Long-term follow-up of early-onset Sneddon syndrome: A case report

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INTRODUCTION

Sneddon syndrome is a rare vasculopathy of small and medium-sized arteries, characterized by the clinical occurrence of livedo racemosa together with ischemic cerebrovascular events.1 First cases of patients with livedo racemosa and neurologic symptoms were reported in the 1950s and 1960s.1-3 This syndrome is rare with an estimated incidence of 4 of 1 million per year and mainly affects young women with a mean onset in the third decade of life.4,5 We present an early-onset idiopathic form of Sneddon syndrome with a long-term follow-up of 19 years in a young male.

CASE REPORT

In 1998, a 3-year-old boy presented in our department with violaceous, erythematous, irregular netlike maculae, that first appeared 3 months earlier at the face, back of the hands, lower arms, feet, and legs with slight manifestation on the trunk. The irregular netlike maculae were persisting and increased in intensity with cold temperature (Fig 1).

The boy had no other symptoms and felt healthy. Medical examination found no signs of concomitant internal or rheumatoid disease. Screening for antinuclear antibodies, antiphospholipid antibodies, cryoglobulins, or deviations in the coagulation system found no abnormalities. We performed a biopsy out of the white center of the irregular netlike maculae, which found an occluding lymphohistiocytic vasculitis of the deep dermal plexus (Fig 2).

Serologic diagnostic testing still found no signs of antinuclear antibodies, antiphospholipid antibodies, or cryoglobulins. Creatinine clearance was not impaired. Cardiac ultrasound scan found no evidence of heart valvulopathy. Meanwhile, the arterial

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hypertension was treated with amlodipine and enalapril and was well controlled.

We initiated antiplatelet therapy with acetylsalicylic acid (ASA), 100 mg once daily, to prevent further cerebrovascular complications. Because of the persisting skin pain, we started treatment with intravenous immunoglobulin (IVIg) 2 g/kg body weight, administered over 5 days.

After 1 cycle, the patient stated distinct reduced pain as well as reduced joint rigidity. Because skin pain increased 10 month after initial treatment, a second and third cycle of IVIg were performed with renewed improvement of symptoms.

**DISCUSSION**

The pathophysiologic correlate of Sneddon syndrome is a vasculopathy leading to livedo racemosa on the skin and ischemic cerebrovascular events.

Histologic analyses, taken from the white skin at the center of livedo racemosa, showed inflammation, occlusion, and fibrosis of small and medium-sized arteries in the deep dermal plexus. A stepwise process of inflammation and secondary tissue reorganization is proposed in the pathogenesis of Sneddon syndrome. Starting with detachment of endothelial cells, edema of the surrounding tissue, and a lymphohistiocytic inflammatory infiltrate in the initial phase, followed by lumen occlusion by...
mononuclear cells, fibrin, and red blood cells. The third step involves subendothelial proliferation of smooth muscle cells leading to occlusion of the vessel. The late phase is then characterized by fibrosis and atrophy of the affected artery. In our case, the histologic changes can be classified as initial-to-early phase (Fig 2).

Besides the syndrome defining cutaneous and neurologic symptoms, systemic hypertension, and valvular and ischemic heart disease, renal disease, retinopathy, Raynaud phenomenon, and fetal loss are also commonly seen in Sneddon Syndrome. Our patient had systemic hypertension diagnosed in 2013. There were no signs of cardiac, renal, or ophthalmic disease.

Sneddon syndrome can be classified as idiopathic with no causative factor identified, primary anti-phospholipid syndrome associated, and systemic lupus erythematosus related. In this case, Sneddon syndrome was classified as idiopathic.

Therapy of patients with Sneddon syndrome is yet an unresolved problem, as there are no controlled trials available because of the rare incidence of the disease. The main goal is to prevent further cerebrovascular events and to lessen skin symptoms. The use of corticosteroids and immunosuppressants seems to be detrimental. Antiplatelet therapy and anticoagulation both decrease the risk of secondary ischemic events. In patients with antiphospholipid syndrome or coagulation disorder, anticoagulation with high-dose warfarin (international normalized ratio, <3) seems to be more effective than ASA treatment, whereas in antiphospholipid-negative patients, antiplatelet therapy with ASA seems to be equally effective as anticoagulation treatment.

In our patient, the diagnosis of Sneddon syndrome was not made until the cerebrovascular event appeared, so antiplatelet therapy was regrettably not started at the age of 3 years. Because our patient is at higher risk of hemorrhage after suffering hemorrhagic stroke, is negative for antinuclear or antiphospholipid antibodies and cryoglobulines, we initiated antiplatelet treatment in consultation with our neurologic department.

Because the antiplatelet therapy did not reduce skin and joint pain in our patient, we decided to additionally initiate IVIg treatment in analogy to patients suffering from livedo vasculopathy. As reported, IVIg significantly reduces erythema, ulceration, and particularly pain in patients with livedo vasculopathy, possibly via anti-inflammatory and anticoagulatory effects.

Because our patient experienced distinct pain relief after the first cycle of IVIg (2 g/kg body weight), we propose IVIg as an additional treatment option for patients with Sneddon syndrome.

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