stimulating hormone level of 21.7 mu/l (normal 0.5–5.0), but serum thyroxine was normal. Other routine bloods including full blood count, urea and electrolytes, serum glucose and liver function tests were also normal. Thyroid autoantibodies and TSH receptor assays were not performed. This subclinical hypothyroidism[1] supported our diagnosis of dysthyroid ocular myopathy. Treatment with oral thyroxine was commenced with a subsequent reduction in this patient's serum cholesterol. He remains visually asymptomatic with normal visual fields, unchanged disc appearances, and normal intraocular pressures in the primary gaze position.

Comment

The English, medieval, Franciscan, philosopher William of Occam, proposed the principle of *Pluralitas non est ponenda sine necessitate* meaning that plurality should not be posited without necessity. Physicians understand this to mean that a patient's diverse symptoms and signs be explained by a single pathophysiology.

Our asymptomatic patient's abnormal lipids and IOP were discovered by separate, ad hoc 'screening' procedures. Initially they were considered separate matters; ultimately a common causation became clear—illustrating Occam's razor.

Both elevated lipids[1] and intra-ocular pressure[2] are recognised features of hypothyroidism in Graves disease. Elevated intra-ocular pressure is due to the inelastic inferior rectus muscle compressing the globe as it fails to relax against the upward pull of its antagonist.[3]

Failure to recognise underlying hypothyroidism was of practical importance for this patient, who suffered the adverse effects from oral lipid lowering agents, lipid levels only becoming controlled on treatment with Thyroxine. In addition topical Timolol treatment was been shown to cause lipid derangement in healthy volunteers.[4]

We feel that hypothyroidism should be considered in patients who present with elevated lipids[1] and elevated IOP—especially when optic discs or visual fields are normal.

Subclinical hypothyroidism may present with a spectrum of clinical ophthalmic signs, but the presence of raised IOP particularly on up gaze, lid lag on down gaze, and the presence of deranged thyroid profiles are sufficient evidence of dysthyroid ocular myopathy in our case. In our opinion the presence of raised intraocular pressure in these patients contraindicates the use of ocular hypotensives in the presence of normal disc appearances and visual fields.

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Sir,

Severe progression of glaucomatous optic neuropathy in patients with Alzheimer's disease

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Several studies have dealt with the association of different systemic diseases and the progression of glaucomatous optic neuropathy. To our knowledge, we report the first cases of severe progression of glaucomatous optic neuropathy associated with Alzheimer's disease, a neurodegenerative disease with apoptotic cell death.[1]

Case reports

From lists of patients treated for glaucoma, who were followed quarterly as outpatients, seven patients (five women, two men) with primary open-angle glaucoma (POAG) were diagnosed with Alzheimer's disease from May to August 2000. The medical records of these seven patients were then reviewed (chart review) by both investigators (unmasked fashion) for pertinent information in a retrospective study of 24 months and are shown in Table 1. During the period from May to

Table 1 Brief clinical data from patients' records (24-month period)

