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A REVIEW OF SNEDDON'S SYNDROME

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ABSTARCT

The confluence of cerebrovascular disease and livedo racemosa characterises Sneddon's syndrome (SS), a rare, slowly developing non-inflammatory thrombotic vasculopathy (LR). Sneddon syndrome (SS) is becoming more widely considered as a major cause of ischemic stroke in teenagers. Because the natural progression of SS is not clearly specified. Nearly all LR patients report symptoms in the trunk and/or buttocks, although it may take years before LR presents as a stroke. Ischemia is the main cause of most cerebrovascular symptoms (transient ischemic attacks and cerebral infarct). Small and medium-sized arteries are engaged in skin histology at the dermal-epidermal junction. Neurological symptoms include vertigo, headaches, dementia, and recurrent strokes. Although in many cases the significance of the skin lesion is only realised after the stroke reveals itself, recurrent strokes first appear before livedo racemosa. Antithrombotic and antiplatelet drugs are administered as a preventative precaution for a second stroke, despite immunomodulatory therapy's conflicting results.

Keywords: Sneddons syndrome, stroke, skin disease

INTRODUCTION

Sneddon syndrome (SS) is a rare, episodic, or chronic neurocutaneous disorder distinguished by generalised livedo racemosa (symptoms of LR: patchy, violaceous, skin discoloration) and recurrent cerebrovascular episodes such as transient ischemic attacks and stroke[1]. Six patients with severe and widespread livedo reticularis and "many cerebrovascular events of circumscribed and benign cause" were described by Sneddon[2]. Estimates place the prevalence of SS in the general population at 4 cases per 1 million per year, with women between the ages of 20 and 42 being the most common category[3]. However, there have been accounts of the illness beginning in childhood[2]. Additionally, a few people who have the illness, which is assumed to have an adult start, have mild symptoms and indicators ranging back to their earliest infancy[13]. Secondary Sneddon syndrome would be used to describe cases that are thought to occur secondary to another disorder or thrombophilic state[5]. Primary Sneddon syndrome would be used to describe situations where there is no known cause (idiopathic)[6]. According to some studies, the presence or absence of antiphospholipid antibodies (aPL-positive or aPL-negative) should be used to distinguish Sneddon syndrome from other inflammatory or autoimmune diseases rather than thrombophilia[7].

CLASSIFICATION

If no aetiologic cause can be found, patients should be labelled as having "primary Sneddon's syndrome[7]." Clinically, this condition differs from numerous kinds of "secondary Sneddon's syndrome," which typically manifests as a thrombophilic condition or as a component of an autoimmune disorder[8].

EPIDEMIOLOGY

The incidence of SS in the general population is estimated to be 4 per 1 million per year. In hospital-based series, SS is present in 0.25–50% of stroke patients. Sneddon syndrome is more common in women than in men[4]. Between the ages of 20 and 42, women make up about 80% of those with Sneddon syndrome[8]. SS, on the other hand, can strike at any age, including girls as young as 10 and women as old as 64[14].

CLINICAL FEATURES

Dermatological Features

The term LR refers to a net-like, irregular, black erythematous to violaceous skin pattern. LR occurs in more than half of individuals prior to cerebrovascular events[3]. At the time of the stroke, some patients' livedo manifests as an erythematous-to-violet, irregular, net-like skin pattern[3].

Additional dermatological signs of Sneddon syndrome include:

• Acrocyanosis[14]

• Raynaud syndrome[14].

Neurological Features

Neurological symptoms associated with Sneddon syndrome often appear in three stages[1].

Prodromal symptoms include vertigo, wooziness, and headaches[1].

Ischemia in the regions supplied by the middle or posterior cerebral arteries causes individuals to have strokes or transient ischemic episodes regularly in the second stage[2]. Typical symptoms include aphasia, visual field abnormalities, hemiparesis, and sensory difficulties[5].

The third stage is distinguished by significant cognitive decline and early-onset dementia as a result of the cumulative impact of many cerebral infarcts[6]. 77% of people with Sneddon syndrome exhibit cognitive dysfunction, which affects memory, attention, and visuospatial domains, as well as mental disorders such as depression[8].

