DIABETIC PAPILLOPATHY IN TYPE II DIABETIC PATIENTS

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Purpose: To evaluate the patient characteristics and fundus findings of patients with type II diabetes presenting with diabetic papillopathy.

Methods: The authors retrospectively reviewed the medical records of 3,235 patients with diabetes followed in their institution since 1986 and identified the patients with unilateral or bilateral transient disk swelling and without significant deterioration of best-corrected visual acuity. The authors investigated patient demographics, symptoms, fundus findings, ancillary test results, and clinical course of those patients.

Results: Twenty-four eyes of 16 patients with type II diabetes mellitus met the criteria. Patients had a mean age of 57.1 (±8.8) years and had diabetes mellitus of long duration (mean 10.0 ± 8.6 years). Approximately half of the patients had poor metabolic control. Disk swelling was bilateral in 8 (50%) patients and resolved in an average of 7.8 ± 3.7 months. A total of 13 (54%) eyes had nonproliferative and 2 (8%) eyes had proliferative diabetic retinopathy at presentation. In 4 (17%) eyes retinopathy progression into the proliferative stage occurred and panretinal photocoagulation was performed.

Conclusions: Diabetic papillopathy may be found in older patients with type II diabetes. Nonproliferative or proliferative diabetic retinopathy as well as macular edema may also be associated with this disorder.

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Unilateral or bilateral transient optic disk swelling associated with minimal deterioration of visual function especially in young people with type I diabetes mellitus (DM) has been described by many investigators since 1971.[1-4] Because of the benign course of this disease it was referred to as diabetic papillopathy. The young age of affected patients, minimal optic nerve dysfunction, and remission usually without significant sequela helped distinguish the disease from anterior ischemic optic neuropathy (AION).[5-8] This disease has also been reported in elderly patients with type II DM.[9] In this study we evaluated the demographic characteristics and clinical findings of older patients with type II DM diagnosed with diabetic papillopathy at our institution.

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Patients and Methods

We retrospectively evaluated the medical records of all patients with diabetes followed and treated in our institution since 1986 and identified all patients with disk swelling. Patients with unilateral or bilateral (simultaneous or sequential) transient disk swelling without accompanying significant visual loss or visual field defect and resolving with no permanent sequel (such as optic atrophy) were included in the study (Table 1).

Patient age, race, and sex; type and duration of DM; data about metabolic control; systemic blood pressure; renal function; best-corrected visual acuity; characteristics and duration of disk swelling (from the fundus photographs); fundus fluorescein angiography find-

Table 1. Patient Characteristics

Patient No.	Sex	Age, yr	DM Duration, yr	Diabetic Retinopathy	Metabolic Control	Involved Eye	BCVA Initial	BCVA at Presentation	BCVA After Resolution	Disk Swelling	Papillopathy Duration, mo	Follow-up, mo
1	F	55	8	NPDR	Good	Left	Unknown!	20/25	20/25	Diffuse	5	36
2	F	65	19	NPDR	Poor	Right	20/60	20/200	20/60	Diffuse	16	48
						Left	20/25	20/200	20/30	Diffuse	8	
3	M	50	1	NPDR	Good	Right	20/20	20/20	20/20	Diffuse	4	24
						Left	20/20	20/20	20/20	Diffuse	6	
4	M	61'	3	Absent	Good	Right	20/20	20/20	20/20	Diffuse	6	12
5	M	43	10	NPDR	Poor	Right	Unknownt	20/200	20/60	Diffuse	7	12
				NPDR		Left	Unknown!	20/60	20/60	Diffuse	7	
6	M	68	22	NPDR	Poor	Right	20/20	20/30	20/25	Diffuse	12	36
				NPDR		Left	20/20	20/25	20/25	Diffuse	12	
7	M	48	1	Absent	Poor	Right	Unknown!	20/25	20/20	Diffuse	6	36
				Absent		Left	Unknown!	20/25	20/20	Diffuse	7	
8	F	57	20	NPDR	Poor	Right	20/20	20/30	20/20	Diffuse	7	12
9	M	70	1	NPDR	Poor	Right	20/25	20/30	20/25	Diffuse	9	36
10	M	64	1	Absent	Good	Right	Unknown!	20/30	20/30	. Diffuse	8	10
11	F	58	1	Absent	Good	Right	Unknown!	20/30	20/30	Diffuse	12	36
				Absent		Left	Unknown!	20/30	20/30	Diffuse	12	
12	M	54	10	NPDR	Poor	Right	20/50	20/60	20/50	Diffuse	3	24
				NPDR		Left	20/50	20/60	20/60	Diffuse	3	
13	F	40	10	Absent	Good	Right	20/20	20/20	20/20	Focal	4	12
14	M	64	25	NPDR	Good	Left	Unknown!	20/50	20/30	Diffuse	8	15
15	F	64	20	NPDR	Good	Right	Unknown!	20/60	20/60	Diffuse	1	24
16	F	53	8	Absent	Good	Right	20/30	20/50	20/30	Diffuse	12	36
				Absent		Left	20/20	20/25	20/20	Diffuse	12	