Patient No. Gender/Age	*Eye*	*Intraocular pressure range during study period (mmHg)*	*Number of antiglaucoma topical agents*	*Humphrey perimetry (30–2 SitaFast) Pattern standard deviation Progression of visual field loss*			*Cup-to-disc ratio*	
				Initial	*After 12 months*	*After 24 months*	*Initial*	*24 months*
1 m/69	R	12–15	2	2.64	6.73 enlarging superior arcuate scotoma	12.43	0.5	0.9
	L	13–16	3	2.96	4.92 paracentral scotomas merging into an arcuate scotoma	10.68	0.6	0.9
2 m/73	R	13–18	3	3.94	8.62 superior and inferior arcuate scotomas forming an annular scotoma	19.41	0.6	1.0
	L	10–13	2	5.21	9.18 superior and inferior arcuate scotomas forming an annular scotoma	12.37	0.5	0.9
3 f/65	R	15–18	3	2.24	7.65 enlarged blind spot deteriorating to a large superior arcuate scotoma	12.10	0.4	0.8
	L	12–18	3	4.12	8.23 enlarging superior arcuate scotoma	10.64	0.5	0.9
4 f/69	R	11–16	2	5.26	8.47 paracentral scotoma extending toward the blind spot and fanning out nasally (arcuate scotoma)	17.42	0.5	1.0
	L	11–17	3	6.13	7.93 paracentral scotoma extending toward the blind spot and fanning out nasally (arcuate scotoma)	19.31	0.6	1.0
5 f/70	R	12–13	2	5.92	9.34 superior arcuate scotoma deteriorating to an altitudinal defect	20.43	0.4	0.7
	L	10–17	2	2.79	6.32 enlarging inferior arcuate scotoma	10.96	0.6	1.0
6 f/71	R	11–18	3	3.92	11.25 paracentral scotomas merging into an arcuate scotoma	14.07	0.7	1.0
	L	10–14	3	4.83	7.21 paracentral scotomas merging into an arcuate scotoma	10.62	0.7	1.0
7 f/74	R	15–17	3	3.98	6.31 localized paracentral scotoma deteriorating to several paracentral scotomas	8.42	0.6	0.9
	L	12–18	3	4.17	8.21 localized paracentral scotoma deteriorating to several paracentral scotomas	9.39	0.6	1.0

August 2000, from the lists of patients with glaucoma, only seven POAG patients were diagnosed with Alzheimer's disease. In all these seven patients, the diagnosis of Alzheimer's disease was confirmed by magnetic resonance imaging (MRI), cranial computerized tomography (CCT) and/or single photon emission computed tomography (SPECT). With the application of strict criteria the accuracy of clinical diagnosis may reach 100%.[2] In none of the patients was the clinical diagnosis of Alzheimer-type dementia confirmed by histopathology.

The diagnosis of glaucoma required a characteristic pattern of glaucomatous visual field loss with corresponding optic nerve head appearance. In no instance was the diagnosis of glaucoma dependent on the level of intraocular pressure. During the 24-month period, all patients were examined by one of the investigators (AUB) with subspecialty training in glaucoma.

The age of the patients ranged from 65 to 74 years. During the 24 months studied, each of the 14 eyes had been subjected to five or more reliable consecutive Humphrey Sita Fast 30–2 tests (Humphrey Field Analyzer, HFA 750). Reliable visual fields contained tests with false-positive answers of less than 10% and showed evidence of the physiological blind spot at its expected location. Visual field tests were evaluated in terms of Pattern Standard Deviation (PSD). The PSD is a weighted standard deviation of the pointwise differences between the measured and the normal, age-corrected reference fields. An irregular field with localized field defects, will result in a large PSD; thus, the PSD is an index of localized change in the field. In addition, the characteristic types of visual field abnormalities and changes over the 24-month period are described. Cup-to-disc (C/D) ratios evaluated by biomicroscopy using the 78D Volk lens in dilated pupils and intraocular pressure (IOP) readings by Goldmann applanation tonometry as recorded in the patients' records were used.

Visual acuity throughout the 24 months remained stable with best corrected visual acuity of 20/25 or better. Refractive errors ranged from −2.25 D to +3.25 D. At the beginning of the period studied, all patients showed bilateral glaucomatous visual field defects with Humphrey PSD ranging from 2.25 to 6.13 and C/D ratios ranging from 0.4 to 0.7. Over the next 24 months, treated IOPs ranged from 10 to 18 mmHg. Timolol (b.i.d.) and dorzolamide (b.i.d.) were given to all eyes; some eyes additionally received latanoprost (once daily). As shown in Table 1, all eyes showed a severe progression of glaucomatous optic neuropathy with significant worsening of the pre-existing sotomas. After 24 months, Humphrey PSD ranged from 8.42 to 20.43 and C/D ratios ranged from 0.7 to 1.0. Although the arcuate defect is probably the most reliable form of glaucomatous visual field loss, it is not pathognomonic, and the following additional causes must be considered, especially when the field and disc do not seem to correlate. In all eyes of the seven patients, there were no other possible causes of visual field defects in the arcuate area (eg, chorioretinal lesions, optic nerve head lesions, anterior optic nerve lesions, and posterior lesions of the visual pathway) and the visual field defects corresponded with optic disc cupping. In addition, all visual field tests were performed before the onset of symptoms of senile dementia.

