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SHORT COMMUNICATION

Case report

Susac syndrome: a vasospastic disorder?

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PURPOSE. *The Susac syndrome is a microangiopathy that leads to visual symptoms, hearing loss and neurological symptoms.*
CASE REPORT. *We report on a young woman suffering from this syndrome who also presented the following signs and symptoms typical of a vasospastic syndrome; 1) a history of cold hands, low blood pressure and migraine; 2) a typical alteration of conjunctival vessels; 3) prolonged flow arrest time after cooling in nailfold capillaromicroscopy; 4) increased resistivity in the orbital vessels measured by color Doppler imaging; and 5) an increased plasma level of endothelin-1.*
CONCLUSIONS. *We postulate that the Susac syndrome is a manifestation of the vasospastic syndrome. (Eur J Ophthalmol 2001; 11: 175-9)*

KEY WORDS. *Susac syndrome, Vasospastic syndrome, Nailfold capillaromicroscopy, Endothelin-1*

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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 vaso-spastic 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.

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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-

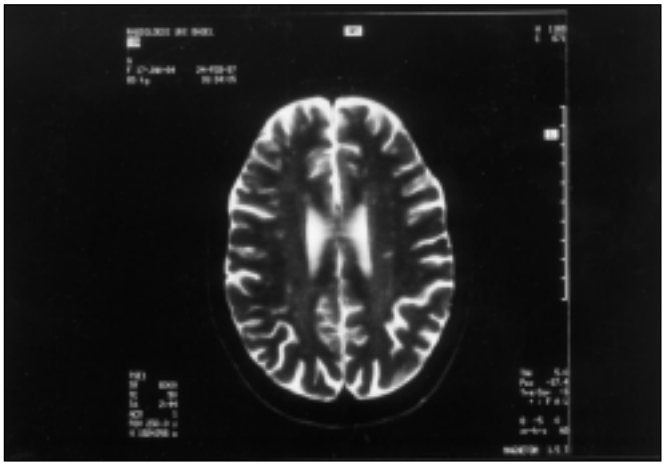

Fig. 1 - *MRI (1997) of the brain showing multiple hyperintensive spots in both hemispheres in a T2 weighted image.*

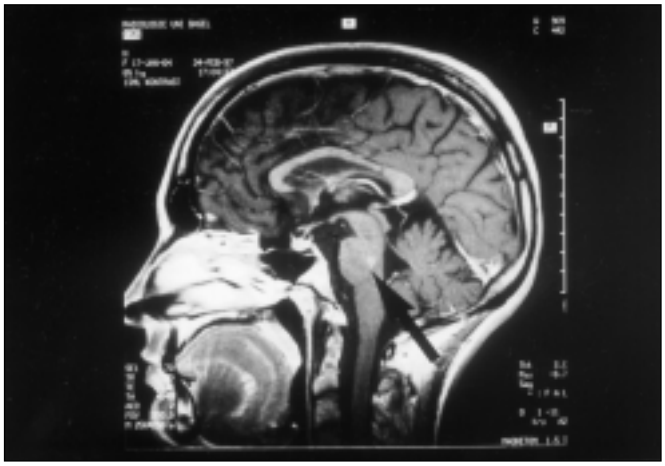

Fig. 2 - *MRI (1997) of the pons with a hyperintensive lesion in a T1 weighted image enhanced with gadolinium.*

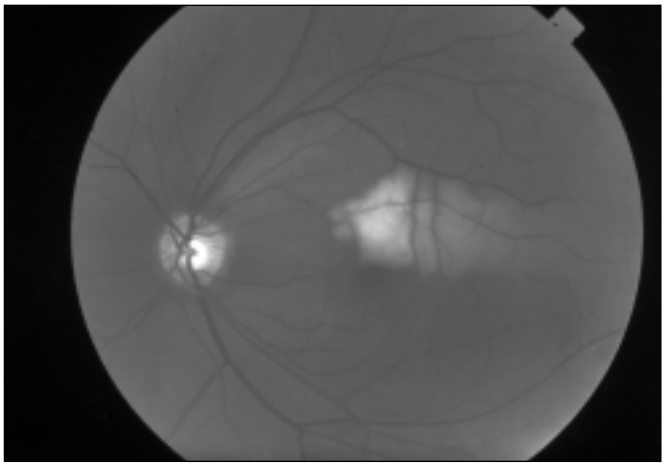

Fig. 3 - *Fundus of the left eye showing a localised infarction of the retina due to an arterial branch occlusion.*

