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Coexisting Normal-Tension Glaucoma and Deficiencies of Folic Acid and Vitamin B6 (Pyridoxal)

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Abstract

A 43-year-old man presented with bilateral visual field defect. Large disc cupping, retinal nerve fiber layer defect, and normal intraocular pressure were found in both eyes. Although the patient was prescribed an anti-glaucoma eye drop, the visual field defect deteriorated after two months of treatment. The patient was diagnosed with sensory, taste, and hearing impairments, as well as depression, caused by folic acid and vitamin B_6 (pyridoxal) deficiencies at an internal medicine department. The Visual field and ocular blood flow improved after two months of treatment with folic acid and pyridoxal, but the visual field deteriorated again when the treatment was discontinued. Because normal-tension glaucoma can be accompanied by systemic disorders including folic acid and vitamin B_6 (pyridoxal) deficiency, attention should be paid to general conditions as well as ocular findings.

Keywords

Normal-tension glaucoma, Vitamin B_6 deficiency, Visual field defect, Ocular blood flow, Folic acid, Pyridoxal

Introduction

Global surveys indicate that glaucoma is second only to cataract as a leading cause of visual impairment [1]. Most aspects of the pathogenesis of glaucoma, particularly normal-tension glaucoma (NTG), remain unknown, and the only evidence-based therapy for glaucoma is reducing intraocular pressure (IOP) [2-4]. Nevertheless, some cases of NTG progress in spite of sufficiently reduced IOP, suggesting that factors independent of IOP may be involved in its pathogenesis. Several preliminary studies have revealed the effectiveness of neuroprotective therapies for glaucoma [5-7], but few have been verified clinically. Epidemiological studies have suggested lower ocular perfusion pressure is associated with an increased prevalence or progression of glaucoma [8,9], and local and systemic vascular factors have been confirmed to play a role in the pathophysiology of glaucoma [7]. In addition, treatment with vitamin B group agents, particularly B_{12}, has been performed for glaucomatous optic neuropathy, albeit without sufficient evidence of its efficacy.

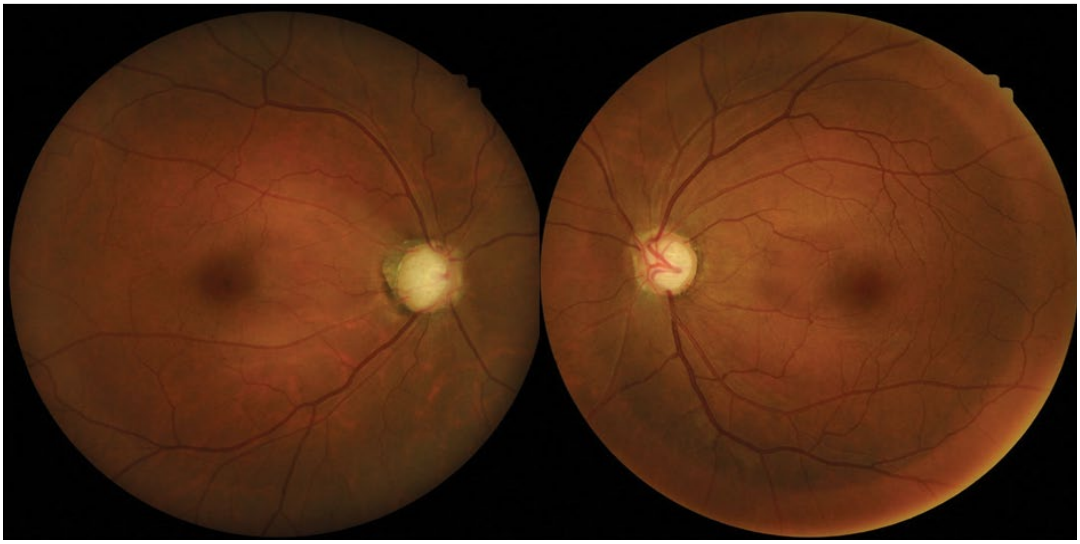

Figure 1: Fundus photographs at the first visit to our clinic.

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In the current report, we present a case of NTG accompanied by folic acid and vitamin B_6 (pyridoxal) deficiency.

