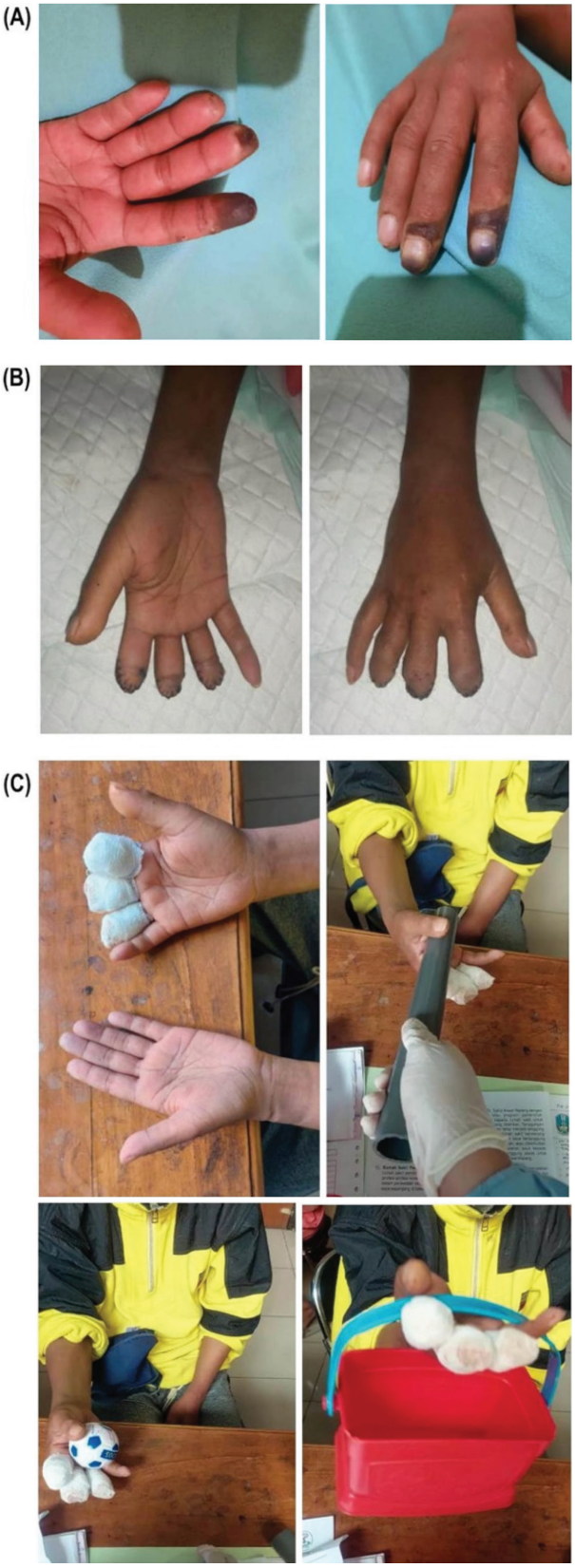

Figure 2. Clinical feature of digital ischemia in our patient on the second admission. **(A)** Before amputation. **(B)** After amputation. **(C)** Isometric strengthening exercise.

respectively. Diffusing capacity of the lungs for carbon monoxide was 9,520 and 470 for prediction and actual, respectively.

Patient was diagnosed having systemic sclerosis with interstitial lung disease and Raynaud's phenomenon with ischemic fingers. In the initial management, patient was treated with mycophenolic acid, beraprost, aspirin, sildenafil, bisoprolol, valsartan, and nifedipine. Lung function showed improvement after one week treatment. For the management of ischemic fingers, we administered additional treatment using heparin conformed to the protocols of arterial disease, followed with warfarin. Two days after heparin administration, there was an improvement in finger ulcers (fig. 1B). However, two weeks after heparin administration, the ischemic fingers had worsened (fig. 2A). Thereafter, patient was readmitted and amputation of the fingers was performed (fig. 2B). After digital amputation, isometric strengthening exercise was also performed to improve the quality of life (fig. 2C).

