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Systemic Lupus Erythematosus with Initial Symptoms of Extensive Digital Gangrene: A Case Report

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Abstract: Systemic lupus erythematosus (SLE) is a chronic, diffuse connective tissue disease primarily caused by the abnormal activation of the immune system, leading to autoimmune attacks on the body's own tissues. Circulatory disorders resulting in gangrene of the extremities as an initial complication of SLE are exceedingly rare. This case report describes a 23-year-old Asian female who was admitted with severe gangrenous involvement of both hands and the right lower extremity. She tested positive for multiple autoantibodies and was diagnosed with SLE, although she lacked other typical signs or symptoms of the disease. Treatment included methylprednisolone, hydroxychloroquine, and plasma exchange; however, these interventions failed to halt the progression of terminal gangrene, necessitating amputation. This case highlights the rarity and poor prognosis associated with SLE presenting with extremity gangrene. Immediate and aggressive treatment is imperative for better outcomes.

1. Introduction

Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disorder characterized by multisystem involvement, primarily affecting the skin, mucosa, bones, joints, cardiovascular system, and kidneys. Clinical manifestations include butterfly erythema, rash, mucosal ulcers, pleuritis, alopecia, arthritis, pericarditis, photosensitivity, thrombocytopenia, and nephrotic syndrome. Digital gangrene represents a rare and severe manifestation of vascular damage in SLE, often leading to significant disability or mortality [1]. Extremity gangrene in SLE patients is believed to result from the formation of immune complexes and thrombi within the walls of relevant blood vessels, leading to vessel wall narrowing or occlusion, inadequate blood supply, and subsequent soft tissue necrosis [2-4]. Timely diagnosis and early initiation of anticoagulation therapy are critical for improving patient outcomes. This case report details a 23-year-old female who presented with digital gangrene and was subsequently diagnosed with SLE. A comprehensive treatment regimen was implemented.

2. Case Report

A 23-year-old Asian female presented with acute pain in both hands and the right lower extremity, accompanied by lavender discoloration of the skin, five months prior. Concurrently, she experienced limited mobility in the affected limbs. Over time, these areas developed progressive swelling, blister formation, spontaneous rupture, and eventual gangrene. The previous hospital provided symptomatic treatments, including hormone therapy and immune modulation, but failed to control the disease effectively, leading to a noticeable spread of cyanosis and gangrene from the distal ends bilaterally towards the proximal regions. The patient had no past medical history of joint pain, hair loss, photosensitivity, oral ulcers, malar rash, or saddle nose deformity, nor were there signs suggestive of Raynaud's phenomenon.

Physical examination revealed erythema on both palms. The fingers of both hands, except the thumbs, exhibited dryness and carbon black discoloration, along with tissue atrophy and well-defined margins. Notably, the nails remained intact, while dysfunction of flexion and dorsalis movement was observed at the distal interphalangeal joints. The right foot showed similar changes, with longitudinal fissures and exposed superficial nerves. The boundary of necrotic tissue was clear, located in the ankle joint area, with obvious junction tenderness. Skin temperature in both hands and the right foot was low, and pulses were absent in the gangrenous areas (Figure 1A/B). All other systemic examinations were within normal limits.

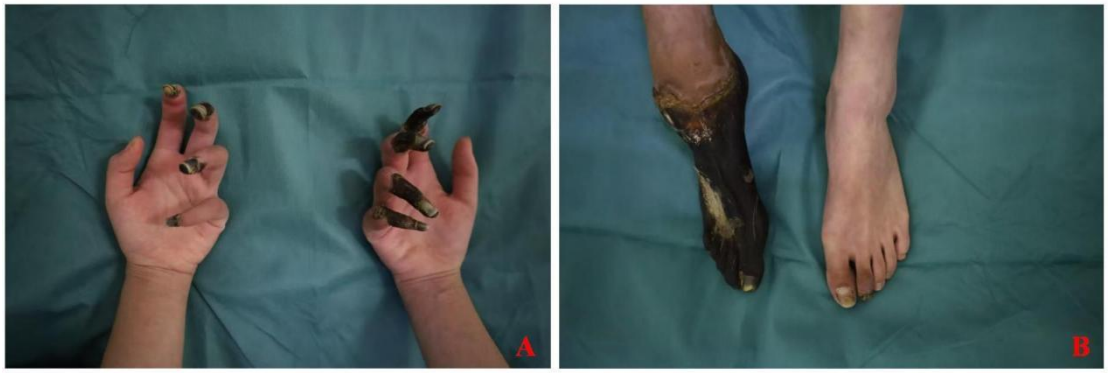

Figure 1: Presented Physical Examination

Biochemical examination revealed prolonged prothrombin time (24.7 s; NV: 11-13 s), activated partial thromboplastin time (APTT: 49.1 s; NV: 31-43 s), elevated fibrinogen (4.16 g/L; NV: 2-4 g/L), and high sedimentation rate (ESR: 115.0 mm/h; NV: 0-20 mm/h). Immunological tests showed positive anti-nuclear antibody (ANA) with a titer of 2560 (> 1/160) and positive anti-ds DNA antibody. Lupus anticoagulant (LA) screening results were LA1: 67.20 s, LA2: 49.20 s, LA1/LA2 ratio 1.37 (NV: 0.8-1.2). Anti-phospholipid antibodies (APA) and anti-neutrophil cytoplasmic antibodies (ANCA) were negative. Echocardiography showed normal atrial and ventricular diameters, normal systolic and diastolic function of the left heart, and slight tricuspid valve regurgitation. Electrocardiogram results were normal.

