Case Report

Ophthalmologica

Ophthalmologica 2003;217:451–453
DOI: 10.1159/000073079

Received: December 11, 2002
Accepted after revision: April 24, 2003

Transient Raise of Endothelin-1 Plasma Level and Reduction of Ocular Blood Flow in a Patient with Optic Neuritis

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Key Words
Endothelin-1 · Optic neuritis · Multiple sclerosis · Vascular dysregulation

Abstract
Purpose: To analyze how far an ischemic component might have been involved in optic neuritis. ***Methods:*** Case report: a 32-year-old man with symptoms characteristic for optic neuritis underwent extensive clinical, laboratory/serological and vascular examination for systemic associations and vascular involvement. ***Results:*** The patient was found to have a temporary ocular blood flow dysregulation and increased plasma endothelin-1 levels which decreased after the acute phase of the optic nerve. ***Conclusions:*** We conclude that there might be an ischemic component in this patient with optic neuritis and hypothesize that this ischemic component is at least in part due to a temporarily increased endothelin-1 level.

Introduction

Optic neuritis occurs characteristically in relatively young patients. The etiology is often unknown. In other cases it is a manifestation of a systemic disease as multiple sclerosis. The fact that initially the visual field is often extensively altered and the optic nerve head is sometimes pale already in the acute phase raises the question whether, beside the inflammatory process, a relative ischemia might contribute to the symptoms.

Case Report

A 32-year-old otherwise healthy male patient was seen 4 days after onset of the initial symptoms (reduced visual acuity, pain during eye movements and disturbed color vision in the right eye). The symptoms aggravated during physical activity (Uhthoff phenomenon). Visual acuity was 20/100 in the right and 20/16 in the left eye. Furthermore, a relative afferent pupillary defect on the right side could be observed and a subjective desaturation of red color on the right side was described. Funduscopic examination showed a pale optic disc swelling.

The resistivity index of the central retinal artery measured with Color Doppler imaging (CDI) was increased and the HRF 'flow' parameter decreased on the right side and normal in the left eye. The latencies of the visual-evoked potentials (VEP) were prolonged and the amplitudes reduced on the right side but normal on the left side (table 1). The visual field (measured with the Octopus program G 1) revealed marked defects in the right eye (MD: 17.8), especially in the lower hemifield (fig. 1). MRI scan was normal. A 24-hour blood pressure monitoring revealed normal values. C-reactive protein (CRP), plasma and full-blood viscosities were normal. The measured serological parameters (EBV-VCA IgG, HSV IgG, VZV IgG, HIV, lues, borreliosis) were normal. Mitochondrial DNA examination for Leber's opticus neuropathy was negative.

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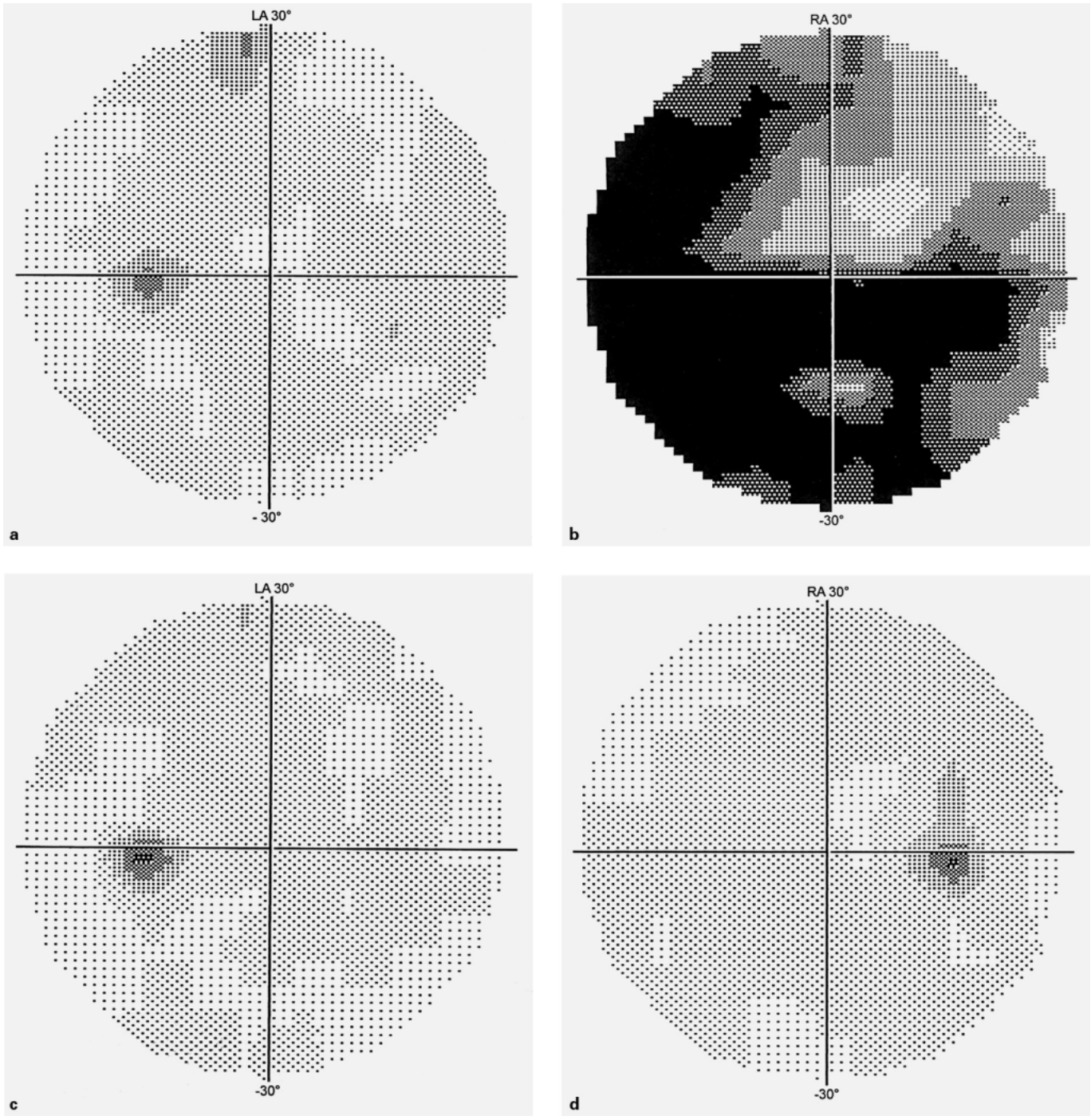

