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Ocular Ischemic Syndrome in Diabetic Patients

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Purpose: Diabetes mellitus aggravates carotid occlusive disease, that can manifest as ocular ischemic syndrome (OIS). Ocular manifestations and visual prognosis of OIS in diabetic patients were retrospectively analyzed.

Methods: Twenty-three consecutive diabetic patients with OIS were divided into two groups according to the presence of iris neovascularization, and the clinical features were reviewed.

Results: In the first group, 14 eyes of 12 diabetic patients (11 men and 1 woman) had no iris neovascularization. Two patients had bilateral OIS. The ages in this group ranged from 50–75 years. Four eyes with optic atrophy or ischemic optic neuropathy had severe visual loss. Six eyes with hypoperfusion retinopathy or retinal vein obstruction and 2 eyes with cataract had mild visual loss. Each eye with amaurosis fugax or retinal neovascularization had no visual deterioration. Asymmetrical retinopathy was observed in 2 patients. Carotid surgery stabilized and resolved amaurosis fugax and hypoperfusion retinopathy. In the second group, 11 eyes of 11 patients had iris neovascularization. The patients were all male and their ages ranged from 53–77 years. All eyes with iris neovascularization had severe visual deterioration. In 5 patients, asymmetrical ocular manifestation was observed. Carotid reconstruction surgery and ophthalmological treatment were not successful for recovering a satisfactory visual outcome in OIS.

Conclusion: The features of OIS in diabetic patients mimic diabetic retinopathy and manifest with asymmetrical ocular findings. Iris neovascularization is an indicator of poor visual prognosis. It is essential to recognize the early stages of OIS associated with diabetes mellitus. **Jpn J Ophthalmol 1999;43:31–35**

Key Words: Asymmetric retinopathy, diabetes mellitus, iris neovascularization, ocular ischemic syndrome, visual prognosis.

Introduction

The vascular complications in diabetic patients comprise large vessel disease, macroangiopathy, and also diabetic microangiopathy that is considered to be specific to diabetes. Macroangiopathy is characterized by ischemic heart disease, cerebrovascular disease and peripheral vascular disease.[1] Carotid occlusive disease, one of the cerebrovascular diseases, is a common cause of stroke and presents with several ocular manifestations, collectively referred to as the ocular ischemic syndrome (OIS).[2,3] Signs of OIS are uveitis and iris neovascularization in the anterior segment of the eye.[3] In the ocular fundus, the retinopathy due to chronic hypoperfusion consists of dilated and beaded vessels, dot and blot hemorrhages, and neovascular proliferations.[3] In addition, amaurosis fugax, retinal artery occlusion, and ischemic optic neuropathy can develop due to emboli from the carotid arteries.[3] Previous reports [3–5] have emphasized the responsibility of the ophthalmologist in recognizing OIS and planning the evaluation and treatment of this disease. When OIS is associated with diabetes mellitus, the ocular manifestations of both diseases may be superimposed, which may lead to some confusion. In this study, we retrospectively analyzed the ocular manifestations of diabetic patients

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with ocular ischemic syndrome, and discussed the relationship between diabetic retinopathy and carotid atherosclerosis as a manifestation of macroangiopathy.

Materials and Methods

The clinical features of 23 consecutive diabetic patients with OIS seen at the Diabetes Unit of the Kobe University Hospital Eye Clinic were retrospectively reviewed. Among the 23 patients with non-insulin–dependent diabetes mellitus (NIDDM), there were 22 men and 1 woman. Their ages ranged from 50–77 years, with a mean age of 64.8 years.

Evaluation of the carotid artery in 19 patients was done by conventional carotid angiography or digital subtraction angiography of the carotid vessels. In the remaining 4 patients, carotid duplex scanning and magnetic resonance (MR) angiography revealed carotid stenosis or occlusion.

Medical history was recorded for each subject, including current smoking habits and morbidity, and each patient received a standard physical examination. All patients underwent slit-lamp biomicroscopy, fundoscopy, and visual acuity tests. Fluorescein angiography was also performed when necessary. All patients were followed for longer than 6 months.

Ten patients underwent carotid artery surgery. Carotid endartectomy (CEA) was performed on 7 patients and superficial temporal artery to middle cerebral artery bypass was performed on 3 patients who had 100% occlusion.

Results

Of the 23 diabetic patients, 2 were treated by diet therapy alone, 17 received oral hypoglycemic agents, and none was given insulin injections. The rest had no management of diabetes at the initial ophthalmologic examination. Carotid evaluation disclosed a 60% or greater stenosis ipsilateral to the ischemic eye.