Based on the 2019 ACR/EULAR classification criteria, the patient scored 11 points, confirming a definitive diagnosis of SLE [5]. She was also diagnosed with lupus digital gangrene combined with antiphospholipid syndrome (APS).

3. Treatment

Following diagnosis, intravenous methylprednisolone (initial dose of 40 mg/day, gradually increased to 520 mg/day), oral hydroxychloroquine (0.2 g/day), heparin (4000 u/day), and plasma

exchange were administered. Despite these interventions, the extent of gangrene stabilized but did not regress. The patient underwent right lower leg amputation and finger amputations on both hands. The amputation planes were located at the lower middle third of the tibia and fibula for the right lower limb and at the proximal interphalangeal joints of the gangrenous fingers. Postoperative wound healing was satisfactory. Re-examination after surgery showed improved coagulation function (APTT: 32.70 s, fibrinogen: 6.64 g/L, ESR: 15 mm/h). Immune-related tests showed a positive ANA with a titer of 1:640 and decreased complement C3 and C4 levels.

4. Discussion

Systemic lupus erythematosus (SLE) rarely manifests with gangrene of the extremities as an initial symptom. Digital gangrene is observed as the presenting feature in only 0.2% of SLE patients [6]. Previous reports indicate that this condition typically appears in later stages of the disease. In a 1962 study, Dubois and Attebury observed that the incubation period from SLE diagnosis to the onset of extremity gangrene ranged from 1 to 18 years [7]. In a study of 2684 SLE patients, only 18 developed digital gangrene (incidence of 0.67%), with a mean age of onset of 33.1 ± 11.8 years. Independent risk factors included Raynaud's phenomenon and elevated serum CRP [3]. Rosato et al. noted that digital gangrene is not usually the initial presentation of SLE [8]. However, in our case, digital gangrene was the first symptom, without any prior typical features of SLE. Reports of digital gangrene as an initial manifestation of SLE exist [1, 9, 10], but cases involving extensive digital gangrene leading to disability are exceedingly rare and primarily involve middle-aged patients [11, 12].

The exact etiology of acrogangrene in SLE remains unknown, but possible mechanisms include thromboembolism, premature atherosclerosis, vasospasm, hypercoagulability, and vasculitis [3]. Among these, antiphospholipid syndrome (APS) represents a significant risk factor. Jeffery et al. identified APS as a contributing cause of severe ischemia [13]. Extremity gangrene is associated with hypercoagulability. Notably, APTT prolongation rates in SLE patients are higher than in other patients, indicating potential abnormal blood coagulation. Early laboratory findings in our patient showed abnormally prolonged APTT, likely due to the presence of LA, an autoantibody causing abnormal blood clotting. Although LA is not a diagnostic criterion for SLE, APAs, including LA, are found in approximately 50% of SLE patients, making SLE a recognized risk factor for venous and arterial thrombosis [14].

The level of ANA titer also serves as an indicator of thrombotic risk. Research indicates a positive correlation between ANA titers and anticardiolipin antibody (ACA) positivity rates. The presence of ACA holds significant value in indicating whether patients with SLE are in a pre-thrombotic state, crucial for assessing thrombotic risk and implementing proactive intervention measures [15]. Hypercoagulability markedly increases the incidence of venous thrombosis and, less frequently, arterial thromboembolism events, as well as cardiovascular complications [16].

Anticoagulant therapy is essential for managing combined APS. In cases of Raynaud's phenomenon or gangrene, vasodilators should be prescribed [17]. Early and aggressive corticosteroid treatment is critical to control gangrene progression and improve prognosis [3]. Ziaee et al. reported a case of a 12-year-old girl treated with steroids and mycophenolate for finger gangrene, achieving good results [4]. Another case of SLE with digital gangrene treated with corticosteroids and cyclophosphamide showed significant improvement [11]. In our case, the decision regarding treatment choice was complex, requiring multidisciplinary discussion. Surgery was deemed necessary after combination therapy had stabilized the gangrene. Interestingly, rapid remission followed amputation.

5. Conclusion

SLE with gangrene at the extremities is a dangerous condition. Immune complex deposition in the vascular wall can cause endothelial dysfunction, induce hypercoagulability, and lead to acute vascular injury, resulting in platelet aggregation and venous thrombosis. Health care professionals, especially dermatologists and plastic surgeons, should be aware of the possibility of limb embolism, diagnose it promptly, treat it immediately, and use invasive strategies and drug combinations if necessary. Such therapies include intravascular therapy (EVT) or bypass grafting, as well as antiplatelet agents, anticoagulants, statins, rituximab, steroids, and mycophenolate. When the disease stabilizes and gangrene is well defined, amputation is often the last and most effective treatment.

Declarations

Not applicable.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the First Affiliated Hospital of the University of South China. The informed consent of the patient was obtained.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Authors' contributions

Study design and conception of this manuscript were performed by CJ, JZ. CL, YF, JL were responsible for drafting, revising the article. Date collection was done by SJ. All authors read and approved the final manuscript.

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