Fig. 1. Visual fields in the acute phase (**a** left eye, **b** right eye) and 3 weeks later (**c** left eye, **d** right eye).

Immediately after the first visit, a therapy was introduced which consisted of high doses of intravenous methylprednisolone (b.i.d. 500 mg) for 3 days followed by oral prednisone (1 mg/kg daily for 11 days) and tapered down during the next 10 days, the calcium channel blocker nimodipine (t.i.d. 30 mg p.o.) and dipyridamole (t.i.d. 75 mg p.o.)

During the next 3 weeks the visual acuity on the right eye improved to 20/16 and the visual field normalized. The resistivity index of the central retinal artery measured with CDI decreased and the HRF 'flow' parameter increased and revealed normal values after 7 months (table 1).

Table 1. Clinical parameters evaluated in the acute phase and 7 months later after full recovery of visual function

	Right eye		Left eye	
	June 1997	January 1998	June 1997	January 1998
Visual acuity	20/40	20/16	20/16	20/16
Resistivity index	0.76	0.63	0.69	0.64
Central retinal artery; CDI; norm 0.63–0.78				
Flow (Heidelberg retina flowmeter)	744	1,101	1,069	907
VEP (amplitudes); norm 5.7–12.1 μm	4.4	8.1	7.1	6.4
VEP (latencies); norm 92–110 ms	121	109	101	92

Endothelin-1 (ET-1) plasma levels were determined as previously described [1]. ET-1 plasma level measured 5 days after the onset of the initial symptoms (and 1 day after institution of therapy), was 5.0 pg/ml (reference value for males in our laboratory: 1.67 ± (SD) 0.34 pg/ml). The ET-1 plasma level was measured again 7, 10 and 48 months after the acute episode in a stage in which the patient had clinically fully recovered. Samples were always taken at the same time in the morning as it had been done with our normal values. The ET-1 levels decreased continuously from 5.0 pg/ml to 4.15, 3.43 and 2.21 pg/ml, respectively, which was less than during the acute phase, but still above the normal range.

Discussion

We describe a young male patient with an optic neuritis, a temporary ocular blood flow reduction and increased ET-1 level which may lead to decreased blood flow. Interestingly, in our patient, the blood flow was decreased only in the right eye, although the ET-1-level was increased systemically. A hypothesis might be that, in the affected eye, circulating ET-1 may reach directly the smooth muscle cells and pericytes, due to a disturbed blood-brain barrier. Indeed, it has been shown that the ocular vasculature is particularly sensitive to changes in ET-1 plasma levels [2].

Whether the optic disc swelling had a partial influence on the altered CDI and HRF parameters is not known. How far the systemic treatment might have influenced the ET-1 plasma levels is also not known. If steroids had any influence, then they rather decreased the ET-1-plasma levels. Calcium channel blockers also seem to decrease the ET-1 plasma level [3]. We can therefore assume that the ET-1 plasma levels were indeed markedly increased. Whether the continuously decreasing but still slightly elevated ET-1 level 48 months after the acute phase have an impact is not yet clear [4]. In fact, elevated ET-1 levels have been described in several other diseases including multiple sclerosis [5, 6].

Whether the increased ET-1 plasma level reflects a possible cause of the optic neuritis or is secondary to it is not yet clear. The clinical relevance of such a temporary ocular blood flow reduction together with a temporary increase of ET-1 plasma level in patients with optic neuritis remains to be established.

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