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SNEDDON SYNDROME: A RARE CAUSE OF ISCHAEMIC STROKE IN A YOUNG WOMAN

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ABSTRACT

Introduction: Sneddon syndrome is an uncommon vasculopathy, thrombotic rather than inflammatory, in which livedo racemosa coexists with ischaemic cerebrovascular events. It mainly affects young women and remains under-recognised.
Case presentation: A 36-year-old woman with a history of two miscarriages and recurrent, spontaneously resolving transient ischaemic attacks presented with right hemiparesis and dysarthria. Skin examination revealed livedo racemosa on the forearms, thighs and legs. Brain magnetic resonance imaging showed a recent ischaemic lesion on diffusion-weighted imaging and bilateral white matter hyperintensities in the centrum semiovale and periventricular regions, with cortical and subcortical lesions. Skin biopsy was normal, antiphospholipid antibodies were repeatedly negative and the etiological work-up for stroke in the young was unremarkable. The diagnosis of antiphospholipid-negative Sneddon syndrome was made, and the patient was treated with oral anticoagulation (acenocoumarol, target INR 2–3).
Conclusion: Ischaemic stroke in a young adult should prompt a careful skin examination. The finding of livedo racemosa points to Sneddon syndrome, a diagnosis that remains clinical and requires the exclusion of antiphospholipid syndrome and other causes of stroke in the young.

KEYWORDS

Sneddon syndrome, Livedo racemosa, Ischaemic stroke, Young adult, Antiphospholipid antibodies, Case report

MAIN ARTICLE

INTRODUCTION

Sneddon syndrome (SS), described by Sneddon in 1965, combines livedo racemosa with ischaemic cerebrovascular events [1]. This uncommon disorder, considered a thrombotic rather than inflammatory vasculopathy, has an estimated incidence of about four cases per million inhabitants per year [2]. It predominantly affects young women and follows a chronic, progressive course caused by involvement of small and medium-sized arteries [2,3]. Its cause remains unknown, and the debate between a primary occlusive arteriopathy and a thrombotic process is still open [2].

We report a case of SS in a young woman, to underline the diagnostic value of a careful skin examination in patients with ischaemic stroke at a young age.

CASE PRESENTATION

A 36-year-old woman was admitted to the Department of Neurology for right hemiparesis and dysarthria. Her history included two miscarriages and recurrent transient ischaemic attacks that had resolved spontaneously. She had no hypertension, did not smoke and did not use oral contraception.

Skin examination revealed livedo racemosa, made of irregular, broken violaceous rings, on the forearms, thighs and legs (Figure 1).

Brain magnetic resonance imaging (MRI) showed bilateral hyperintensities on fluid-attenuated inversion recovery (FLAIR) sequences in the white matter of the centrum semiovale and in periventricular regions, together with cortical and subcortical lesions (Figure 2). Diffusion-weighted imaging showed a recent ischaemic lesion in the left cerebral hemisphere, consistent with the right hemiparesis. Cervical and intracranial vascular imaging was normal.

Skin biopsy was normal. Antiphospholipid antibodies (anticardiolipin, anti-β2-glycoprotein I and lupus anticoagulant) were negative and remained negative on repeat testing 12 weeks later, and the rest of the immunological work-up, including antinuclear antibodies, was also negative. Transthoracic and transoesophageal echocardiography, electrocardiogram and Holter monitoring, and thrombophilia screening were all normal.

The diagnosis of SS was made on the association of livedo racemosa and cerebral ischaemic lesions, after exclusion of other causes of stroke in the young. The patient was started on oral anticoagulation with acenocoumarol (Sintrom®), with a target international normalised ratio (INR) of 2–3, without antiplatelet therapy.

DISCUSSION

SS is a neurocutaneous disorder of unknown cause, defined by livedo racemosa occurring together with cerebral ischaemic events [1,2]. Around 80% of patients are women, and the median age at diagnosis is about 40 years [3,4]. In the series of Tourbah et al., the first cerebral ischaemic event occurred between 22 and 58 years of age [5]. Our patient, a 36-year-old woman, fits this typical profile.