Case Presentation

A 43-year-old man complained of bilateral visual disturbance and visited an ophthalmologist. He was subsequently referred to our clinic because of suspected NTG. His personal medical history included hemorrhagic gastric ulcer and a surgery for atrial septal defect. His family history revealed that his father suffered from diabetes mellitus. Refraction examination revealed myopia of -2.25 D in the right eye (OD) and -0.5 D in the left eye (OS). His best corrected visual acuity (BCVA) was 20/20 OD and 14/20 OS. His IOP was 13 mmHg in both eyes. His corneal thickness was within normal range in both eyes (547 μm OD and 552 μm OS). The cup-to-disc ratio was 0.9 OD and 0.8 OS (Figure 1). Optical coherence tomography revealed retinal nerve fiber layer defect (NFLD) in the superior and inferior regions (Data not shown). Centripetal narrowing of the visual field was detected in both eyes, particularly OD, by visual field tests using the Goldmann perimeter (Figure 2A). We prescribed carteolol solution (Otsuka, Tokyo, Japan), methylcobalamin tablets (Eisai, Tokyo, Japan), and kallidinogenase tablets (Sanwa Kagaku Kenkyusho Co., Ltd., Nagoya, Japan). Methycobalamin and kallidinnogenase were prescribed for optic neuropathy and for reduced ocular blood flow, as shown in figure 3A, respectively. However, the patient took hardly any of the tablets because of nausea.

Two months later, the patient's visual field had obviously deteriorated (Figure 2B) although his BCVA was not significantly altered (18/20 OD and 16/20 OS). His central flicker frequency had