DISCUSSION

The diagnosis of systemic sclerosis is challenging and may require careful examination. In our case, patient had skin thickening in fingers, fingertip lesions, Raynaud phenomenon, and abnormal nail fold capillaries. Following the American College of Rheumatology classification criteria for systemic sclerosis,[11] our patient had score 20, suggesting that he had fulfilled the systemic sclerosis classification. Moreover, ANA profile indicated that he had positive Scl-70. As widely known, Scl-70, having the target to the catalytic region of DNA helicase topoisomerase I, is a specific biomarker for systemic sclerosis and serves as a useful adjunct in confirming a clinical diagnosis of systemic sclerosis.[12] To identify organ involvement in systemic sclerosis, we performed HRCT, considering that he had chronic shortness of breath. In HRCT, cylindrical bronchial dilatation with tram-track sign and signet ring sign, as well as interlobular septa thickening with pulmonary fibrosis and ground-glass opacification were found, consistent with interstitial lung disease.[13,14] Additionally, the findings of body plethysmography were also consistent with interstitial lung disease.[15] The treatment using immunosuppressive agent (mycophenolic acid) improved the symptoms. Previous study also reported that mycophenolic acid was associated with the beneficial impact for the management of patients with interstitial lung disease.[16] On the other hand, our patient also had severe thickness of right and left fingers. Corresponding to modified Rodnan score (score 5),[17] our patient had skin involvement with digital ischemia, a primary concern of our case report.

The management of digital ischemia in patients with systemic sclerosis remains challenging. To date, there is no specific recommendation for the management of digital ischemia in patients with systemic sclerosis. Previous study revealed that digital necrosis needing amputation was often preceded by ischemia, and the prevalence was found approximately one third of the affected population.[8] On the other hand, several previous studies had reported the various management of digital ischemia in patients with systemic sclerosis (tab. 1).[18–24] Treatment using standard of care and the additional bosentan provided the improvement of the digital ischemia.[19–22,24] Moreover, study also reported that adjuvant heparinization was also found to provide beneficial outcome for treating digital ischemia patients.[18] In our case, beside administering calcium channel blockers, phosphodiesterase type 5 inhibitors, angiotensin II receptor blockers, alpha blockers, and prostacyclin analogues; we also gave heparinization. Those drugs are available at our National Drugs Catalog.[9] While no randomized controlled trial had elucidated the efficacy of heparin in digital ischemia related to systemic sclerosis, theoretically, this method might be appropriate in cases where symptoms are suggestive of a new arterial occlusion thought to be due to an acute thrombosis or embolization.[25] However, further investigation on this context should be conducted. On the other hand,

Table 1. Previous case reports and case series on the management of digital ischemia in patients with systemic sclerosis.

Author and year	Study design	Case	Complication	Treatment	Outcome
Zaima et al, 2011[19]	Case report	Systemic sclerosis	Digital ischemia	SOC + bosentan	Died
Soares et al, 2007[21]	Case report	Systemic sclerosis	Digital ischemia	SOC + bosentan	All signs of ischemia disappeared
Acharya et al, 2015[18]	Case report	Systemic sclerosis	Digital ischemia	SOC + heparin + methylprednisolone	Improvement
Blaise et al, 2017[23]	Case report	Systemic sclerosis	Digital ischemia	SOC + amputation	No improvement
Ngcozana et al, 2014[24]	Case series	Systemic sclerosis	Digital ischemia	SOC + bosentan	Improvement
Yu et al, 2007[20]	Case report	Systemic sclerosis	Digital ischemia	SOC + bosentan	Improvement
Humbert et al, 2003[22]	Case report	Systemic sclerosis	Digital ischemia	SOC + bosentan	Improvement

