SCIENTIFIC CORRESPONDENCE

Amiodarone induced optic neuropathy

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Aim: To determine the clinical features of amiodarone induced optic neuropathy, which may help distinguish it from non-arteritic anterior ischaemic optic neuropathy.

Methods: Retrospective observational case series of patients diagnosed with amiodarone induced optic neuropathy at the neuro-ophthalmology service from March 1998 to February 2001. Amiodarone was discontinued after discussion with the patient's cardiologist. Visual acuity, colour vision, automated perimetry, and funduscopy were performed on initial and follow up examinations.

Results: Three patients with amiodarone induced optic neuropathy presented with mildly decreased vision, visual field defects, and bilateral optic disc swelling. Upon discontinuing the medication, visual function and optic disc swelling slowly improved in all three patients.

Conclusion: Amiodarone induced optic neuropathy can present with visual dysfunction, and is typically a bilateral process. Upon discontinuation of amiodarone, slow resolution of optic disc swelling occurs and visual function improves in some patients.

Amiodarone is an anti-arrhythmic drug used in the treatment of ventricular tachycardia and fibrillation, and in restoration of sinus rhythm in atrial fibrillation. The widespread use of this drug has increased after approval, by the American Heart Association, for its use in advanced cardiac life support protocols.¹ Common systemic side effects of amiodarone include thyroid dysfunction, pulmonary toxicity, drug interactions (especially with other commonly used cardiac medications such as digoxin and warfarin), peripheral neuropathy, ataxia, photosensitivity, and gastrointestinal problems.^{2,3} Ocular side effects have been noted, the most common being corneal microdeposits, which are found in 70–100% of patients.⁴ Other ocular side effects, which rarely cause visual impairment, include anterior subcapsular lens opacities, multiple chalazia, and dry eye syndrome.^{2–4}

Amiodarone has also been reported to cause optic neuropathy, which may result in permanent visual loss. The clinical presentation of amiodarone induced optic neuropathy may be similar to that of non-arteritic anterior ischaemic optic neuropathy (NAION).^{5–10} We present three patients with amiodarone induced optic neuropathy to emphasise the sight threatening visual effects of the drug and to better define the clinical features of this entity.

PATIENTS AND METHODS

This was a retrospective observational case series. Three patients were diagnosed with amiodarone induced optic neuropathy from March 1998 to February 2001 at a major neuro-ophthalmology referral centre. In these three patients, visual acuity, colour vision, automated perimetry, and funduscopy were performed as part of the initial and follow up examinations. In the two patients who were taking amiodarone on ini-

tial examination, the medication was discontinued after discussion with the patient's cardiologist.

Case 1

A 72 year old man was referred because of optic disc oedema initially detected in his right eye, followed by the recognition of bilateral disc oedema 3 weeks later. He was visually asymptomatic and a computed tomography (CT) scan of the head and orbits was normal. His past medical history was significant for two coronary artery bypass surgeries, atrial fibrillation requiring a pacemaker, aortic aneurysm, hypothyroidism, and sleep apnoea. He had sustained trauma to the left eye years earlier and was surgically aphakic. His medications included sotalol, warfarin, levothyroxine, omeprazole, fluoxetine, beclomethosone nasal spray, multivitamins, and psyllium. He had been taking amiodarone 200 mg daily for atrial fibrillation for 3 months, but this had been discontinued by his cardiologist 6 weeks before presentation because the patient developed mild ataxia.

Visual acuity was 20/30 in the right eye and 20/60 in the left eye. He recognised 10 of 10 Ishihara pseudoisochromatic colour plates with the right eye and none with the left eye. A relative afferent pupillary defect (RAPD) was noted in the left eye. Slit lamp examination revealed nuclear sclerosis in the right eye, and a corneal scar, irregular pupil, and aphakia in the left eye. Humphrey automated perimetry (24-2) showed an inferior arcuate defect on the right, and generalised depression with an inferior and superior nasal step on the left (Fig 1A). Funduscopy revealed swollen optic discs in both eyes with overlying haemorrhages.

A diagnosis of amiodarone induced optic neuropathy was made. Four weeks later, his vision was 20/30 in the right eye and 20/40 in the left eye. He identified seven of 10 Ishihara pseudoisochromatic colour plates with the right eye and six of 10 colour plates with the left eye. Repeat automated perimetry of the right eye was within normal limits, and the left eye showed improvement in the nasal step and overall depression (Fig 1B). The optic disc swelling was improved from his previous examination. Three months after initial presentation, the optic disc oedema remained. Four months after initial presentation, the patient was noted to have minimal oedema, which was fully resolved on examination 2 months later.

Case 2

A 70 year old man complained of decreased vision in his left eye, which he initially noticed 5 months before presentation. Four months before his referral, he was noted to have bilateral optic disc swelling. He denied symptoms of giant cell arteritis or polymyalgia rheumatica. His past medical history was significant for pacemaker/defibrillator placement, and his medications included digoxin, warfarin, and amiodarone at a daily dose of 200 mg, which he had been taking for the past year.

His visual acuity was 20/60 in both eyes. He recognised eight of eight Ishihara pseudoisochromatic colour plates with the right eye and seven of eight with the left eye. His pupils reacted equally without a RAPD. Slit lamp examination revealed bilateral cornea verticillata. Humphrey automated perimetry (24-2) showed a superior arcuate defect with a

Figure 1 Case 1. (A) left eye, superior and inferior nasal step; right eye, inferior nasal step, (B) improved bilaterally. Case 2. (C) left eye, superior arcuate defect; right eye, superior and inferior arcuate defects, (D) improved bilaterally. Case 3. (E) bilateral inferior altitudinal defects, (F) left eye, stable; right eye, improved. Right eyes on right side of figure, left eyes on left side of figure.

nasal step on the right and a superior arcuate defect with a nasal step and early inferior arcuate on the left (Fig 1C). Funduscopic examination revealed bilaterally elevated, hyperaemic optic discs with sectoral swelling superiorly (Fig 2A, B).

