SFO COMMUNICATION

Two cases of bilateral amiodarone-associated optic neuropathy

À propos de deux cas de neuropathie bilatérale à l’amiodarone

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Summary
Introduction. — The widespread use of amiodarone is limited by its toxicity, notably to the optic nerve. We report two cases of bilateral optic nerve neuropathy due to amiodarone, and provide a detailed description of the disease.

Observations. — The first case was a 59-year-old man complaining of insidious monocular loss of vision within ten months of initiating amiodarone. Funduscopy and optical coherence tomography showed bilateral optic disc edema. The second case was a 72-year-old man presenting with a decrease in visual acuity in his left eye for a month. Funduscopy showed a left optic nerve edema, and fluorescein angiography showed bilateral papillitis. In both cases, the clinical presentation was not suggestive of ischemic neuropathy, because of the preservation of visual acuity and the insidious onset. In addition, both cardiovascular and inflammatory work-up were normal. An amiodarone-associated neuropathy was suspected, and amiodarone was discontinued with the approval of the cardiologist, with complete regression of the papilledema and a stabilization of visual symptoms.

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Introduction

Amiodarone has become a widely used class III antiarrhythmic drug. However, its use can be limited by serious toxicities and side effects, with almost 50% of long-term users resultantly discontinuing the drug [1]. Due to its lipophilic nature, amiodarone has strong tissue affinity, and its toxicity is ubiquitous, affecting the lungs, thyroid, skin, nervous system, liver, and eyes. There are a number of ocular adverse effects including corneal microdeposits, anterior subcapsular lens opacities, multiple chalazia, dry eye syndrome, halo vision and optic neuropathy [2]. Proper diagnosis of toxic optic neuropathy can justify drug withdrawal and hope of restored visual function. Every cardiologist must be aware of this potential adverse effect and ask their patients about visual symptoms.

Discussion.

Differentiating between amiodarone-associated optic neuropathy and anterior ischemic optic neuropathy may be complicated by the cardiovascular background of such patients. The major criterion is the absence of a severe decrease in visual acuity; other criteria are the normality of cardiovascular and inflammatory work-up, and the improvement or the absence of worsening of symptoms after discontinuation of amiodarone.

Conclusion.

Amiodarone-associated neuropathy remains a diagnosis of exclusion, and requires amiodarone discontinuation, which can only be done with the approval of a cardiologist, and sometimes requires replacement therapy.

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Observations

Case 1

A 59-year-old man complained of non-painful insidious decreased vision, with a visual field defect in his right eye. This man had been undergoing amiodarone treatment (200 mg daily) for tachyarrhythmia for eleven months. He had a history of hypertension, dyslipidemia, cardiomyopathy and hyperuricemia. His medication included warfarin, bisoprolol, irbesartan, simvastatin, allopurinol and pantoprazol. Neurological examination was normal. The brain MRI was normal. Visual acuity was 20/25 in the right eye and 20/20 in the left eye. Funduscoppy showed a bilateral optic disc swelling predominating on the left eye (Fig. 1). His pupils reacted equally with no relative afferent pupillary defect.
There was a central scotoma in the right visual field and an arciform scotoma in the left visual field (Fig. 2). Spectral domain optic coherency tomography (SD-OCT) showed a bilateral increase in optic nerve fiber thickness predominating on the left papilla (Fig. 3). SD-OCT is an optical signal acquisition and processing method that captures micrometer-resolution three-dimensional images from the retina. The peripapillary retina nerve fiber layer (RNFL) scan showed an increase in the left eye RNFL thickness that was above the 95th percentile of the normative data. The right eye RNFL thickness increase was sectoral, predominating on the lower quadrant. After discussion with the patient’s cardiologist, amiodarone was discontinued, and bisoprolol increased. After 3 months, the visual recovery was total, in terms of both visual acuity and visual field, with no cardiac disturbances. Fundus examination had normalized. No relapse occurred after a four-year follow-up.