! Presented with diabetic papillopathy.
DM, diabetes mellitus; BCVA, best-corrected visual acuity; NPDR, nonproliferative diabetic retinopathy.

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ings; visual field test results; and neurologic examination results were obtained from the records.

Patients with DM diagnosed before 30 years of age and receiving insulin therapy were classified as type I and others (regardless of insulin use) were classified as type II DM. A total of 3,235 patients were evaluated for the current study. Of these, 3,123 (96.5%) were diagnosed as type II and 112 (3.5%) as type I according to the above criteria.

Patients with Hb A1e levels of 6 mg% or less were described as under good metabolic control, those with Hb A1e levels between 6 mg% and 8 mg% were described as moderate metabolic control, and those with Hb A1e levels greater than .8 mg% were described as under poor metabolic control.

Patients with systemic blood pressure equal to or greater than 180/100 mmHg during the episode of disk swelling and with clinically evident renal failure were excluded from the study.

Patients who had concurrent uveitis or vasculitis at the time of disk swelling were also excluded. Patients with Westergren erythrocyte sedimentation rates higher than 40 mm/hour were excluded to rule out arteritic ischemic neuropathy due to giant cell arteritis.

Best-corrected visual acuities were measured with the Snellen chart. Patients with severe visual loss that was not proportional and could not be explained by the diabetic retinopathy status during disk swelling and those with permanent visual deficit after resolution of disk swelling were excluded from the study.

Characteristics of the disk swelling were obtained from fundus photographs. Extent of swelling, hemorrhages, and telangiectatic vessels on or around the disk were noted. Severity of diabetic retinopathy was classified as nonproliferative or proliferative. Data about diabetic retinopathy were obtained also from the fundus photographs. Patients with macular edema according to the Early Treatment Diabetic Retinopathy Study criteria were verified.[10]

Data about macular edema, capillary perfusion, and status of disk vessels were obtained from fundus fluorescein angiograms. Patients with optic disk neovascularization diagnosed by fundus fluorescein angiography were excluded from the study.

Visual field examinations were done by Humphrey" automated perimetry or Goldmann manual perimetry.

Patients with pathologic neurologic examination and those having abnormal computerized tomography or magnetic resonance imaging were excluded.

Results

Between 1986 and 1999, 45 patients (66 eyes) with optic disk swelling were evaluated in our institution. This represented 1.4% of the total diabetic patient population. Only 24 eyes of 16 patients (0.5% of our total diabetic patient population) met the above inclusion criteria; 42 eyes of 29 patients were excluded. The reasons for exclusion were inadequacy of follow-up, which did not allow differential diagnosis, in 4; definite ischemic optic neuropathy in 19; hypertensive retinopathy plus papilledema in 4; pseudotumor cerebri in 1; and intracranial mass in 1 patient.

The mean age at presentation was 57.1 ± 8.8 years (range 40-70 years). There were nine men and sever, women. All of these patients had type II DM. Of the patients with type II diabetes, 0.5% (16/3,123) were identified as having diabetic papillopathy. Two additional patients (1.8%, or 2/112 of our type I diabetic patient population) with type I diabetes presenting with optic disk swelling were also identified as having diabetic papillopathy from the patient records, but they had to be excluded from the current study because clinical foliow-up of those patients was too short and differential diagnosis could not be made accurately.

Average duration of DM was 10.0 ± 8.6 years (range 1-22 years). At presentation, 7 (44%) patients had poor metabolic control and 9 (56%) had good metabolic control. None of those patients had any abrupt change in blood glucose level such as initiation of insulin therapy before the onset of disk swelling. Characteristics of the patients are summarized in Table 1.