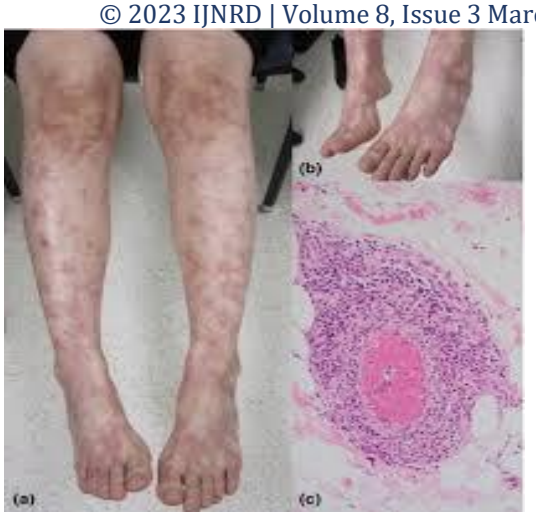

Figure 1:a,b,c shows rashes on the lower limb (symptoms of livido racemosa)[8]

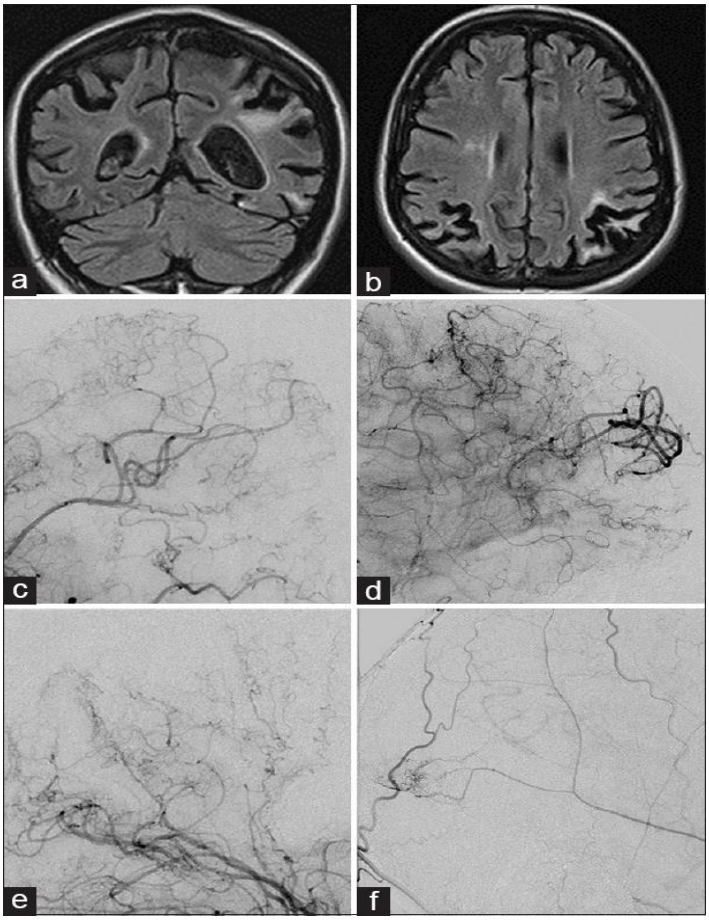

Figure 2 : Diffuse cerebral atrophy and numerous chronic ischemic lesions in the subcortical white matter are visible on brain MRI images (a and b). The distal intracranic branches (c), areas of slow flow (d), thin and flattened distal branches (e), and transdural anastomosis are all visible on cerebral angiograms (c–f) ,(f)[9].

ETIOLOGY

Half of all cases are idiopathic, with no known cause[2]. Oral contraception, high blood pressure, and female reproductive hormones have all been linked to disease progression[7]. The disorder's potential causes, which may include immunological, environmental, genetic, and/or other factors,

are being investigated[3]. It has been documented in a few cases in more than one family member, lending credence to the hypothesis that hereditary vulnerability may occasionally play a role[4]. A person who is genetically susceptible to the disease has a gene (or genes) for the disease, but they may not express it until certain situations lead it to be "activated" or triggered[8].

PATHOLOGY

Dermatopathology

Livedo racemosa, a Sneddon syndrome characteristic, arises more than ten years before recurrent strokes. The significance of the livedo racemosa, which commonly begins in childhood, is only realised in the 20s and 30s after the initiation of the cerebrovascular events[5].

• Occlusion of small or medium-sized arteries results in a persistent restriction of peripheral blood flow, resulting in livedo racemosa.

• It appears as a netting-like branching pattern of violaceous or dark broken circles.

