INTRODUCTION

In 1979, Susac et al (1) described two young women who presented with multiple branch arterial occlusions in both eyes, hearing loss and neurological symptoms suggestive of a brain microangiopathy. Many similar cases, the majority women, have since been described (2-8). In the last few years we have had an opportunity to see several patients with Susac syndrome, and made the interesting observation that these patients were all vasospastic. This paper describes the history of one of these patients and we formulate the hypothesis that the underlying etiology of the Susac syndrome is a vasospastic dysregulation.

What is a vasospastic syndrome? Raynaud's disease is characterized by attacks of white fingers provoked by cold exposure or emotional stress (9). Although some symptoms of the vasospastic syndrome are common to Raynaud's disease, the vasospastic syndrome is a different entity (10). Patients with this syndrome also suffer from cold hands but they rarely turn white. The majority of these patients are female and have a tendency to low blood pressure. Some also suffer from migraine, tinnitus or variant angina (11), and the plasma endothelin level is elevated in most patients (12). The syndrome is normally mitigated after the menopause.

The vasospastic syndrome can be diagnosed using capillaromicroscopy of the nailfold combined with a standard cooling test (11, 13). The flow arrest time after cooling separates spastic from non-spastic patients (14). In vasospastic patients there is a relation between blood flow in the nailfold capillaries and blood flow in the ophthalmic artery (15) and visual field behavior (16), indicating an involvement of the eye circulation. For that reason the term "ocular vasospastic syndrome" was introduced (17). This ocular vasospastic syndrome is a risk factor for glaucoma (18, 19), anterior ischemic optic neuropathy (AION) (20), vein occlusion (21) and central serous chorio-retinopathy (22). In this case report we describe a patient with this vasospastic diathesis who developed the classical symptoms of the Susac syndrome.
Case report

R. T. was born in 1964. She had no major childhood diseases. She had used contraceptives between 1982 and 1986 without concurrent medication. In the early nineties she suffered from several episodes of diplopia lasting several minutes but without accompanying headaches. In 1992, after major emotional stress at her place of work, she suffered from dizziness, diarrhea, vomiting and disturbance of the sense of balance for a few days. She recovered completely. In 1996 she experienced a loud tinnitus, followed by sudden loss of hearing on the right side.

After about two months the hearing improved and the tinnitus decreased. In February 1997 she experienced marked dysbasia and dizziness and was admitted to a neurological clinic. MRI revealed multiple hyperintensive spots in both hemispheres of the brain (Fig. 1) and in the pons (Fig. 2) but their etiology remained unclear. She had no signs of inflammation in the blood or cerebrospinal fluid. Otolaryngological examination revealed no pathological abnormalities except for the hearing problem on the right side. Transcranial Doppler sonography was normal. The patient recovered clinically after a few weeks.

In April 1998 the patient again experienced extreme stress at her place of work, and became conscious of a scintillating scotoma in her left eye which per-
sisted during the whole day. The next day she still had the scotoma but also had a very strong headache. Four days after the first symptom appeared she had a stable scotoma on her left eye and still some headache.

She visited our clinic and we found a retinal artery branch infarction on her left eye (Fig. 3). Visual acuity was 1.0 in the right eye and 0.8 in the left. Perimetry showed visual field defects on both sides with a paracentral scotoma on the left (Fig. 4), together with marked concentric narrowing of the right visual field. Capillary microscopy showed prolonged flow arrest time after cooling, 69 seconds (normal: less than 11 seconds). Fluorescence angiography confirmed the arterial occlusion. Indocyanine green angiography showed normal choroidal perfusion.

Color-Doppler imaging (CDI) of the retroocular vessels showed a slight decrease in flow in the central retinal artery on both sides, more pronounced on the left.

An extensive clinical and laboratory work-up found no vascular risk factors except the vascular dysregulation. Endothelin-1 in the plasma was markedly increased (3.23 pg/mL vs. our normal lab value of 1.5±0.6). A 24-h blood pressure monitoring showed a tendency to hypotension. Lowest systolic blood pressure was 78 mm Hg.

Short-term therapy with prednisone (500 mg intravenously per day) and long-term therapy with nimodipine (30 mg orally twice daily) was introduced. In the next few days and weeks the patient reported subjective improvement. The visual fields improved slightly but remained pathological on both sides. The retinal edema resolved and the fundus was morphologically close to normal. After six months the plasma endothelin-1 concentration had fallen to 2.62 pg/mL, still pathologically elevated.

DISCUSSION

We have described a patient with the Susac syndrome. This young lady very clearly suffers from a vasospastic syndrome and we propose that there may be a causal relationship between this syndrome and the Susac syndrome. The diagnosis of the vasospastic syndrome in this patient was based on the following indices: 1) her history of cold hands and low blood pressure; 2) a typical alteration of the conjunctival vessels (23); 3) the prolonged flow arrest time after cooling in the nailfold capillary microscopy (24); 4) the increased resistivity in the orbital vessels measured with CDI (25); and 5) the increased level of endothelin-1 (26). This endothelin-1 increase is typical but not specific for vasospastic disorders (27). Other diseases associated with increased endothelin-1 plasma levels were excluded.

The ocular vasospastic syndrome describes the condition where the vasospastic syndrome involves the eye. While the syndrome is normally harmless and reversible, it does increase the risk for many eye diseases, especially for normal tension glaucoma. Retinal (28) and optic nerve head infarctions (29) have been described in rare cases, and especially in vasospastic patients who also suffer from migraine. In our patient the scotoma was due to retinal infarction that had occurred during an episode of severe headache. Less is known about the relationship between vasospasm and sudden loss of hearing although it has been discussed (30). Small infarctions of the brain in vasospastic patients have also been described (31). MRI reveals more frequent brain lesions in patients with migraine (32) and patients with normal tension glaucoma (33) than in normals.

Considering all these observations we now postulate that vascular dysregulation is at least one of the possible causes of the Susac syndrome.

A vascular dysregulation can be primary or secondary. The major causes of a secondary vasospastic syndrome are autoimmune diseases (27). Indeed, findings typical of Susac syndrome were described in a patient with scleroderma (34). The patient we describe, however, suffered from a primary vasospastic syndrome.

For patients with Susac syndrome we recommend a hemodynamic work-up including nailfold capillaroscopy, and the measurement of plasma endothelin concentrations. The therapeutic approach is not firmly established. We treat vasospasm in the acute stage with calcium channel blockers (35) followed by longer term treatment with Mg (36). In the future endothelin blockers might be helpful (37).

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