A total of 8 (50%) patients had unilateral and 8 (50%) patients had bilateral involvement. There was a time delay of 1 and 12 months between the occurrence of disk swelling in 2 (12%) patients who had bilateral involvement. A total of 6 (37%) patients had bilateral involvement at presentation.

Average follow-up was 25.6 ± 12.3 months (range 10-36 months). Average duration of papillopathy was 7.8 ± 3.7 months (range 1-16 months). Duration was more than 3 months in all but 1 (4%) eye and more than 12 months in 7 (29%) eyes. Initial best-corrected visual acuities ranged between 20/200 and 20/20. They were 20/40 or better in 15 (63%) eyes and between 20/200 and 20/40 in 9 (37%) eyes. Eyes presenting with 20/20 visual acuity were usually asymptomatic and papillopathy was diagnosed during routine follow-up visits for diabetic retinopathy.

At presentation, disk swelling was focal in 1 (4%) eye and diffuse in 23 (96%) eyes. In 7 (29%) eyes with diffuse disk swelling, radially oriented dilated telangiectatic vessels were observed on the disk surface (Figures 1A and 2A). In 5 (21%) eyes, flame-shaped small hemorrhages were also found on the disk.

Diabetic retinopathy was absent in 9 (37%) of 24 eyes at presentation. A total of 13 (54%) eyes had

Fig. **1.** A, Disk photograph of Patient 10, right eye. B, Fundus fluorescein angiography (FFA) of Patient 10, hyperfluorescence on the disk, early phase. C, FFA of ratient 10. leakage from telangiectatic vessels, late phase.

nonproliferative and 2 (9%) had proliferative diabetic retinopathy. In 4 (17%) eyes (2 with nonproliferative diabetic retinopathy and 2 with proliferative diabetic retinopathy at presentation) diabetic retinopathy worsened during follow-up and proliferative retinopathy requiring panretinal photocoagulation developed. A total of 6 (25%) eyes with clinically significant macular edema underwent grid laser photocoagulation treatment after resolution of the disk swelling.

In all eyes, fundus fluorescein angiography showed focal or diffuse early hyperfluorescence on the disk (Figures IB and 2B). There was no evidence of posterior ciliary artery occlusion, choroidal filling defects, or segmental hypofluorescence of the optic disk (Figure 2B). Late extensive leakage from telangiectatic disk vessels was seen in 7 (29%) eyes (Figures 1C and 2C). During follow-up. fundus fluorescein angiography of 4 (17%) eyes showed extensive capillar}' nonperfusion areas.

Visual field examination was performed in 12 (50%) eyes. Of those eyes, 7 (29%) had blind spot enlargement and the remaining 5 (21%) eyes had no significant visual field defect. Blind spot enlargement was found in eyes with diffuse disk swelling.

After resolution of disk swelling, best-corrected visual acuity was found to be between 20/200 and 20/20. hi 22 (92%) eyes it remained unchanged and in 2 (8%) eyes it was decreased. At the last visit best-corrected visual acuity was better than 20/40 in 18 (75%) eyes and between 20/200 and 20/40 in 6 (25%) eyes.

Fig. **2.** A, Disk photograph of Patient 3, left eye. B. Fundus fluorescein angiography (FFA) of Patient 3, hyperfluorescence on the disk, early phase. C. FFA of Patient 3, leakage from telangiectatic vessels, late phase.

Discussion

Transient, idiopathic unilateral or bilateral optic disk edema without any significant visual disturbance in young patients with type I diabetes has been published by many investigators since 1971.[1-4-9] Although the risk population and associated clinical findings have been described, the exact pathogenesis and clinical significance of this peculiar disorder (or finding) have not been understood. In 1971, Lubow and Makley described three young patients with type I diabetes with bilateral disk swelling.[1] In 1980, Appen et al described two young patients with type I diabetes with bilateral papilledema.[2] The same year, Pavan et al published eight patients and Barr et al published 12 patients with unilateral or bilateral optic disk edema without any visual disturbance.[3-4] All of the patients were younger patients with type I diabetes. In 1995, Regillo et al published 19 patients with diabetic papillopathy.[9] In their series most of the patients were older patients with type II diabetes and the age range was 19 to 79. In our current study, all of the subjects were older patients with type II DM. The average age in our patients was approximately 57 years. This is probably owing to the older mean age of

our patient population. In our institution, we usually follow and treat patients with type H diabetes: the ratio of type ILtype I patients was approximately 30:1. This may cause a selection bias, but we believe that diabetic papillopathy is not only a disease of young patients with diabetes. The average duration of diabetes was 10 years in our study patients. In previous publications, longer duration of diabetes was pointed out as a risk factor.[2-4,9] In the majority of our patients duration of diabetes was more than 8 years. We agree with the authors that duration of diabetes is an important risk factor for diabetic papillopathy.