SOC: Standard of care

regarding the efficacy of bosentan reported in previous studies, in our case, bosentan and other endothelin receptor antagonist drugs were not available on our National Drugs Catalog.[9] Considering that non-invasive management was the preferred method, we applied heparinization to manage the digital ischemia in our patient. Previous study had provided the comparison between the use of bosentan and heparinization, platelet inhibitors, vasodilators, and alprostadil for the management of digital ischemia in patients with thrombo-angiitis obliterans. They found that bosentan was the therapeutic option when classical therapeutic option failed.[26] However, due to bosentan being unavailable in our hospital, we used heparinization. In our case, the failure of heparinization was found two weeks after treatment, and thereafter, we considered to perform digital amputation. Previous study revealed that digital amputation was indicated in patients with both micro- and macrovascular involvement.[4] In our case, he had digital necrosis with no oxygen saturation detected in the affected fingers, suggesting that he had micro- and macrovascular involvement. Therefore, it was reasonable that we perform digital amputation in our patient.

In this paper, we reported a case of the challenging management of digital ischemia in patients with systemic sclerosis. To the best of our knowledge, our case is the first case in Indonesia and the second case worldwide on the use of heparin for the management of digital ischemia in patients with systemic sclerosis. In our case, we could learn how to manage patient with digital ischemia in the case of systemic sclerosis. Multifactorial consideration should be performed before deciding the management method of digital ischemia in patient with systemic sclerosis. We suggested that a proper recommendation should be established for managing patient with digital ischemia.

Our case had several important limitations. First, systemic sclerosis is a chronic disease, and the previous investigation and treatment for managing our patient was unknown as our patient visited the different hospitals before admitted to our hospital. Second, when admitted to our hospital, the digital ischemia condition had already worsened. Therefore, there was a delay in providing intervention to the patient, and we were unable to implement comprehensive pharmacological interventions. Third, our hospital had limitation in providing the pharmacological products for the management of digital ischemia. Therefore, comprehensive pharmacological intervention referring to previous studies and recommendation was unable to be applied.

In conclusion, the diagnosis of digital ischemia in patients with systemic sclerosis requires a holistic investigation. Moreover, for the selection of the method for the management of digital ischemia in patients with systemic sclerosis, multifactorial analysis should be considered.

ΠΕΡΙΛΗΨΗ

Ισχαιμία δακτύλων σε ασθενή με σκληρόδερμα

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Ένας 49χρονος άνδρας εισήχθη στο νοσοκομείο λόγω πόνου στα δάκτυλα από έτους. Παρουσίαζε επίσης δύσπνοια, μείωση της δραστηριότητας και βελτίωση με την ανάπαυση. Πληρούσε τα κριτήρια ταξινόμησης του Αμερικανικού Κολλεγίου Ρευματολογίας για σκληρόδερμα. Επίσης, είχε συστηματική συμμετοχή, περιλαμβανομένης της διάμεσης πνευμονοπάθειας και του φαινομένου Raynaud με την ισχαιμία των δακτύλων. Μετά τη χορήγηση της συνήθους αγωγής και της ηπαρινοθεραπείας η νεκρωτική βλάβη βελτιώθηκε, αλλά ο ασθενής εισήχθη και πάλι λόγω επιδείνωσης της ισχαιμίας μετά την έξοδο με χορήγηση βαρφαρίνης και στη συνέχεια έγινε ακρωτηριασμός. Συμπεραίνουμε ότι η διάγνωση του σκληροδέρματος και ο εντοπισμός της επιπλοκής του θα πρέπει να περιλαμβάνει μια ολοκληρωμένη διερεύνηση και διαχείριση της ισχαιμίας των δακτύλων, ενώ θα πρέπει να δοθεί προτεραιότητα στη μη επεμβατική μέθοδο, καθώς προς το παρόν δεν υπάρχει καθιερωμένη σύσταση για την αντιμετώπιση των δακτυλικών ελκών στο φαινόμενο Raynaud.

Λέξεις ευρετηρίου: Ακρωτηριασμός, Θεραπεία με ηπαρίνη, Ισχαιμία δακτύλων, Σκληρόδερμα

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