Individual patients were categorized according to the presence or absence of iris neovascularization. The first group of 12 patients had no iris neovascularization. Clinical profiles of the 14 eyes of these patients are presented in Table 1. Eleven were men and 1 was a woman. Their ages ranged from 50–75 years (mean age 64.6 years). Two cases were bilaterally affected. Associated risk factors included hypertension in 6 patients, cigarette smoking and prior stroke in 2 other patients. Arteriosclerosis obliterans (ASO) was present in 4 patients and cardiac disease in 3. Transient ischemic attacks (TIA) were observed in 1 patient. A decrease in visual acuity in the affected eyes was observed in 12 eyes in this group, 2 of these 12 eyes had slight visual deterioration due to cataract. In 4 eyes with optic atrophy, anterior or posterior ischemic optic neuropathy and severe visual loss was observed. In 6 eyes with hypoperfusion

Table 1. Clinical Presentation of Ocular Ischemic Syndrome Without Iris Neovascularization

Case No.	Age/Sex	Carotid Stenosis (%)	General Condition	Visual Acuity		Ocular Manifestation Symptom and Sign	Treatment
				Initial	Final		
1	66/M	60	HT, stroke, smoking	0.6	0.6	AF, cataract	CEA
2	70/M	70	HT, ASO	0.6	0.6	AF, cataract	CEA
3	68/M	90	HT	1.2	1.2	AF	CEA
4	61/F	80	Stroke	0.6	HM	Hypo R, Chol E, CRAO	CEA
		100		HM	LP(−)	Optic atrophy	
5	59/M	90	ASO	1.0	0.1	Hypo R, RNV, (SDR)	PC
6	72/M	90	TIA	0.6	0.6	Hypo R	CEA
7	61/M	100	HT, angina	0.5	0.6	Hypo R, RNV, (SDR)	Bypass
8	69/M	60	HT	0.6	0.03	Hypo R, glaucoma (SDR)	PC
9	75/M	70	HT, ASO	0.2	CF	Hypo R	
		100	Angina	LP(−)	LP(−)	Optic atrophy	
10	50/M	60	ASO, angina	0.01	CF	AION	
11	52/M	99		0.03	0.01	PION, soft patch Chol E	
12	72/M	100		0.5	0.04	BRVO, glaucoma	Trabe

AF: amaurosis fugax. AION: arterior ischemic optic neuropathy. ASO: arteriosclerosis obliterance. BRVO: branch retinal vein obstruction. bypass: superficial temporal artery to middle cerebral artery bypass. CEA: carotid endartectomy. CF: counting fingers. Chol E: cholesterol emboli. CRAO: central retinal artery obstruction. HM: hand motion. HT: hypertension. hypo R: hypoperfusion retinopathy. LP(−): no light perception. PC: retinal photocoagulation. PION: posterior ischemic optic neuropathy. RNV: retinal neovascularization. (SDR): simple diabetic retinopathy in fellow eye. TIA: transient ischemic attack. Trabe: trabeculectomy.

retinopathy or retinal venous obstruction, mild or moderate visual loss was found. One patient with amaurosis fugax had no visual deterioration. In 1 patient with good visual acuity, retinal neovascularization was observed. Simple diabetic retinopathy (SDR) was found in 3 fellow eyes (Table 1). Retinal neovascularizations were found in 2 of 3 cases and the affected eyes showed asymmetric retinopathy. There was resolution of amaurosis fugax or hypoperfusion retinopathy in 5 eyes after carotid reconstruction surgery, including CEA and bypass surgery. However, 1 patient had retinal artery occlusion after CEA, leading to severe visual loss. In the remaining 8 eyes without carotid reconstruction surgery, 2 eyes received retinal photocoagulation and 1 eye had trabeculectomy for glaucoma. However, visual acuities were 0.1, 0.03, and 0.04 at the end of follow-up for these 3 eyes. The other 5 eyes had no treatment because of poor visual acuity, except case 9 who wanted no further treatment.

The second group of 11 patients with iris neovascularization is presented in Table 2. All patients were men and had unilateral carotid involvement. Their ages ranged from 53–75 years (mean age, 65.1 years). Systemic arterial hypertension was found in 6, stroke in 5, smoking in 2, and TIA in 1 patient. ASO was found in 2 cases and hyperlipidemia in one. At the initial ophthalmologic examination, iris neovascularization was found in 6 eyes (cases 1–6), all of which had hypoperfusion retinopathy. Four eyes had a visual acuity of 0.1 or less. The remaining 2 eyes had progressive visual deterioration despite trabeculectomy and retinal photocoagulation. Carotid reconstruction surgery resulted in neither regression of the iris neovascularization nor visual improvement. In eyes with hypoperfusion retinopathy iris neovascularization was not present at the initial visit (cases 7–10), and slight or moderate visual deterioration was observed. However, iris neovascularization developed 3 months later in cases 7 and 8, 4 months later in case 9, and 12 months later in case 10. One eye (case 11) with optic atrophy developed iris neovascularization 3 months later. Severe visual loss occurred despite photocoagulation, trabeculectomy, and carotid reconstruction surgery in all eyes. In 5 patients with iris neovascularization, the contralateral eyes had signs of simple diabetic retinopathy (SDR) (Table 2). The ocular manifestations were asymmetrical in these patients.