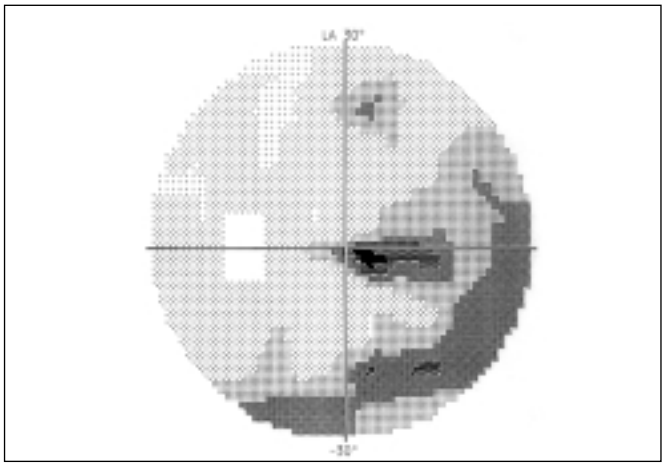

Fig. 4 - *Visual field (Octopus Program G1) of the left eye with a paracentral scotoma corresponding to the arterial branch occlusion.*

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 II 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 leves 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 capillaromicroscopy, 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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REFERENCES

1. Susac JO, Hardman JM, Selhorst JB. Microangiopathy of the brain and retina. Neurology 1979; 29: 313-6.
2. Monteiro ML, Swanson RA, Coppeto JR, Cuneo RA, DeArmond SJ, Prusiner SB. A microangiopathic syndrome of encephalopathy, hearing loss, and retinal arteriolar occlusions. Neurology 1985; 35: 1113-21.
3. MacFadyen DJ, Schneider RJ, Chisholm IA. A syndrome of brain, inner ear and retinal microangiopathy. Can J Neurol Sci 1987; 14: 315-8.
4. Heiskala H, Somer H, Kovanen J, Poutiainen E, Karli H, Haltia M. Microangiopathy with encephalopathy, hearing loss and retinal arteriolar occlusions: two new cases. J Neurol Sci 1988; 86: 239-50.
5. Schwitter J, Agosti R, Ott P, Kalman A, Waespe W. Small infarctions of cochlear, retinal, and encephalic tissue in young women. Stroke 1992; 23: 903-7.
6. Notis CM, Kitei RA, Cafferty MS, Odel JG, Mitchell JP. Microangiopathy of brain, retina, and inner ear. J Neuroophthalmol 1995; 15: 1-8.
7. Papo T, Biousse V, Lehoang P, et al. Susac syndrome. Medicine 1998; 77: 3-11.
8. O'Halloran HS, Pearson PA, Lee WB, Susac JO, Berger JR. Microangiopathy of the brain, retina, and cochlea (Susac syndrome). A report of five cases and a review of the literature. Ophthalmology 1998; 105: 1038-44.
9. Raynaud M. De l'asphyxie locale et de la gangrène des extrémités. Thèse. Paris, 1862.
10. Saner H, Wurbel H, Mahler F, Flammer J, Gasser P. Microvasculatory evaluation of vasospastic syndromes. Adv Exp Med Biol 1987; 220: 215-8.
11. Mahler F, Saner H, Wurbel H, Flammer J. Local cooling test for clinical capillaroscopy in Raynaud's phenomenon, unstable angina, and vasospastic visual disorders. Vasa 1989; 18: 201-4.
12. Zimmermann M. Endothelin in cerebral vasospasm. Clinical and experimental results. J Neurosurg Sci 1997; 41: 139-51.
13. Gasser P. Video-nailfold-microscopy and local cold test: morphological and hemodynamic correlates in 124 healthy subjects. Vasa 1991; 20: 244-51.
14. Gasser P, Flammer J. Blood-cell velocity in the nailfold capillaries of patients with normal-tension and high-tension glaucoma. Am J Ophthalmol 1991; 111: 585-8.
15. Gasser P, Orgul S, Dubler B, Bucheli B, Flammer J. Relation between blood flow velocities in the ophthalmic artery and in nailfold capillaries. Br J Ophthalmol 1999; 83: 505.
16. Guthauser U, Flammer J, Mahler F The relationship between digital and ocular vasospasm. Graefes Arch Clin Exp Ophthalmol 1988: 226: 224-6.