After consultation with his cardiologist, amiodarone was discontinued. One month later, his vision improved to 20/30 in the right eye, 20/40 in the left eye, and he recognised all of the colour plates with each eye. Automated perimetry of the right eye showed improvement, while the left eye was unreliable because of a large number of fixation losses. Funduscopic examination showed persistent optic disc swelling in both eyes. Repeat examination, 2 months after discontinuing the amiodarone, demonstrated minimal optic disc swelling bilaterally. Four months following discontinuing amiodarone, visual fields showed improvement (Fig 1D). Minimal optic disc swelling was noted in the right eye, and swelling of the left optic disc had resolved (Fig 2C, D).

Case 3

A 59 year old man noted that objects appeared darker in his left eye for 2 weeks. He was referred to a retina specialist who noted bilateral optic disc swelling. Magnetic resonance imaging showed no signs of hydrocephalus, optic nerve enhancement or mass lesion within the visual pathways. The patient was referred for neuro-ophthalmic evaluation.

His past medical history was significant for hypertension, atrial fibrillation for which he underwent cardioversion 1 year earlier, and coronary artery disease. Medications included hydrochlorothiazine/losartan, aspirin, and amiodarone, which had been started 3 months before presentation, with a loading dose of 800 mg daily for 2 months, followed by a daily maintenance dose of 200 mg over the past month.

Visual acuity was 20/25 in the right eye and 20/60 in the left eye. He recognised 11 of 11 Ishihara pseudoisochromatic col-

our plates with the right eye and five of 11 with the left eye. His pupils had been pharmacologically dilated. Slit lamp examination revealed bilateral cornea verticillata, and Humphrey automated perimetry (24-2) demonstrated bilateral inferior altitudinal defects, worse in the left eye (Fig 1E). The optic discs were swollen bilaterally with streak peripapillary haemorrhages. The amiodarone was discontinued.

Three weeks later, his visual acuity was 20/25 in the right eye and 20/40 in the left eye. His pupils were slightly sluggish to light, but no RAPD was noted. He recognised 11 of 11 colour plates in the right eye and nine of 11 in the left eye. His visual field defects persisted, and the optic disc swelling in each eye was unchanged.

Four months after the initial presentation, visual acuity and colour plates remained stable, and optic disc swelling persisted on the superior aspect of each disc. Six months after presentation, the visual field defect in the right eye was improved while the left eye remained stable (Fig 1F). The optic disc swelling had resolved.

DISCUSSION

Our three patients with amiodarone induced optic neuropathy presented with mild visual loss, and all had bilateral optic disc swelling. Two patients had unilateral subjective visual complaints, and the remaining patient was asymptomatic. All three patients were on a daily dose of 200 mg of amiodarone and had been taking the drug between 3 and 12 months. All of the patients were able to discontinue the medication, with subsequent improvement in visual acuity, dyschromatopsia, and visual field defects. All of our patients had documented optic disc swelling for more than 6 months, a finding which would be unusual in the optic disc swelling in NAION.¹¹ Additionally, the disc swelling persisted for at least 4 months after discontinuing amiodarone in all of our patients.

Figure 2 Fundus photographs on initial presentation in case 2 showing superior sectoral optic disc swelling in the right (A) and left eye (B). Four months later, minimal disc swelling persists in the right eye (C), with resolution in the left (D).

The diagnosis of amiodarone induced optic neuropathy should be a diagnosis of exclusion. Most patients taking this drug have vasculopathic risk factors, which at times makes the differentiation of this optic neuropathy from NAION difficult. In their review of 16 published case reports and 57 patients on the National Registry of Drug Induced Ocular Side Effects, US Federal Drug Administration, and World Health Organization, Macaluso and coworkers highlighted factors which may help distinguish between these two optic neuropathies. They suggested that amiodarone induced optic neuropathy typically has an insidious onset, a milder degree of visual loss, a longer duration of disc oedema, and is more commonly bilateral than NAION.⁷

Amiodarone has a long half life (21–78 days), owing to its cationic amphophilic structure, allowing interaction with polar lipids and subsequent accumulation of the drug and its metabolites as lysosomal inclusion bodies in multiple tissues, including the optic nerve.^{12–13} Therefore, the optic disc swelling may persist for weeks to months after the medication is stopped. Only after discontinuing amiodarone, with the subsequent slow resolution of optic disc swelling and improvement in visual function, is the diagnosis established with certainty.

Although it was not initially recognised when the drug was first released for use in the United States, subsequent reports have suggested that amiodarone induced optic neuropathy is not a rare entity. Feiner and coworkers reported the incidence of optic neuropathy in patients treated with amiodarone at the Mayo Clinic to be 1.79%, compared with the general incidence of optic neuropathy in patients over age 50 in Olmstead County, Minnesota, of 0.3%.⁵ However, because of vascular co-morbidities, patients treated with amiodarone also may be at a greater risk for NAION than the general population.

Some practitioners have suggested regular ophthalmic screening of patients taking amiodarone.^{5,7} As amiodarone induced optic neuropathy has been shown to have an insidious onset, periodic evaluation of the fundus may be warranted. However, examination should be performed expeditiously with the onset of any visual symptoms. If this diagnosis is suspected, attempts should be made to discontinue amiodarone. A slow improvement in visual function, in association with the equally slow resolution of optic disc swelling, may then be expected.

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