Discussion

Major risk factors for macroangiopathy in the white NIDDM population have been identified as dyslipidemia, hypertension, hyperinsulinemia, and obesity.[1] In addition to these factors, the duration and degree of hyperglycemia are significant and are independent risk factors for macroangiopathy. These factors are important for Japanese patients as well.[6,7] Predisposing factors, such as carotid atherosclerosis, are also very prevalent.[8,9]

Ultrasound high B-mode imaging on carotid arteries demonstrated advanced atherosclerosis in diabetic patients.[2,10] Hypertension is found in more than

Table 2. Clinical Presentation of Ocular Ischemic Syndrome With Iris Neovascularization

Case No.	Age/Sex	Carotid Stenosis (%)	General Condition	Visual Acuity		Ocular Manifestation Symptom and Sign	Treatment
				Initial	Final		
1	75/M	100	HT, stroke	0.01	HM	hypo R	PC, Trabe, Cry
2	53/M	100		0.9	0.1	hypo R, (SDR)	Trabe
3	72/M	70	Stroke	LP(−)	LP(−)	hypo R, (SDR)	PC
4	72/M	100	Hyperlipidemia	0.4	0.01	hypo R, (SDR)	PC
5	64/M	100	HT, stroke	0.1	LP(−)	hypo R, VH	PC, bypass
6	66/M	100	HT	0.1	LP(−)	hypo R	Bypass
7	60/M	100	HT, stroke	0.7	LP(−)	hypo R→CRAO→INV	PC
8	60/M	100	HT, stroke	0.2	0.01	hypo R→INV, (SDR)	PC
9	55/M	100	TIA, smoking	0.2	CF	hypo R→INV	PC, bypass
10	67/M	99	ASO, smoking	0.3	LP	hypo R→INV, (SDR)	CEA
11	72/M	90	HT	0.03	HM	Optic atrophy→INV	Trabe

ASO: arteriosclerosis. bypass: superficial temporal artery to middle cerebral artery bypass. CEA: carotid endartectomy. CF: counting fingers. CRAO: Central retinal artery obstruction. cry: retinal cryopexy. HM: hand motion. HT: hypertension. hypo R: hypoperfusion retinopathy. INV: iris neovascularization. LP: light percetion. LP(−): no light perception. PC: retinal photocoagulation. (SDR): simple diabetic retinopathy in fellow eye. TIA: transient ischemic attack. Trabe: trabeculectomy. VH: vitresus hemorrhage.

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two thirds of the patients with OIS, and diabetes mellitus is observed in greater than one half.[11] The prevalence of both diabetes and hypertension was higher among patients with OIS than in the Framingham population.[12]

In this study, in addition to diabetes mellitus, other risk factors, including hypertension, cigarette smoking, hyperlipidemia, and prior stroke, were observed in 17 of 23 patients. Ocular ischemic syndrome has been reported to occur more frequently in men than in women, by a ratio of approximately 2:1.[3,11] However, there was an even higher preponderance of men in this study. We need to analyze this preponderance of male patients in Japan.

The acute symptoms and signs of OIS are amaurosis fugax, cholesterol emboli of the retina, retinal artery occlusion, and ischemic optic neuropathy due to atheromatous plaques from carotid arteries. In this study, these symptoms and signs were observed in 8 eyes. The stroke rate after retinal artery occlusion or hemispherical TIA is more frequent for patients with amaurosis fugax.[13] A retrospective study of 71 patients with ischemic optic neuropathy showed a two- to three-fold higher mortality than expected.[14] The five-year mortality in patients with OIS has been demonstrated to be about 40%, which is significantly higher than the 11% mortality rate in the Framingham group.[11,12] High mortality in patients with OIS, especially associated with hypertension and diabetes, may suggest severe atherosclerosis with additional affects on the heart and kidney.

Carotid occlusive disease can lead to progressive chronic hypoperfusion of the eye. In the ocular fundus, hypoperfusion retinopathy was observed in 16 of the 25 eyes. In addition to retinopathy, iris neovascularization is often encountered.[3–5] The features of OIS resemble diabetic retinopathy, which is a common diabetic complication of microangiopathy. Moreover, high-grade carotid stenosis may worsen the retinopathy of diabetic patients. In this study, 7 eyes were found with asymmetrical ocular changes. Eyes ipsilateral to the carotid atheroma in diabetic patients had further compromised retinal microcirculation due to macroangiopathy. Previous studies[15–17] reported an association of carotid occlusive disease and diabetes in the development of neovascular glaucoma or asymmetric retinopathy. Diabetic patients who have unilateral retinopathy and iris neovascularization or marked asymmetry of retinopathy should be examined for possible carotid occlusive disease.

The visual prognosis following ophthalmological treatment for iris neovascularization in OIS, including retinal photocoagulation, cryopexy, and glaucoma procedures, is not encouraging,[5] though it is promising in diabetic retinopathy, to a certain extent. Carotid surgery was not beneficial in stabilizing iris neovascularization, as also shown in this study.[18] The presence of iris neovascularization indicates poor visual prognosis. The incidence of OIS is unknown. It is possible that this syndrome is underdiagnosed, especially when associated with diabetes. It is important to recognize the underlying carotid occlusive disease in diabetic patients because of the poor visual prognosis and high mortality. We should manage not only the diabetic retinopathy, but also the carotid atherosclerosis to preserve good visual function in diabetic patients. It is essential to detect the early stage of OIS before the onset of iris neovascularization.

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