17. Flammer J, Gasser P, Prunte CH, Yao K. The probable involvement of factors other than ocular pressure in the pathogenesis of glaucoma. In: Drance SM, Buskirk Van EM, Neufeld AH, eds. Pharmacology of glaucoma. Baltimore: Williams and Wilkins, 1992; 273-83.
18. Flammer J, Guthauser U, Mahler F. Do ocular vasospasm help cause low tension galucoma? Doc Ophthalmol Proc Ser 1987; 49: 397-9.
19. O'Brien C. Vasospasm and glaucoma. Br J Ophthalmol 1998; 82: 855-7.
20. Kaiser HJ, Flammer J, Messerli J. Vasospasm - A risk factor for nonarteritic anterior ischemic optic neuropathy? J Neuroophthalmol 1996; 16: 5-10.
21. Messerli J, Flammer J. Central vein thrombosis in younger patients. [Article in German]. Klin Monatsbl Augenheilkd 1996; 208; 303-5.
22. Prunte C, Flammer J. Choroidal capillary and venous congestion in central serous chorioretinopathy. Am J Ophthalmol 1996; 121: 26-34.
23. Orgül S, Flammer J. Perilimbal aneurysms of conjunctival vessels in glaucoma patients. Ger J Ophthalmol 1995; 4: 94-6.
24. Gasser P, Flammer J, Guthauser U, Mahler F. Do vasospasms provoke ocular diseases? Angiology 1990; 41: 213-20.
25. Kaiser HJ, Schötzau A, Flammer J. Blood-flow velocities in the extraocular vessels in normal volunteers. Am J Ophthalmol 1996; 122: 364-70.
26. Miyauchi T, Masaki T. Pathophysiology of endothelin in the cardiovascular system. Annu Rev Physiol 1999; 61: 391-415.
27. Flammer J, Pache M, Resink TH. Vasospasm, its role in the pathogenesis of diseases with particular reference to the eye. Prog Retin Eye Res 2001; 20: 319-49.
28. Graveson CS. Retinal artery occlusion in migraine. Br J Ophthalmol 1949; 2: 838-40.
29. Weinstein JM, Feman SS. Ischemic optic neuropathy in migraine. Arch Ophthalmol 1982; 100: 1097-100.
30. Viirre ES, Baloh RW. Migraine as a cause of sudden hearing loss. Headache 1996; 36: 24-8.
31. Prunte CH, Flammer J. Mikrozirkulationsstörungen als pathogenetischer Faktor des Glaukoms - wird der Verdacht zur Gewissheit? In: Prunte C, Flammer J, Hrsg. Das Glaukom in der Praxis. Basel: Karger, 1997; 39-52.
32. Arnold G, Reuter U, Kinze S, Wolf T, Einhaupl KM. Migraine with aura shows gadolinium enhancement which is reversed following prophylactic treatment. Cephalalgia 1998; 18: 644-6.
33. Stroman GA, Stewart WC, Golnik KC, Cure JK, Olinger RE. Magnetic resonance imaging in patients

with low-tension glaucoma. Arch Ophthalmol 1995; 113: 168-72.
34. Sahin O, Goldstein DA, Tessler HH. Findings typical of Susac's syndrome in a patient with scleroderma . Retina 1999; 19: 476-7.
35. Gasser P, Flammer J. Short-and long-term effect of nifedipine on the visual field in patients with presumed vasospasm. J Int Med Res 1990; 18: 334-9.
36. Dettmann ES, Lüscher THF, Flammer J, Haefliger IO. Modulation of endothelin-1-induced contractions by magnesium/calcium in porcine ciliary arteries. Graefes Arch Clin Exp Ophthalmol 1998; 236: 47-51.
37. Meyer P, Flammer J, Luscher THF. Endothelium-dependent regulation of the ophthalmic microcirculation in the perfused porcine eye: role of nitric oxide and endothelins. Invest Ophthalmol Vis Sci 1993; 34: 3614-21.