DIGITAL GANGRENE AS THE INITIAL PRESENTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS WITHOUT SECONDARY ANTIPHOSPHOLIPID SYNDROME: CASE REPORT

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ABSTRACT

This is a case of a 28-year-old female presented with an extensive cutaneous gangrene of her fingers and toes with history of a livedo reticularis rash in both lower limbs. Her work-up showed positive serology for Systemic Lupus Erythematosus (SLE). There were no other symptoms suggestive of SLE. Interestingly, the patient adequately responded to rituximab therapy. Such a case of digital gangrene as the initial presentation of SLE without secondary antiphospholipid syndrome has rarely been reported in the literature.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic inflammatory disorder affecting different organs and systems. Vascular injury is an important characteristic of SLE. Digital gangrene in SLE is a rare form of vascular injury and considered to be a severe complication of SLE that generally leads to digital amputation (1,2). The mechanisms include vasculitis, premature atherosclerosis, vasospasm, and hypercoagulability related to antiphospholipid antibodies. This is a report of an adult female presented with digital gangrene as the initial presentation of SLE; such presentation is rarely reported in the literature. There was no evidence of antiphospholipid antibodies. Initially treated with glucocorticoid, anti-platelets, anticoagulation, and potent vasodilator agents. Surprisingly, her digital ischemia improved dramatically after tow cycles of rituximab (RTX) administration. Up to our knowledge, the dramatic response of digital ischemia in systemic lupus erythematosus (SLE) to rituximab (RTX) is rarely reported in the medical literature.

CASE DESCRIPTION

A 28-year-old female presented to the emergency department, complaining of a black discoloration of the tip of her fingers and toes which progressed over a period of 2 weeks and was associated with severe pain. The patient reported a lower limb net-like rash (livedo reticularis) 1 month earlier but without any other associated symptoms. There was no previous history of joint pain, oral ulcers, hair loss, photosensitivity, or Reynaud's phenomena.

Based on the physical examination, the positive findings were observed in her extremities. In her right hand, the third and fourth fingers were cyanotic and gangrenous (figure1). In her left hand, the fifth finger was cyanotic and gangrenous (figure2). In her right foot, the tip of the big toe was cyanotic (figure3). In her left foot, the first and second toes were cyanotic (figure3). The dorsal pedis artery was not palpable. Both her legs showed a livedo reticularis rash (figure4).

Laboratory findings were as follows: WBC: 2.45 × 109/L, Hb: 8.9 g/dL, platelet: 233 × 109/L, Hct: 29.4%, ESR: 115 mm/h, CRP: 99.9 mg/L, trace proteinuria on urinalysis.

Immunologic studies revealed an ANA titer of > 1:160 (homogenous pattern),

ds-DNA titer of > 240, c- and p-ANCA negative, and anti-beta 2 GP1-IgA/IgM/IgG isotype were negative. Anti-cardiolepin antibodies and lupus anticoagulant were negative. Hypocomplementemia was observed (C3: 0,371 g/L, C4: 0,035 g/L; normal: 0.9–2 g/L and 0.1–0.4 g/L, respectively) although rheumatoid factor was negative (table1).

Table1: laboratory result

WBC	2.45 × 109/L
Hb	8.9 g/dL
platelet	233 × 109/L
Hct	29.4%
ESR	115 mm/h
CRP	99.9 mg/
urinalysis	trace proteinuria
ANA titer	> 1:160 (homogenous pattern)
ds-DNA titer	> 240
c-ANCA	negative
p-ANCA	negative
anti-beta 2 GP1-IgA/IgM/IgG isotype	negative
Anti-cardiolepin antibodies	negative
lupus anticoagulant	negative
C3	0,371 g/L
C4	0,035 g/L
rheumatoid factor	negative

