Bilateral Optic Neuropathy Associated with Amiodarone Therapy: Case Report

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Abstract

We report the case of a 70-year-old man whose medical history is characterized by cardiac arrhythmia (atrial fibrillation diagnosed 2 months ago) and hypertension. He is being treated with Xarelto, statins, amlodipine and Cordarone (since 2 months). He presents with rapidly progressive bilateral loss of visual acuity. His visual acuity was 2/10 in the right eye and 6/10 in the left eye. Examination of the fundus revealed a bilateral verticillate cornea.

anertior segment examination showed bilateral verticillata cornea, Fundus examination reveals bilateral papilledema OCT Fluorescein and indocyanine green (ICG) angiography confirmed bilateral papilledema

Imaging and blood tests were negative In the absence of an identifiable cause for the bilateral optic neuropathy, after normal results for all tests and imaging, and given the stable appearance of bilateral papilledema after 2 weeks, amiodarone was discontinued in consultation with his cardiologist and switched to flecainide.

Three weeks after discontinuation of amiodarone, the bilateral papilledema resolved and bilateral visual acuity improved progressively.

Two months after discontinuation of amiodarone, the ophthalmologic examination revealed a visual acuity of 7/10 in the right eye and 10/10 in the left eye, a regression of the papilledema as well as the development of temporal disk pallor in both eyes.

Keywords: Amiodaron, Bilateral Optic Neuropathy, Optic Nerve Atrophy, Optic Disc Edema,

Introduction

Amiodarone (Cordarone®) is used to treat symptomatic arrhythmias and angina pectoris. While effective, it is associated with several ocular side effects, including corneal microdeposits, subcapsular lens opacities, dysthyroid eye disease, enlargement of the extraocular muscles, keratitis sicca, multiple chalazia, electrophysiological disturbances, and, more rarely, optic neuropathy. The most frequently observed ocular side effect is the appearance of corneal whorl-like opacities, known as cornea verticillata, occurring in approximately 70–100% of cases. This form of keratopathy is typically asymptomatic, does not impair vision, and is generally considered a benign and potentially reversible condition. More severe systemic side effects have also been reported, including thyroid dysfunction (both hypo- and hyperthyroidism), interstitial pneumonitis, drug interactions, dermatological reactions, gastrointestinal disturbances, and peripheral neuropathy. Fortunately, most of these adverse effects tend to resolve after discontinuation of the drug.[1.2] In this report, we present the case of a male patient who developed bilateral optic neuropathy during treatment with amiodarone.

Case Report

A 70-year-old patient presents with rapidly progressive bilateral loss of visual acuity. His medical history is characterized by cardiac arrhythmia (atrial fibrillation diagnosed 2 months ago) and hypertension. He is being treated with Xarelto, statins, amlodipine and Cordarone (since 2 months).

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On clinical examination, best-corrected visual acuity is reduced to 2/10 in the right eye and 6/10 in the left eye.

The anterior segment examination shows a bilateral verticillata of the cornea without further abnormalities.

The fundus examination shows a right-sided papilledema with flame-shaped hemorrhages around the optic disk. The left fundus shows moderate papilledema. The peripheral retina of both eyes is normal (Figure 1).

Papillary OCT shows a retinal nerve fiber layer (RNFL) thickness of 167 µm in the right eye and 138 µm in the left eye (Figure 2).

Macular OCT shows hyperreflective spots in the outer layers and bilateral thickening of the interpapillo-macular retina with a serous retinal detachment in the retrofoveolar region of the left eye (Figure 2).

On questioning, there are no signs suggestive of Horton's disease or possible intracranial hypertension.

Fluorescein and indocyanine green (ICG) angiography confirms bilateral papilledema and the absence of signs of vasculitis or granuloma (Figure 2).

An emergency MRI of the brain was performed. No intracranial expansive process or cerebral thrombophlebitis was detected. Laboratory tests, including CBC, ESR, CRP, EPP, and ACE, are normal, and AAN quantification is also normal.

Given the bilateral papilledema with no obvious etiology, hospitalization was decided. A lumbar puncture revealed a pressure of 17 mmHg, ruling out idiopathic intracranial hypertension. CSF analysis was normal (with negative serologies for borreliosis, syphilis, Bartonella henselae, HIV, HBV and EBV).

A biopsy of the temporal artery revealed no pathology suggestive of giant cell arteritis (Horton's disease).

In the absence of an identifiable cause for the bilateral optic neuropathy, after normal results of all tests and imaging, and in view of the stable appearance of bilateral papilledema after 2 weeks, amiodarone was discontinued in consultation with his cardiologist and he was switched to flecainide.

Three weeks after discontinuation of amiodarone, the bilateral papilledema resolved and bilateral visual acuity improved progressively.

Two months after discontinuation of amiodarone, the ophthalmologic examination revealed visual acuity of 7/10 in the right eye and 10/10 in the left eye, regression of papilledema, and development of temporal pallor of the disc in both eyes (figure 4).