• Unlike livedo reticularis, skin discolouration does not change with warming, but it is more noticeable after cold exposure and during pregnancy.

• Livedo racemosa first affects the buttocks and lower back, then moves on to the dorsal areas of the thighs and arms[5].

Lesions are painless and have no relationship to oedema, ulceration, or pruritus. It sometimes affects the face, hands, or feet[2].

Brain pathology

A generalised vasculopathy characterised by intima and medial growth, with certain vessels displaying fibrotic obstruction and recanalization and affecting small to medium-sized arteries (including brain vessels)[5]. The primary pathologic findings in the presented case were many mild cortical infarcts connected to medium-sized artery blockage and significant localised smooth muscle hyperplasia of smaller artery vessels. Inflammation had little effect on blood vessels[8].

DIAGNOSIS

Sneddon syndrome is diagnosed by the presence of livedo racemosa, specific histological findings on skin biopsy, and localised neurological abnormalities. A history of transient ischemic attacks, a stroke, or imaging evidence of these illnesses can help support the diagnosis[7].

Patients with a possible Sneddon syndrome diagnosis should undergo a cerebral MRI, cardiovascular examination, skin biopsy, and blood testing to rule out coagulopathies and autoimmune disorders[5].

The periventricular deep white matter, often known as the pons, is a common location for the microscopic, multifocal lesions that MRI reveals[3]. Cerebral angiography is abnormal in up to 75% of patients with Sneddon syndrome[6].

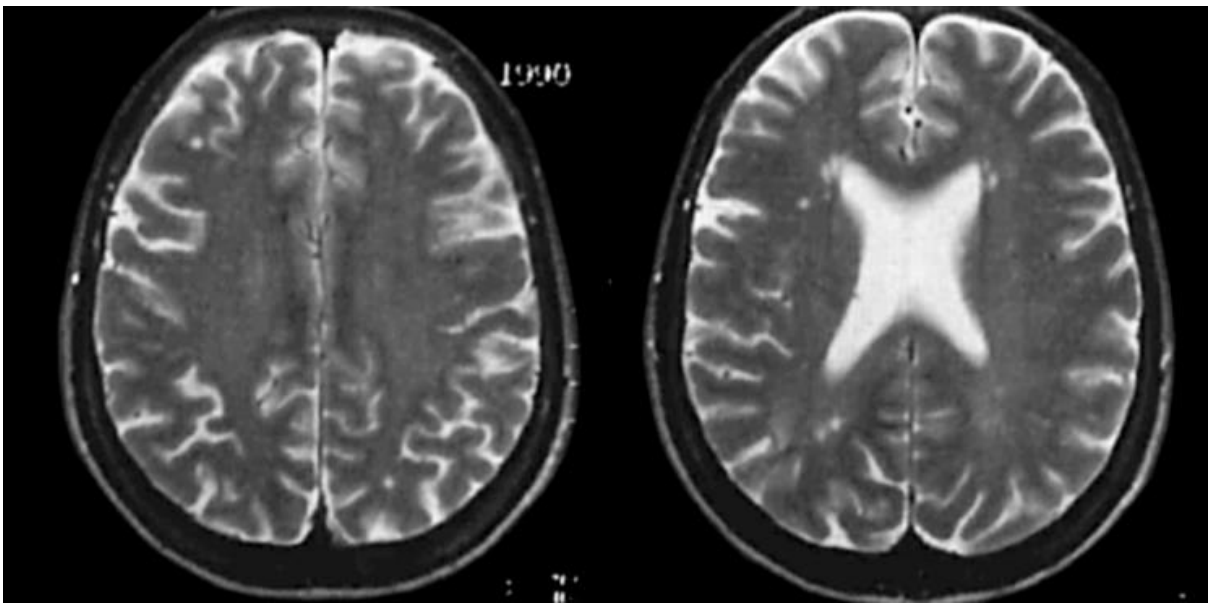

Figure 3 : The scan shows tiny hyperintense foci ranging in size from 1 to 6 mm between the subcortical U fibres and the periventricular region, with one highlighted in the left hemisphere[10].