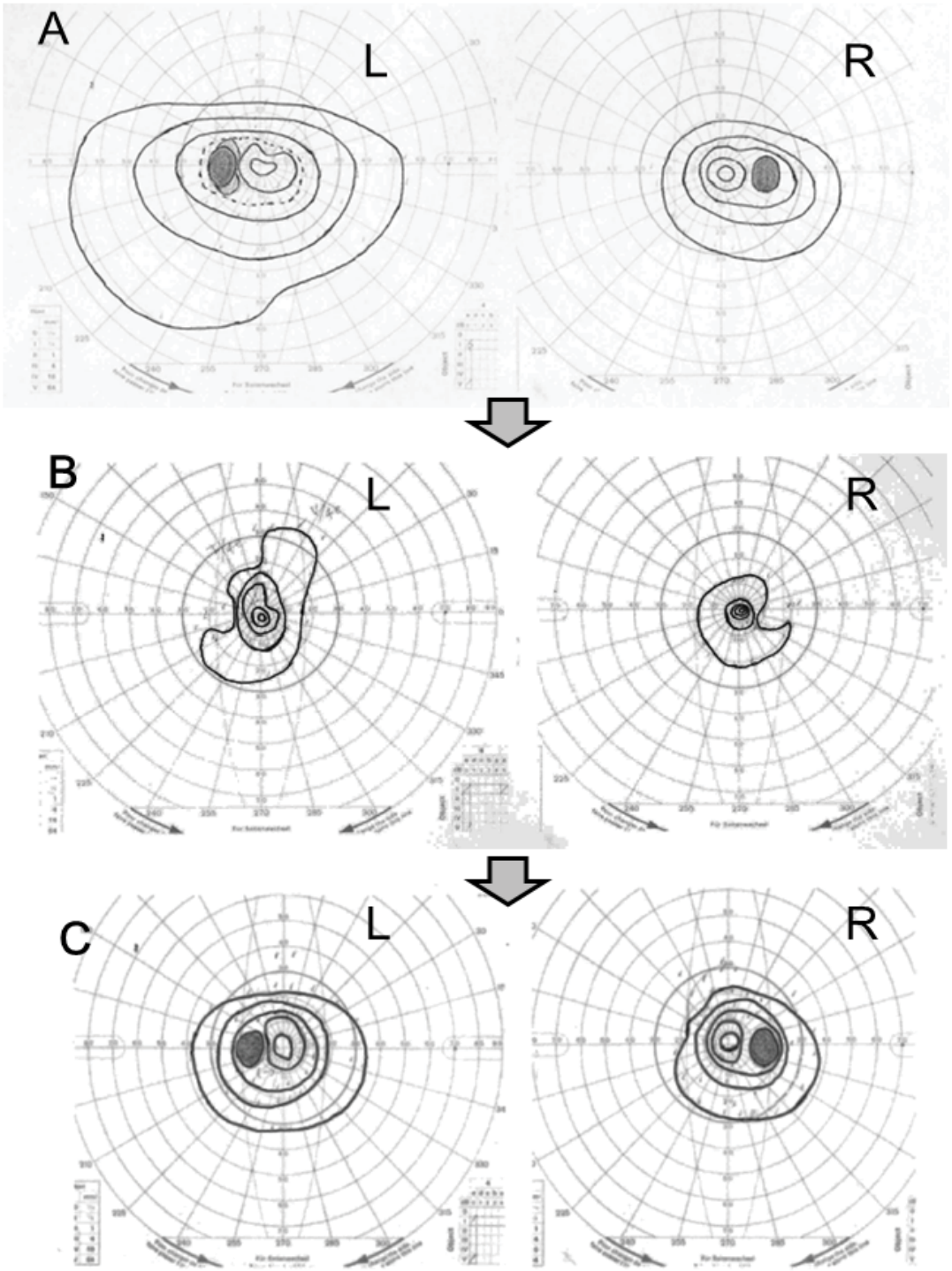

Figure 2: Visual field findings obtained with the Goldmann perimeter at the first visit (A), the 2-month visit (B), and the 4-month visit to our clinic (C; 2 months after beginning the treatment with folic acid and pyridoxal).

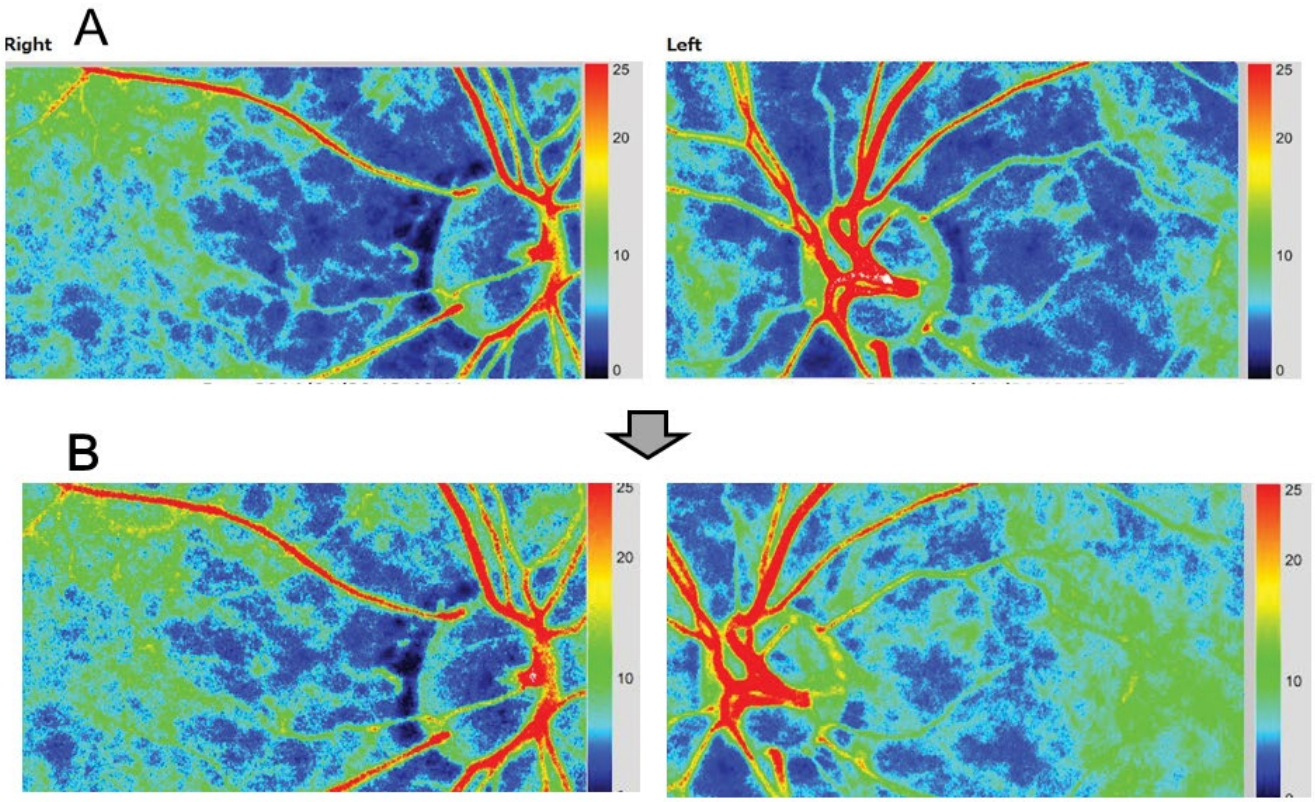

Figure 3: Findings obtained on laser speckle flowgraphy at the first visit (A) and the 4-month visit (B). Relative ocular blood flow, shown as color codes, increased particularly in OS after the treatment.