The skin lesion is the key to the diagnosis. Livedo reticularis is a transient, vasomotor phenomenon; livedo racemosa, by contrast, is fixed and reflects obstruction of dermal arteries of small and medium calibre, which durably reduces cutaneous perfusion [2]. Livedo racemosa forms irregular, broken rings, persists in a warm environment and is typically widespread, involving the limbs and often the trunk or buttocks [2]. It usually precedes the neurological events by several years and is often overlooked by both patients and physicians [2]; a systematic skin examination is therefore essential in any young patient with stroke.

Neurological manifestations are polymorphic and often multifocal, including transient ischaemic attacks, ischaemic strokes, headache, seizures and, over time, cognitive decline that can progress to dementia because of the cumulative effect of repeated ischaemic lesions [2]. On brain MRI, infarcts typically involve more than one arterial territory and are frequently accompanied by white matter changes [6]. In the series of 26 patients reported by Tourbah et al., MRI patterns were classified into six groups, and the extent of MRI lesions correlated with clinical disability, whereas antiphospholipid antibodies did not [5,7]. Extracerebral involvement may include valvular heart disease, fluctuating blood pressure and retinal abnormalities [3].

The main differential diagnosis is antiphospholipid syndrome (APS), which shares several features with SS but does not require livedo for its diagnosis [4]. Antiphospholipid antibodies are found only in a subset of patients with SS: in a series of 53 patients, 14 were antibody-positive, and the main clinical features did not differ between antibody-positive and antibody-negative patients [4]. In our patient, the history of two miscarriages made it essential to rule out APS; antiphospholipid antibodies were negative on two determinations 12 weeks apart, which supports antiphospholipid-negative SS. In early-onset or familial forms, deficiency of adenosine deaminase 2 (DADA2), caused by loss-of-function mutations in the ADA2 gene, should also be considered, as it can produce a Sneddon-like phenotype [8,9].

No single investigation confirms SS, and the diagnosis rests largely on clinical findings [6]. Skin biopsy may support it by showing an occlusive arteriopathy of the deep dermis, but its sensitivity is limited: in a case-control study, sensitivity rose to 70% only with a standardised

protocol of three deep samples, obtained from the pale central areas of the livedo and extending to the junction between dermis and subcutis, compared with 50% for unstandardised samples [6]. A normal skin biopsy, as in our patient, therefore does not rule out the diagnosis.

Treatment is not codified and relies mainly on case reports and small series [3]. Long-term antiplatelet agents and/or oral anticoagulation are the most widely used options; anticoagulation is generally favoured in patients with antiphospholipid antibodies. However, in the series of Starmans et al., recurrent strokes occurred under both antiplatelet and anticoagulant therapy [4]. Our patient was treated with acenocoumarol alone, with a target INR of 2–3. Control of vascular risk factors, particularly hypertension, is also part of management. The long-term prognosis depends on recurrent ischaemic events and on the progression of cerebral lesions, which can lead to cognitive impairment [2,5].

CONCLUSION

Ischaemic stroke in a young adult, particularly a woman, should always prompt a full skin examination. The presence of livedo racemosa strongly suggests SS. The diagnosis remains clinical and requires the exclusion of antiphospholipid syndrome and other causes of stroke in the young; a normal skin biopsy does not rule it out.

FIGURES:

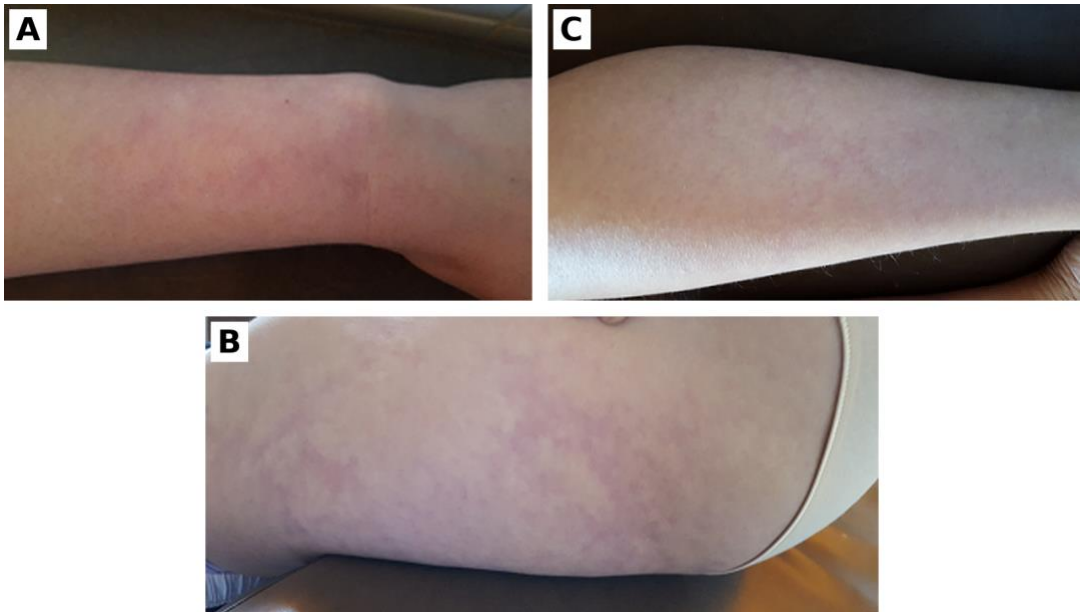


Figure 1: Livedo racemosa of the forearm (A), thigh (B) and leg (C): irregular, broken violaceous rings.

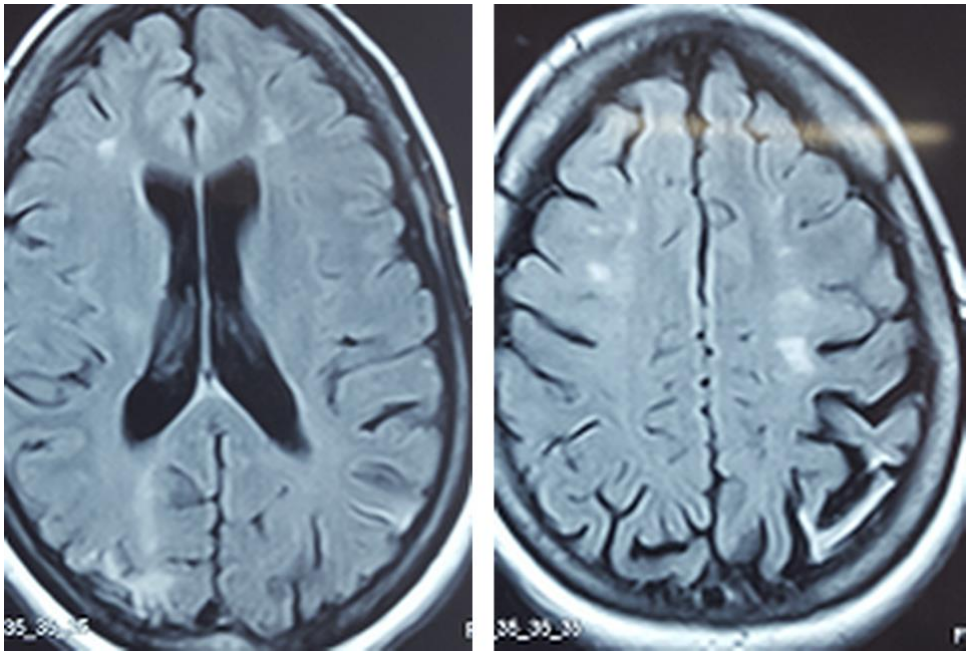


Figure 2: Brain MRI, axial FLAIR sequences: bilateral hyperintensities of the periventricular white matter and centrum semiovale, with cortical and subcortical involvement.

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Author contributions: O.C.R. managed the patient, collected the data, reviewed the literature and wrote the manuscript.

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