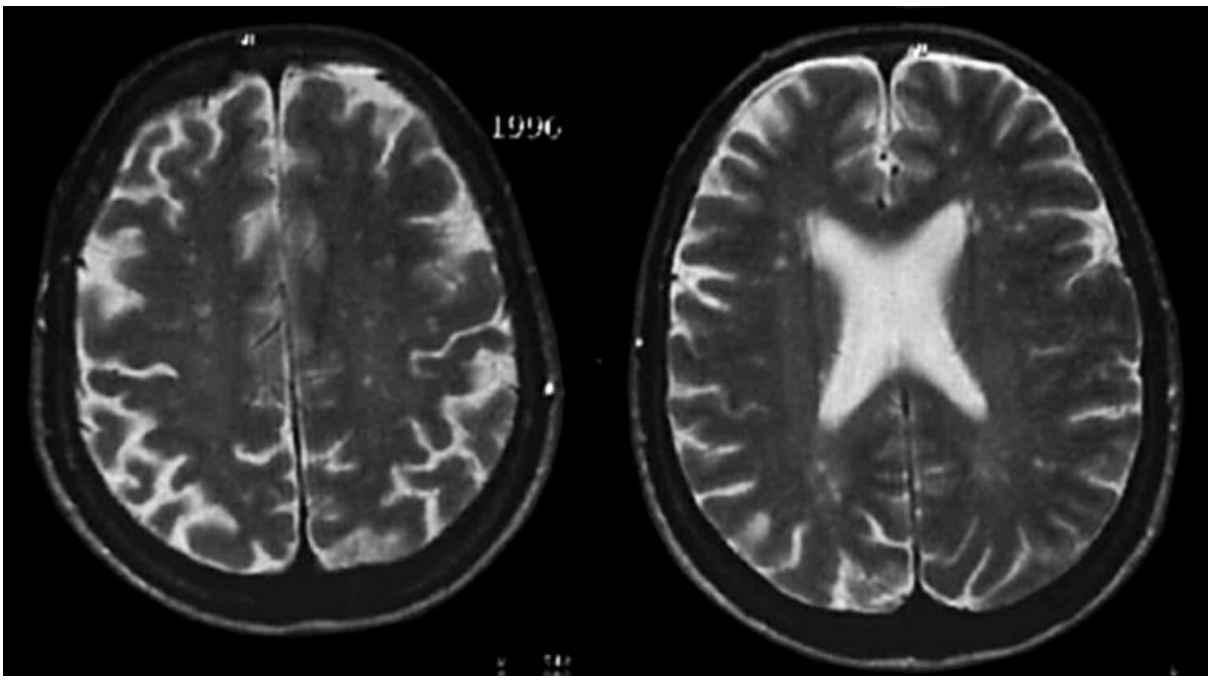

Figure 4: The periventricular region, which ranges in size from 1 to 6 mm, is noticeably enlarged on the image taken six years later. The scan also reveals small hyperintensive foci within the subcortical U fibres[10].

TREATMENT

The optimal technique to treat SS patients is still being debated. For SS patients who have recently undergone an acute ischemic stroke, thrombolytic therapy may be both safe and effective[1]. PGE1 and ACEI (angiotensin-converting enzyme inhibitors) have also been used to treat SS[7]. Nifedipine may help with skin disorders, however it has no effect on preventing cerebrovascular complications[6]. Avoiding smoking and using oestrogen-containing oral contraceptives may help to prevent or alleviate neurological problems[3]. According to one study, patients' neurological and cognitive issues improved after 8 months of monthly intravenous cyclophosphamide therapy[11]. Furthermore, it is critical to address cardiovascular risk factors[4].

Anti-aggregants such as aspirin, direct oral anticoagulants (DOAC), or vitamin K antagonists such as warfarin may be used to thin the blood and prevent the formation of clots[1]. Some doctors recommend that patients with Sneddon syndrome who do not have antiphospholipid antibodies be treated with aspirin less aggressively, and that those who do have antiphospholipid antibodies be treated with DOAC or warfarin with an INR target of 2 to 3[5].

CONCLUSION

Sneddon syndrome is a chronic, progressive disorder caused by the cumulative impact of several cerebral infarcts[12]. It typically causes cognitive impairment and early-onset dementia.[4]

It is a clinical syndrome that mostly affects the cerebral and cutaneous vascular beds and is thought to be caused by a variety of acquired or congenital hemostatic diseases[2]. To some extent, the small number of cases may not fully reflect the syndrome's prevalence because individuals may be unfamiliar with it[1]. More research into the pathophysiology of SS is needed to uncover new etiological groups[5]. Future medicines should identify different therapeutic options for different etiological categories[2].

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