reduced to 25 Hz in both eyes. In addition, brain magnetic resonance imaging (MRI) revealed no abnormal findings. At the same time, he suffered sensory, taste, and hearing impairments as well as depression and was diagnosed with a nervous disorder due to deficiencies of folic acid and vitamin B_6 (folic acid: 3.7 ng/mL, pyridoxal: 5.0 ng/mL) at the Department of Internal Medicine of another hospital. The plasma level of vitamin B_{12} was not markedly reduced (435 pg/mL). The normal plasma levels of folic acid, pyridoxal and vitamin B_{12} were 4.0 ng/mL or more, 6.0~40.0 ng/mL and 180~914 pg/mL at the Department. He began treatment with folic acid (15 mg per day) and pyridoxal (60 mg per day). Two months later, the visual field had improved (Figure 2C), as well as the nervous disorder. Nevertheless, treatment with folic acid and pyridoxal was discontinued when he changed to another physician. Two months later, the visual field had again deteriorated (Data not shown). Measurement of ocular blood flow on laser speckle flowgraphy (LSFG) [10] indicated increased optic nerve head (ONH) and retino-choroidal blood flow, particularly in OS, after the treatment (Figure 3B). By questioning the patient about his daily life, it was found that he had taken an extremely unbalanced diet (mostly instant foods) for several years although he had consumed neither of tobacco nor alcohol.

Discussion

In this case report, a patient with ocular findings of NTG showed bilateral centripetal narrowing of the visual field and reduced concentrations of the vitamin B group, particularly folic acid and pyridoxal. Treatment with vitamin B group agents improved his visual field, while discontinuance of the treatment caused deterioration of his visual field defect again.

The patient was diagnosed with NTG because of obviously large disc cupping, NFLD, and normal IOP level in both eyes. However, the symptoms could not be explained only by NTG because the visual field defect was characterized by centripetal narrowing. The patient suffered sensory, taste, and hearing impairments at about the same time. Therefore, his visual field defect might have been modified by a nervous disorder induced by vitamin B_6 (pyridoxal) deficiency. In addition, his visual field defect was improved with the treatment of folic acid and pyridoxal, and deteriorated without that treatment, suggesting that folic acid and vitamin B_6 (pyridoxal) deficiency was probably involved in the visual field defect.

Although cases with optic neuropathies due to vitamin B_{12} deficiency have often been reported [11-17], those due to deficiencies of folic acid and vitamin B_6 have seldom been reported [11,18-20]. Vitamin B_6 participates in the metabolism of neurotransmitters (e.g., dopamine, noradrenaline, serotonin, and acetylcholine), and vitamin B_6 deficiency may be involved in many disorders of the central nervous system, such as Parkinsonism and Huntington's chorea [21]. On the other hand, low folate levels have been documented in the serum of patients with nutritional optic neuropathy and some malnourished patients with optic neuropathy recover when treated with folic acid supplements [18-20]. The role of pyridoxine and folic acid deficiencies in the pathogenesis of optic neuropathy has been previously reviewed [22], and an association, albeit not fully delineated, has been described between optic neuritis and pyridoxine deficiency [23]. In addition, folic acid and vitamin B_6, as well as vitamin B_{12}, are essential for metabolism of homocysteine. Therefore, deficiencies of these B vitamins cause elevation in blood homocysteine, enhancing arteriosclerosis-one of the underlying causes of vascular diseases (e.g., myocardial infarction and cerebral infarction) [24]. In the current case, the reduced ocular blood flow in the ONH and retino-choroid was improved after the treatment, suggesting that hemodynamic disorders might have been involved in the optic nerve disorder, at least partly, in this case.

Compressive and infiltrative optic neuropathies were excluded on the basis of the patient's MRI findings, and toxic and traumatic optic neuropathies were ruled out by consulting the patient's medical history. In addition, typical ischemic optic neuropathy or hereditary optic neuropathies could not be diagnosed in this patient because of the lack of an obvious reduction in visual acuity. Flammer syndrome was excluded because of the lack of increased general sensitivities, including pain sensitivity [25]. On the basis of the information obtained by questioning the patient about his daily life, an extremely

unbalanced diet (mostly instant foods), neither tobacco nor alcohol, was presumed the most likely cause of the vitamin B deficiency in this case. This seems different form other reports on optic neuropathy from folic acid deficiency [18-20]. However, higher brain dysfunction due to an underlying mental disorder could have been partly responsible for the visual field defect.

In summary, a case of NTG in which folic acid and vitamin B_6 (pyridoxal) deficiency might have played a role in deteriorating symptoms is reported. The importance of systemic examination, including measurement of plasma levels of a vitamin B group, should be noted in NTG patients.

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