Case 2

A 72-year-old man, taking amiodarone (200 mg daily) for 8 months for atrial fibrillation, consulted our department for decreased vision in his left eye for 1 month. His medical history comprised a mantle cell lymphoma in remission, and arterial hypertension. His treatments were telmisartan and acenocoumarol. Visual acuity was measured at 20/20 in his right eye and 20/25 in his left eye. Slit lamp examination showed bilateral amiodarone corneal deposits, and
ocular pressure was normal. Fundus examination showed a papilledema in the left eye, and there was a doubt about the same aspect in the right eye (Fig. 4). Kinetic campimetry showed a significant bilateral narrowing with no special systematization (Fig. 5). Fluorescein angiogram showed a bilateral dye leakage in both optic nerves, confirming bilateral papillitis (Fig. 4). Cardiological and inflammatory assessment and brain imaging were performed, and were normal. An amiodarone-associated neuropathy was suspected, so amiodarone was discontinued after cardiologists’ consent. The evolution was marked by a stabilization of the visual acuity and the visual field; the papilledema completely regressed with no relapse after a two-year follow-up.

**Discussion**

It is important to underline that patients requiring amiodarone therapy have the same vascular risk factors as those with nonarteritic anterior ischemic optic neuropathy (NAION). Symptoms of amiodarone-associated optic neuropathy share features of non-arteritic anterior ischemic optic neuropathy, the most common etiology of visual loss with optic disk edema after the age of 50. The diagnosis of amiodarone-induced optic neuropathy should be a diagnosis of exclusion. However, some differences orient toward amiodarone-associated optic neuropathy [1–4]. As in our two cases, it occurs more often in men, while NAION has equal sex predilection. Its onset is insidious, whereas NAION is acute. Two thirds of amiodarone-associated optic neuropathy cases present bilateral optic disk edema, whereas NAION is usually unilateral. Amiodarone-induced optic neuropathy has a longer duration of disc edema, for weeks to months, as shown in our two cases. A recent review [1] has shown that the most common presentation is insidious onset, which on funduscopy generally revealed bilateral optic disk edema, although most patients reported vision loss in only one eye. In fact, ocular symptoms are varied: one third of patients were asymptomatic, some reported either acute (19%) or insidious (26%) monocular vision loss, or acute (10%) or insidious (14%) bilateral visual loss. This critical review shows that amiodarone ocular toxicity generally occurs within 1 year of drug initiation, with a median duration of 6 months before vision loss. The mechanism of amiodarone-associated optic neuropathy could be similar to amiodarone-induced peripheral neuropathy [1,4,5]; different histopathologic studies have demonstrated...
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Multiple intracytoplasmic lamellar inclusions in axons of the optic nerve, with an irreversible or partially reversible toxicity. In this case, visual findings require several months to stabilize after the drug’s discontinuation. Following drug cessation, around 50% improve visual acuity, whereas around 20% have further decreased visual acuity [1]. Permanent blindness in at least one eye has been reported for 20% of affected individuals. The second mechanism can be the occurrence of a benign intracranial hypertension also called _Pseudotumor cerebri_ [6–8]: amiodarone has been held responsible in such manifestations, in which case visual symptoms are more likely to resolve after treatment discontinuation. In our observations, an amiodarone-associated toxic neuropathy was suspected, but the mechanism remains unsure, as no lumbar puncture with cerebro-spinal fluid pressure evaluation was performed. However, stabilization of visual symptoms with a good visual acuity argues for amiodarone implication. We note that amiodarone is frequently coadministered with digoxin, which can be an important contributing factor in the development of the toxic optic neuropathy. Digoxin similarly decreases vision and alters color perception, and its serum level is increased by amiodarone use.

**Conclusion**

Amiodarone-induced optic neuropathy is rare but serious. There is a risk of severe vision loss and permanent blindness. Thus an ophthalmologic evaluation at baseline is

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**Figure 4.** Retinophotographies of patient no 2 (top imaging): right papilledema and doubt on a left papilledema. Fluorescein angiogram (bottom imaging): bilateral fluorescein leakage in the optic nerve confirming bilateral papillitis.

**Figure 5.** Kinetic perimetry of the patient no 2: bilateral visual field shrinkage, evocative of optic neuropathy.
recommended, in particular for patients with pre-existing visual impairment. If visual symptoms develop, early referral to an ophthalmologist is recommended for evaluation of visual acuity and color vision, automated perimetry, dilated funduscopic examination, and OCT.

Disclosure of interest

The authors declare that they have no conflict of interest concerning this article.

References


