Coexistence of Erythromelalgia and Raynaud’s Phenomenon in a Systemic Lupus Erythematosus Patient

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Erythromelalgia (EM), an uncommon disorder first described by Mitchell in 1878, is characterized by redness, heat, and painful extremities with intense burning sensation. Attacks of EM may be worsened by limb warming, exercise, or dependency of the affected extremity. Although the coexistence of EM and Raynaud’s phenomenon (RP) may appear to be opposites in symptomatology and clinical presentation, recent studies provide an explanation based on a dysfunction of the regulation of vasomotor tone. Here, we report a case of EM in a patient with RP. (J Rheum Dis 2018;25:69-72)

Case Report

A 59-year-old woman was referred to our Dermatology Department due to a burning sensation accompanied by edema and redness on her palms and soles. Her symptoms first occurred 15 days prior to her presentation and were usually exacerbated by warm temperatures and relieved by cooling. Her past medical history included ischemic dilated cardiomyopathy and a 20-year history of RP. Her family history was negative for EM, RP, or other diseases. Although the history of her medication was not clear, there was no change of the medication in recent years. Physical examination showed symmetrical erythematous patches with bean- to pinpoint-sized violaceous...
macules on both soles and palms (Figure 1A and 1B), and ulceration with atrophie blanche lesions on bilateral malleolar areas. She sometimes noticed cyanotic changes in her fingers consistent with a history of known RP (Figure 1C). A punch biopsy obtained from a violaceous macule on her right second finger revealed vascular dilatation with endothelial hyperplasia, fibrin thrombi, fibrinous necrosis, and positive immunoglobulin G (IgG), and IgM in the vessel walls noted on immunofluorescence staining—findings consistent with livedoid vasculitis (Figure 2). Another skin biopsy performed on an erythematous swollen patch on her sole revealed histological findings of only dermal ectatic vessels (Figure 3). Laboratory investigations revealed: hemoglobin (8.7 g/dL), platelet count (78×10^3/μL), C3 (28.1 mg/dL), and C4 (15.3 mg/dL) were decreased while antinuclear antibodies (1:320), perinuclear anti-neutrophil cytoplasmic antibodies, anti-double-stranded DNA antibodies, and direct Coombs test were positive. Peripheral blood smear (PBS) revealed normochromic normocytic red blood cell. C-reactive protein (5.93 mg/dL) and 24 hour urine protein (2,048 mg/day) were also elevated. These findings met two clinical criteria (renal, thrombocytopenia) and four immunological criteria (anti-nuclear antibodies, anti-DNA, low comple-
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Figure 3. Scattered dilated vessels in the upper dermis (H&E, ×100).

ment, direct Coombs test) based on the 2012 systemic lupus international collaborating clinics diagnostic criteria for SLE. Finally, we made a diagnosis of secondary EM and secondary RP with SLE accompanying livedoid vasculitis, which is one of the non-specific skin symptoms indicating systemic activity of SLE.

In rheumatology, for the treatment of SLE, she was prescribed 400 mg hydroxychloroquine per day and 50 mg prednisolone per day, which led to an improvement of livedoid vasculitis and erythromelalgia.

DISCUSSION

Lupus erythematosus is classified as acute, subacute, or chronic cutaneous lupus erythematosus based on distinctive histological findings, and as a non-specific skin disease when no characteristic histological findings are observed [9]. Non-specific skin symptoms associated with lupus erythematosus are mainly observed in SLE and are important symptoms from a dermatologist’s viewpoint because they are critical indicators of disease activity. Cutaneous manifestations related to, but not specific to SLE, include cutaneous vasculitis, periungual telangiectasia, urticarial vasculitis, livedo reticularis, atrophie blanche, and bullous lesions [10]. RP is also seen in 15% to 30% of patients [11] and EM is rarely observed [12].

Based on criteria proposed by Kurzrock and Cohen [1], EM is clinically diagnosed in patients showing: (i) Severe burning discomfort, warmth, and erythema of the feet and/or hands. (ii) Exacerbation and aggravation of symptoms upon exposure to heat or placing the involved extremity in a dependent position. (iii) Amelioration of discomfort by elevation or cooling of the affected extremity. EM may be primary or secondary in nature. Primary EM usually affects younger patients and is more often bilateral. Secondary EM is related to various disorders, such as thrombocythemia, myeloproliferative disorders, arterial hypertension, vasculitis, and SLE [4], and administration of calcium channel blockers or bromocriptine [13,14]. A negative family history, late onset at the age of 59 years, and clinical symptoms of SLE indicated the presence of secondary EM in the patient we reported in our study. In this case, hematologic disease could be ruled out as a cause of EM because normochromic normocytic red blood cell was revealed in PBS and any disease increasing blood viscosity, such as thrombocythemia or polycythemia vera, was not observed. She had a long history of dilated myocardopathy, so calcium channel blocker or beta blocker medication should also be taken into consideration. However, since there was no history of medication change in recent years, the medication could be ruled out as a possible cause of EM.

Similar to EM, RP maybe (i) primary (formerly known as Raynaud’s disease), or (ii) secondary (formerly known as Raynaud’s syndrome). Primary RP most typically affects female patients in the first and second decades, often with a family history of the disease and is always symmetric. Secondary RP is most commonly associated with connective tissue disorders and less frequently with thromboangiitis obliterans, thoracic outlet syndrome, paraneoplastic syndrome, hypothyroidism, administration of beta blockers or ergotamines, and exposure to vibrating machinery [5]. Our patient related no family history and showed an asymmetric pattern of RP; thus, she was more likely to have secondary rather than primary RP.

Although RP and EM are both vascular acrosyndromes, EM is a rare painful disorder of the extremities characterized by redness, a burning sensation, and increase in skin temperature exacerbated by exposure to heat [15]. Unlike EM, in patients having RP, the characteristic symptoms of pallor or cyanosis are aggravated by cold. Therefore, some authors believe that the coexistence of RP and EM is simply coincidental [8]. However, recent studies provide an explanation for the rare instances in which EM and RP are seen to coexist. Berlin and Pehr [5] have postulated that both syndromes have a common basis in that in both conditions, there is a dysfunctional regulation of the vasomotor tone. In both, EM and RP, the initial event seems to be vasospasm. Subsequent to vasoconstriction, reactive hyperemia may occur in both con-
ditions, although it is more apparent and longer lasting in EM. In this case, the patient had livedoid vasculitis with histologic findings of fibrin thrombi and vasculitis. It is thought that this vascular obstructive condition caused vasospasm associated with the development of RP and EM.

**SUMMARY**

In summary, we report a case of EM in a patient with RP, which is supposed to be in the same spectrum of diseases involving a dysfunctional vasomotor tone like EM. Pathophysiological mechanisms underlying both, RP and EM are not yet clearly understood, and further studies may be helpful in understanding the pathophysiology of the two diseases.

**CONFLICT OF INTEREST**

No potential conflict of interest relevant to this article was reported.

**REFERENCES**