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Case Report

Ruptured, fusiform, distal lenticulostriate aneurysm causing intraventricular haemorrhage in a patient with antiphospholipid-negative Sneddon's syndrome

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1. Introduction

Sneddon's syndrome (SS) is a rare, non-inflammatory, occlusive, arterial vasculopathy affecting small to medium calibre arterial vessels and defined by the presence of bluish-purple, lattice-like skin lesions known as *livedo racemosa* in association with ischaemic cerebrovascular events. Predominantly affecting women in early middle age [1]. SS occurs both sporadically and in a familial form and is often accompanied by hypertension and cardiac valvulopathies [1]. Anti-phospholipid antibodies (aPL) are detected in around half of cases [1] and derangement of clotting factors has also been reported. While abnormalities on cerebral digital subtraction angiography (DSA) in SS are common and diverse [1,2], intracranial aneurysms have not, so far, been recognised as a feature.

Aneurysms arising from distal branches of the lenticulostriate arteries are exceedingly rare [3,4]. We report a case of a fusiform, distal lenticulostriate artery aneurysm presenting with intraventricular haemorrhage (IVH) in a patient with SS – the first report of such an association.

2. Case report

A 39-year-old Caucasian woman presented to the emergency department with worsening of an acute onset headache over three days, now with nausea and vomiting. Significant medical history included dilatation of the ascending aorta causing moderate aortic insufficiency, hypertension, one miscarriage, and a small, left temporo-occipital infarct at the age of 24 assumed to be an embolic event secondary to the aortic anomaly. The patient was an ex-smoker and her mother had a history of multiple deep vein thromboses. Neurological examination was normal. Striking, reticulated, bluish-purple *livedo racemosa* skin lesions were noted on the trunk and lower limbs (Fig. 1a).

Lumbar puncture revealed frankly blood-stained CSF containing 150 μL^{-1} predominantly mononuclear leucocytes with an elevated opening pressure of 39 cm H_2O. Unfortunately, data on protein content is unavailable. No organisms were seen or cultured. CT and MRI scans (Fig. 1b) revealed a subacute IVH involving the left lateral ventricle and extending into the third ventricle. Subsequent cerebral DSA demonstrated multifocal, segmental stenoses and beading of distal arterial vessels throughout the cerebral circulation (Fig. 1c and d), consistent with a vasculopathy affecting medium-calibre arterial vessels. In watershed regions, a diffuse network of fine, corkscrew-like collaterals, predominantly white matter perforators, was apparent. Vascular filling of the deep structures was limited and the extant lenticulostriate arteries were of unusually

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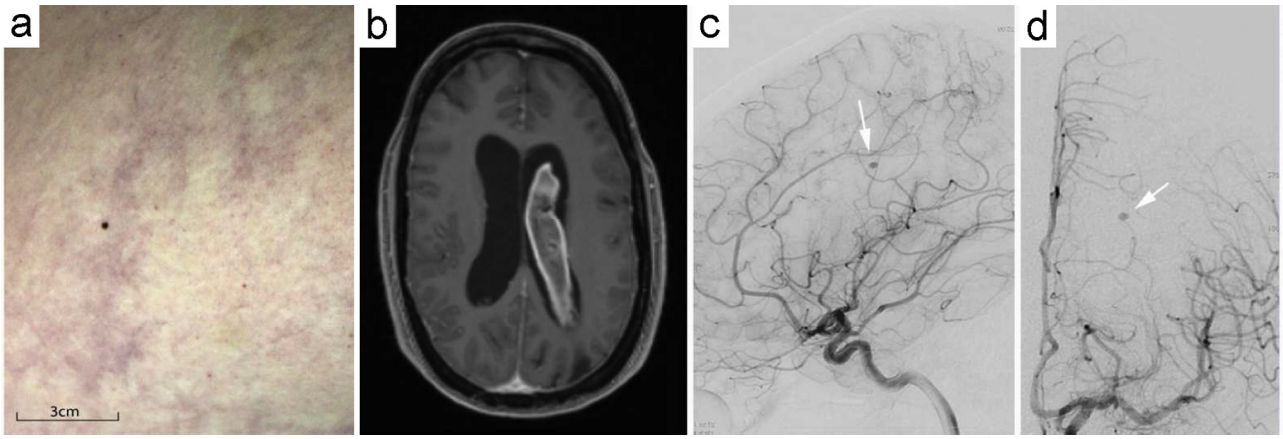

Fig. 1. (a) Photograph of the patient's right lateral thigh demonstrating the characteristic *livedo racemosa* skin lesions which, when associated with cerebral ischaemic events, define Sneddon's syndrome. The patient had widespread lesions over the trunk, buttocks and limbs. (b) Axial T1-weighted cranial MRI showing three-day-old intraventricular haematoma in the right lateral ventricle. (c) Digital subtraction angiography demonstrating 6 mm, fusiform, distal lenticulostriate aneurysm (arrow) arising from a branch of the right middle cerebral artery. Note the diffuse, fine collateral vessels, some of which exhibit beading and corkscrewing. (d) Anterior view of digital subtraction angiogram demonstrating the paucity of flow to deep structures. The aneurysm is once again arrowed.

large diameter. Arising from one of these enlarged and unusually long vessels – a lenticulostriate branch originating just distal to the bifurcation of the left middle cerebral artery (MCA) – was a 6 mm diameter fusiform aneurysm abutting the left lateral ventricle. The circle of Willis and the internal carotid and basilar arteries were of normal appearance and there were no abnormal proximal collaterals typical of moyamoya. To prevent rebleeding, it was decided clip the aneurysm.