A review of the radiological work-up (computed tomography angiography) of the upper and lower limb arteries showed no evidence of occlusion, significant stenosis, or aneurysmal formation. Electrocardiographic, echocardiographic, and computed tomography (CT) imaging studies of the thorax did not show any pathological findings. Because the initial results from laboratory studies indicated a possibility of SLE with high disease activity, initial treatment was started with glucocorticoid (1 mg/kg/day), aspirin (81 mg/day), intravenous prostaglandin (2 mcg/kg/min), and intravenous heparin. After confirmation of SLE and rolling out the secondary antiphospholipid syndrome, we discontinued the intravenous heparin and continued the patient on steroids. The plan was to administer cyclophosphamide; however, the patient refused because she was worried about the side effects. As an alternative to cyclophosphamide, the patient started on rituximab (RTX) with two infusions of 1000 mg at a 14-day interval. The clinical and laboratory response to treatment was observed after RTX therapy. Laboratory evaluation revealed the following: ESR: 30, CRP: 2 mg/dL, and normal levels of C3 and C4 complement levels. (Results from a complete blood count panel were unremarkable). A combined dosage of 100 mg/day azathioprine (AZA) and 200 mg/day hydroxychloroquine were added to the treatment protocol after two infusions of RTX therapy. In addition, the corticosteroid dosage which was started at 1 mg/kg was gradually tapered till it reached 5 mg/day over the 3-month period. Eventually, digital gangrenous lesions started to regress after the first cycle (5 months) of RTX therapy. A second cycle of RTX therapy was started during which a complete recovery of digital lesions and the regression of active disease signs and acute phase responses were seen. The patient has been in clinical remission with glucocorticoid (5 mg/day), aspirin (81 mg/day), azathioprine (100 mg/day), and hydroxychloroquine (200 mg/day) for the last 2 years (table2).

Table2: management plan

• Initial treatment	• glucocorticoid (1 mg/kg/day). • aspirin (81 mg/day). • prostaglandin (2 mcg/kg/min). • therapeutic heparin.
• Induction treatment	• rituximab (RTX) two infusions of 1000 mg at a 14-day interval.
• Maintenance treatment	• glucocorticoid (5 mg/day). • aspirin (81 mg/day). • azathioprine (100 mg/day). • hydroxychloroquine (200 mg/day).

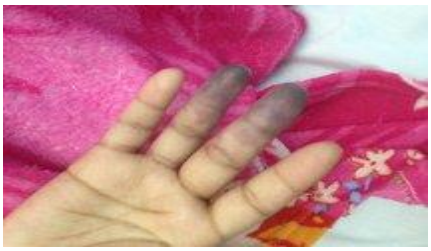

Figure1. cyanosis and gangrene of the third and fourth fingers of the right hand.

Figure2. cyanosis and gangrene of the fourth finger of the left hand.

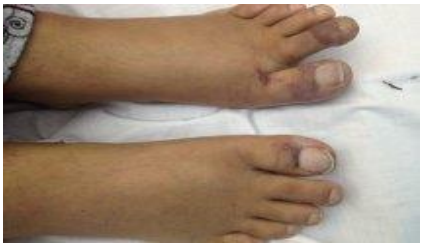

Figure 3. cyanosis of the tip of the big toe of the right foot And the first and second toes of the left foot.

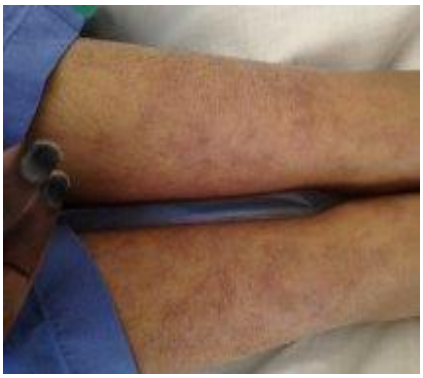

Figure 4. livedoreticularis rash.

DISCUSSION

Digital gangrene as an initial presenting symptom of SLE is rarely reported. Most of the reported cases indicate the presence of antiphospholipid antibodies (3). The mechanisms involved in SLE with digital gangrene are complicated, including hypercoagulability, vasculitis, vasospasm, and atherosclerosis. Liu et al. found that 18 of 2684 SLE patients had digital gangrene, and they found that a long disease duration, Raynaud's phenomenon, and elevated serum CRP were independent predictive factors for SLE to develop digital gangrene. All the 18 patients were treated with cyclophosphamide, although eight cases failed and ultimately received digital amputation (4). Jeffery et al. observed in a cohort study that the prevalence of critical peripheral ischemia in SLE patients was 1.4%. All of these had active

disease and positive antiphospholipid antibodies with one patient responding to Rituximab therapy (5). Zieaa et al. reported a case of a 12-year-old girl presented with digital gangrene as the initial symptom of SLE and treated with steroids and mycophenolate mofetil (2). Orhan et al. reported a case of SLE and jaccoud arthritis in a patient who developed digital ischemia which improved after rituximab therapy (6).

In conclusion, digital gangrene as an initial presenting symptom of SLE is rare. a long disease duration, Raynaud's phenomenon, and elevated serum CRP were independent predictive factors for SLE to develop digital gangrene. Either cyclophosphamide, mycophenolate mofetil,or rituximab (RTX) can be a treatment option. Lastly, our patient presented with digital gangrene as the initial presentation of SLE without evidence of secondary antiphospholipid syndrome. She did not show any other signs or symptoms of SLE and eventually responded to rituximab therapy.

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