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LETTER TO THE EDITOR

Livedo and ischemic strokes: diagnostic hints of a rare condition

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Dear Editor,

Sneddon's syndrome (SS) is a rare condition characterized by the combination of ischemic strokes and cutaneous livedo [1, 2], defined as the "persistent, not reversible with rewarming, violaceous, reticular or mottled pattern of the skin of trunk, arms or legs, consisting of regular unbroken circles (livedo reticularis) or irregular-broken circles (livedo racemosa)". Other well-defined neurological manifestations of SS include headache, seizures, and vascular dementia. Here, we report two cases with clinical and imaging features suggestive of SS. In both patients skin biopsy was performed and sections were stained with hematoxylin and eosin (H&E).

A 54-year-old man (*Case 1*) presented with a 2-year history of lower limbs weakness, seizures, and progressive behavioral changes. He had been having recurrent ischemic strokes since he was 48. He had no history of hypertension, heart arrhythmia, diabetes, migraine, or smoking. His neurological examination revealed dysarthria, ataxic gait, lower limbs hyperreflexia, and right extensor plantar response; general examination revealed diffused livedo racemosa (Fig. 1a). An extensive cardiological evaluation including an electrocardiogram, an echocardiogram and carotid ultrasound evaluation ruled out cardiovascular causes of stroke. Coagulation parameters (including fibrinogen and D-dimer), inflammatory indexes, syphilis serology, and autoimmune antibody panels including, ANA, ENA, ANCA, lupus anti-coagulants (LAC) and antiphospholipid antibodies (IgM and IgG anti-cardiolipin and anti-β2-microglobulin) were negative. A heterozygous mutation of factor V Leiden was detected. Brain MRI showed cortical atrophy and multiple ischemic lesions involving both the superficial and deep territories of posterior and middle cerebral artery (Fig. 1b). Skin biopsy showed intra-capillary and parietal widespread thrombosis (Fig. 1c). Oral anticoagulants and antipsychotic were added to therapy.

A 65-year-old man (*Case 2*) presented with a 3-year history of progressive lower limbs weakness and mixed dysphagia. He had been having recurrent ischemic strokes since he was 55. He had history of myocardial infarcts, hypertension, and smoking. His neurological examination revealed dysphagia, ataxic and spastic gait, limbs hyperreflexia, right extensor plantar response. General examination revealed diffused livedo racemosa at the trunk and lower limbs (Fig. 1a). A cardiological evaluation and electrocardiogram ruled out the presence of heart arrhythmia; echocardiography demonstrated mild hypokinesia of apical and distal septum of lateral ventricle, as consequence of previous myocardial infarcts. Coagulation parameters and thrombophilic screening were normal. Brain MRI showed diffused cortical atrophy and multiple ischemic lesions (Fig. 1b) in both medium-sized superficial and deep, posterior and middle cerebral artery territories. Skin biopsy revealed intra-capillary and parietal widespread thrombosis (Fig. 1c). As for the first patient, oral anticoagulants were added to therapy.