At operation, a ventricular drain was placed and the aneurysm located under image guidance via an inter-hemispheric transcallosal approach. The aneurysm was visualised in the lateral wall of the left lateral ventricle and, after temporary occlusion caused no significant changes to intraoperative sensory and motor evoked potentials, a clip was applied to the feeding artery. Histological examination of the excised fundus revealed a true aneurysm with a tortuous, prominent elastica interna and an atrophic tunica media, findings similar to those seen in more proximal vessels in moyamoya [5].

Postoperatively, the patient had a moderate expressive aphasia which resolved over four months. Her drain was removed on day 5 and hydrocephalus did not develop. In light of the history and the DSA appearances, a full vasculitis workup was performed. Levels of anti-nuclear antibodies, ANCA, ACPA, rheumatoid factor, CRP, anti-cardiolipin IgA, IgG and IgM, complement C3, C4 and C50, protein C, protein S and Factor V Leiden were all within the normal range. Antithrombin III activity was reduced at 57% (normal range 75-120%). Transcranial Doppler ultrasound showed normal findings throughout the cerebral circulation, including in the proximal anterior, middle and posterior cerebral and the vertebral and basilar arteries. Biopsy of the *livedo racemosa* skin lesion showed mural thickening in the small calibre arterioles in the chorion layer of the dermis, consistent with a livedo vasculopathy and confirming a diagnosis of aPL-negative SS.

Over the next three years, the patient went on to develop Raynaud's syndrome and, despite aspirin anticoagulation, suffered a cerebellar infarct 30 months following treatment of her aneurysm, resulting in dysarthria and ataxia. Other than occlusion of the right superior cerebellar artery, repeated DSA showed a stable appearance.

3. Discussion

With an incidence of around 4 per million, SS is defined by cerebrovascular events co-occurring with *livedo racemosa.* Skin biopsies usually show arteriolar stenosis and mural thickening but, beyond this, are often non-specific, leading to uncertainty about the underlying pathological process, with proliferation of subendothelial smooth muscle or endothelial cells variably implicated. Stenosis and occlusion results in reduced oxygen provision to the watershed regions between the supply zones of affected arterioles, which manifests as cyanotic skin mottling in a reticular or irregularly circular pattern.

A similar pathomechanism has been offered to explain cerebral DSA findings in some cases of SS, which include transdural and leptomeningeal anastomoses and, as seen in our case, a network of abnormal collateral vessels, a finding labelled "pseudoangiomatosis" by Gondim et al. [2]. Stenosis and occlusion of cerebral arterioles results in chronic brain hypoxia, in turn leading to angiogenesis and collateral formation, akin to the process seen around more proximal vessels affected in moyamoya. In moyamoya, such collateral vessels are prone to rupture, and alteration of circulatory dynamics is thought to lead to structural abnormalities and aneurysm formation [5]. In the presented case, transcranial ultrasound supported the diagnosis of a more distal arteriopathy over moyamoya, showing normal structure and function of the large calibre vessels arising from the circle of Willis and of the posterior circulation, with the affected arterioles presumably too small and distal for Doppler assessment.

It is disputed whether SS carries an elevated risk of intracerebral haemorrhage (ICH) or IVH, given that the majority of patients have exclusively ischaemic strokes and that known ICH risk factors such as hypertension, anticoagulation and smoking are often present in SS [2,6]. Until now, a lack of structural angiographic abnormalities in SS patients following ICH has also supported this position. It may be necessary to consider whether patients with SS, particularly those with prominent collateral vessel formation on DSA, may be at risk of developing aneurysms or suffering ICH from vessel rupture.

SS is not a benign diagnosis, with a mortality rate of 9.5% seen in a cohort followed for six years and epilepsy and stroke common. In the current case, the patient suffered a further, disabling, cerebellar stroke despite antiplatelet therapy. Anticoagulation may prevent the occurrence of these complications and possibly slow the subtle, general cognitive decline seen in many SS patients, although warfarin did not show significant benefit over antiplatelets in terms of reducing the number of ischaemic events per year in a group of 27 patients with aPL-negative SS, two of whom (7%) suffered ICH while on anticoagulation [6]. Derangements of antithrombin III, in

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this case a deficiency, are occasionally seen in conjunction with SS although their significance is unknown.

4. Conclusion

This report describes the unique finding of a distal lenticulostriate artery aneurysm in a patient with Sneddon's syndrome, treated with microsurgical clipping. Distal lenticulostriate aneurysms are exceedingly rare, with around 36 cases reported to date. Vasculopathy secondary to moyamoya, radiation, lupus and cocaine have been implicated in cases of aneurysms in this region [3,4], but this is the first report of an aneurysm in a patient with SS.

This case adds to the evidence that patients with SS may harbour vascular abnormalities, including aneurysms, associated with the small- to mid-calibre arteries of the brain. It underlines the need for a thorough diagnostic workup in younger patients, with or without hypertension, presenting with ICH or IVH. Our angiographic findings lend support to the concept of a "pseudoangiomatous" pattern of abnormal collateral vessels on DSA in patients with SS. This should be considered a risk factor for bleeding and borne in mind when deciding on an appropriate anticoagulation regimen.

Competing interests

The authors declare that they are not aware of any conflicts of interest relating to this case report.

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