The relationship between diabetic papillopathy and metabolic control has not been thoroughly understood. It was reported that poor metabolic control or abrupt tightening of the glycemic control such as in pregnancy or with initiation of insulin therapy could be associated with optic neuropathy.[11-16] In our study only seven patients had poor metabolic control and there was no abrupt tightening of glucose level before the disease presentation. We believe that fluctuations of blood glucose level may be associated with but probably is not the main factor in the pathogenesis of diabetic papillopathy.

It was reported that there were few if any associated fundus findings in patients with diabetic papillopathy in the early studies.[1-4] In the latest one, however, it was demonstrated that variable stages of diabetic retinopathy and macular edema could be accompanied by diabetic papillopathy.[9] Fifteen eyes were found to have diabetic retinopathy and six of them had macular edema associated with reduced best-corrected visual acuity at presentation in our study.

One interesting finding of our study was that in two eyes in which nonproliferative diabetic retinopathy was evident at presentation, retinopathy worsened and proliferative diabetic retinopathy developed 3 months after the diagnosis of papillopathy. Other previous studies showed that retinal ischemia could be associated with diabetic papillopathy and it was suggested that vascular occlusion could play a role in the pathogenesis of diabetic papillopathy[1,17-22]. Dilated, radial oriented vessels occasionally found on the optic disk during the episode of diabetic papillopathy might indicate the possible association of this rare disorder with vascular disturbance. Those telangiectatic vessels should be distinguished from disk neovascularization to make a correct diagnosis. Although mild leakage of fluorescein from those vessels can usually be detected during fundus fluorescein angiography, true neovascular vessels are usually oriented randomly throughout the vitreous, whereas telangiectatic vessels found in diabetic papillopathy usually do not extend to the vitreous and stay on the disk surface.

Although some researchers suggest that diabetic papillopathy most likely refers to a mild form of AION, we believe that diabetic papillopathy could be distinguished from AION in most patients by the following clinical findings. First, typical patients with AION almost always present with profound and sudden loss of visual acuity, in contrast to patients with diabetic papillopathy, who usually demonstrate a mild decrease in visual acuity.[5-8] Second, a dense visual field defect that almost always persists after the resolution of optic neuropathy is usually present in patients with AION, in contrast to the mild and transient visual field abnormalities in diabetic papillopathy.[5-8] Third, approximately 30% of patients with AION may experience an increase of three or more fines of visual acuity,[8] whereas best-corrected visual acuity of all our patients improved to the initial levels after the resolution of diabetic papillopathy. The distinction between the two diseases is simple for patients on the two opposite ends of the clinical spectrum, but may be artificial and arbitrary in some patients.

The presence of DM was shown to be a strong risk factor for AION.[5-7] In the current study, we did not observe any fundus fluorescein angiography findings that might implicate occlusion of the posterior ciliary arteries or choroidal filling defects.

A small cup:disk ratio was shown to be associated with both .AION and diabetic papillopathy in previous studies.[5-7] The crowded disk could play an important role in the pathogenesis of those two diseases. In our study, we could not measure the disk size or cup:disk ratio so we cannot support or reject this hypothesis. Marked edema of the optic disks in the acute presentation did not permit a precise assessment of either optic disk size or cup:disk ratio.

In this study, we demonstrated that a much higher than previously thought proportion of older type II patients with diabetes are also at risk for papillopathy. Disk swelling might be bilateral or unilateral and duration of disk swelling could be prolonged in some patients. Although this disease was generally assumed to be associated with good visual prognosis, as shown in this study, reduction of visual acuity could occur either during the course or after the resolution of diabetic papillopathy owing to the worsening of diabetic retinopathy or macular edema in some patients.

Key words: diabetic papillopathy, type II diabetes, diabetic retinopathy.

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