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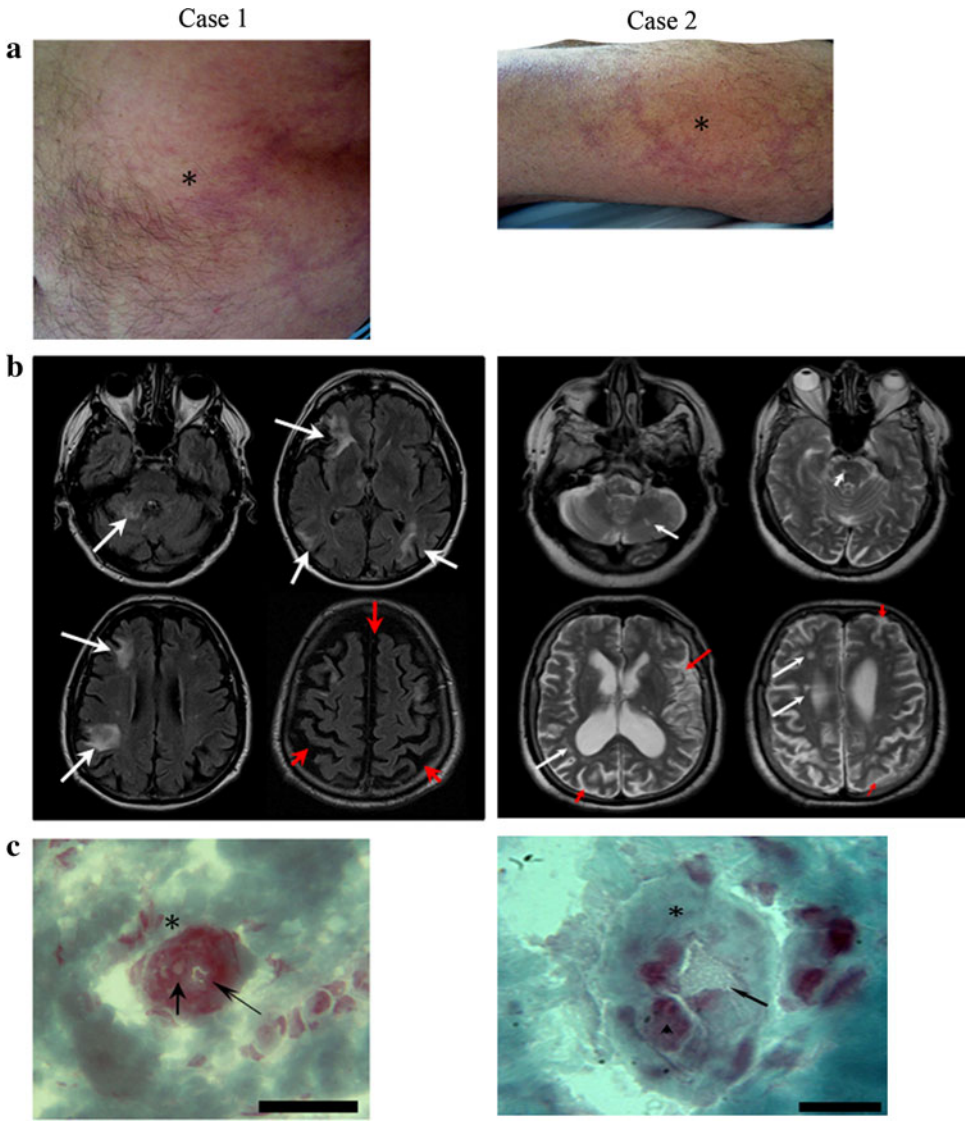

Fig. 1 (Cases 1 and 2) **a** diffused livedo racemosa (*asterisks*); **b** FLAIR/T2 MRI brain scan showing multiple ischemic lesions (*white arrows*) and cortical atrophy (*red arrows*); **c** skin biopsy showed intra-capillary (*thin arrow*) and parietal (*thick arrow*) widespread thrombosis; *scale bar* 100 μm (*Case 1*) and 50 μm (*Case 2*) (color figure online)

The precise etiology of SS is not well defined: some studies reported the evidence of autoimmune mechanisms although an imbalance of thrombotic mechanisms has been suggested [3]. It is considered a progressive non-inflammatory thrombotic vasculopathy affecting medium- and small-sized arterioles [4]. Skin biopsy reveals thrombosis of subcutaneous arterioles and compensatory capillary dilation with blood stagnation causing the mottled discoloration (livedo racemosa). Moreover, recent findings suggest a possible link between the vasculopathy and a primary coagulopathy, as supported by altered levels of coagulation factor V, VII, protein S, and activated protein C resistance. Although SS is considered by some authors an anti-phospholipid syndrome [5], elevated antibodies are usually identified in only half of patients [6] indicating that this syndrome may be a distinct entity or perhaps a group of different disorders.

These two cases draw attention to the differential diagnosis of recurrent/young-onset ischemic strokes, confirming the enigmatic pathogenesis of presumably dysimmune cerebrovascular events, in particular when antibodies are not clearly detected.

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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