None of the patients had diabetes mellitus, cardiovascular disease, thyroid disease, nor high or low blood pressure. Optic disc hemorrhages were not found in any of the eyes. Noncompliance with treatment was not noted (multiple visits with IOPs $<$ 19 mmHg). Meanwhile, 6 out of 14 eyes were trabeculectomized and all other eyes were given additionally brimonidine (b.i.d.). Possible further progression of glaucomatous optic neuropathy will be evaluated.

Comment

Several reports have dealt with the rate of visual field loss in POAG patients.[3,4] The rate of decay of the visual field in these patients despite presumed effective IOP-lowering therapy was estimated at approximately 3% per year. It has been observed that the course of this deterioration varies; some POAG eyes show episodic or curvilinear field loss with time rather than gradual linear deterioration. However, fluctuations of more than 10% within one year are rare. In our report of seven cases, the rate of decay of the visual field was more than 10% in each of the 14 eyes with POAG within the one year prior to the diagnosis of Alzheimer's disease.

Apoptosis has been shown to be at least one of the mechanisms for retinal ganglion cell death in pressure-induced glaucoma in the monkey[5] and the rat.[6] Evidence of necrotic cell death has not been found in the human glaucoma or in the monkey model, and is the basis for the hypothesis that apoptosis is the dominant mechanism of retinal ganglion cell death in glaucoma. The evidence of apoptotic cell death in a brain afflicted with Alzheimer's disease is quite compelling and stems back to work by Cotman and co-workers[1] demonstrating the anatomical and biochemical features of apoptotic cell death in brain tissue affected by Alzheimer's disease.

In postmortem studies, Sadun and Bassi[7] offer clear

evidence of a distinctive histopathologic process in the retinas and optic nerves of patients with Alzheimer's disease. The changes, which included degeneration and loss of axons, were noted in the optic nerves obtained from most of the patients with Alzheimer's disease examined and were easy to distinguish from changes due to aging in a normal control group. The largest retinal ganglion cells, the M-cells, seemed to be selectively involved. Whether these cells are the same large-size ganglion cell population that is affected in glaucoma[8] is not known. There was no retinal but intracranial neurofibrillary degeneration of amyloid angiopathy in optic nerves, which is typically seen in the brains of patients with Alzheimer's disease. By contrast, there is evidence of buildup of amyloid-β in retinal ganglion cells in rats with experimental glaucoma (McKinnon SJ, Paper at the Subspecialty Day *Glaucoma 2000*, American Academy of Ophthalmology, Dallas, Texas, October 2000). Glaucoma may be a chronic neurodegeneration like Alzheimer's disease, and a slow buildup of amyloid-β in the ganglion cell eventually triggers cell death and optic nerve axon loss.

We performed a retrospective chart review and found a more severe progression of glaucomatous visual field defects with corresponding enlarging cup-to-disk ratios in POAG patients with Alzheimer's disease than one would expect in patients with glaucoma. The striking feature of our results is the severe progression of glaucomatous optic neuropathy among patients with Alzheimer's disease when compared to glaucoma patients[3,4] without Alzheimer's disease. We are unaware of previous cases of severe progression of glaucomatous optic neuropathy in patients having Alzheimer's disease and can find no such references in a computer search using the PubMed database (National Library of Medicine). In a very recent clinical study, we reported an association of glaucoma with Alzheimer's disease.[9] However, the validity of our study is not optimal because of possible selection bias, lack of masked observers, and the lack of objective optic disc photographs. In addition, in none of the patients was the diagnosis of Alzheimer's disease confirmed by histopathology. For that reason, this retrospective chart review should serve to alert physicians as to the association of these two diseases and needs to be further studied in a more rigorous nature.

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Sir,

Uncomplicated phacoemulsification—should we see our patients the following day?

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Phacoemulsification with a small self-sealing incision is currently the commonest method of cataract surgery in the UK, and is increasingly becoming a day case procedure.[1]

There remain however, unresolved issues with