The papillary OCT revealed a deficiency in RNFL in both eyes (Figure 5). The macular OCT showed a vitreomacular traction syndrome in the both eyes (Figure 5).

Discussion

Amiodarone is among the most commonly prescribed antiarrhythmic agents, frequently used to manage atrial fibrillation and ventricular tachycardias [2]. Due to its amphiphilic nature, the drug is extensively distributed throughout various body tissues, including ocular structures [2].

Amiodarone induces phospholipidosis, leading to the intracellular buildup of phospholipids in the form of lamellar bodies [3]. Organs affected by phospholipidosis often show inflammatory responses and histopathological alterations [3]. Histological examinations in patients receiving amiodarone have revealed numerous lamellated inclusion bodies within large axons of the optic nerve, although there is no evidence of demyelination or axonal loss [4]. These findings suggest that amiodarone may exert neurotoxic effects on the optic nerve through drug-induced lipidosis.

A rarer, less recognized but clinically significant ocular complication is optic neuropathy. Cases of vision loss linked to amiodarone-associated optic neuropathy (AAON) [2].

AAON typically presents with a gradual onset of visual loss accompanied by slow progression and optic disc edema. Although it often begins in one eye, it can eventually affect both eyes simultaneously. While some individuals experience only mild impairment

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of optic nerve function, others may suffer irreversible vision loss. One study reported that the median time to onset of optic neuropathy was approximately four months following the initiation of amiodarone therapy [5]. Although the incidence of amiodarone-related optic neuropathy has been estimated at up to 2.0%, its true frequency remains uncertain [2].

The diagnosis of amiodarone-associated optic neuropathy (AAON) is clinical ; however, due to its variable presentation, it remains a subject of ongoing controversy. An observational case series involving 55 patients found that 40% presented with sudden vision loss, 80% exhibited optic disc edema, and five individuals demonstrated elevated intracranial pressure on lumbar puncture [5].

AAON encompasses a broad clinical spectrum, with reported presentations including asymptomatic optic disc edema, unilateral optic neuropathy, and bilateral involvement—either simultaneous or sequential [6].

Importantly, AAON must be differentiated from non-arteritic anterior ischemic optic neuropathy (NAION), which is the most prevalent cause of optic neuropathy in individuals over 50 years of age [7]. Although both conditions share overlapping clinical features such as optic disc swelling and vision loss they differ in several key respects. Epidemiologically, AAON is more commonly observed in male patients with systemic hypertension, while NAION shows no gender predilection [8]. Additionally, optic disc edema in AAON tends to persist longer, typically ranging from one to eight months (median duration of three months), whereas in NAION, disc swelling usually resolves within two to six weeks [9].

Further distinctions exist in the funduscopic and anatomical characteristics of the optic nerve. Patients with NAION frequently have small, crowded optic discs, a finding not consistently associated with AAON [9]. In terms of onset, NAION typically presents acutely, while AAON generally follows an insidious course. Laterality also differs: NAION is predominantly unilateral, whereas approximately two-thirds of AAON cases are bilateral at presentation, often with simultaneous involvement [9,13].

Although AAON and NAION share certain clinical manifestations, such as vision impairment and optic disc edema, they can be distinguished based on sex distribution, temporal profile of disc swelling, pattern of laterality, and optic nerve head morphology. Accurate differentiation is essential for guiding appropriate management and assessing prognosis.

Amiodarone-associated optic neuropathy (AAON) can be categorized into five distinct clinical subtypes based on either the temporal profile of onset or optic nerve appearance. The most prevalent form is the insidious-onset subtype, typically characterized by bilateral, simultaneous optic disc edema [9]. The second most common presentation resembles non-arteritic anterior ischemic optic neuropathy (NAION), manifesting as acute unilateral or bilateral visual loss [5].

The third subtype is retrobulbar optic neuropathy, which poses diagnostic challenges due to the absence of visible optic disc abnormalities. Diagnosis in such cases requires neuroimaging and laboratory investigations to exclude other causes of visual field loss [5]. The fourth category involves elevated intracranial pressure, defined as cerebrospinal fluid pressure exceeding 200 mmH_2O. The fifth and final category is delayed-onset progressive neuropathy, in which optic disc edema may develop several days to weeks after discontinuation of amiodarone therapy [5].

Given the potential for serious ocular toxicity, annual ophthalmologic evaluation should be considered for patients receiving long-term amiodarone therapy. If AAON is suspected, prompt cardiology consultation is advised to assess the feasibility of discontinuing amiodarone or transitioning to an alternative antiarrhythmic regimen.

Conclusion

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Although rare, AAON represents a significant adverse effect of amiodarone therapy, warranting heightened clinical awareness. This case underscores the importance of early recognition and monitoring for optic nerve toxicity in patients receiving the drug. Due to amiodarone's critical role in the management of life-threatening arrhythmias, risk stratification is essential in deciding whether to continue therapy, reduce the dosage, or switch to alternative treatments. Timely involvement of cardiology is crucial when AAON is suspected, to balance the therapeutic benefits of amiodarone with its potential for ocular toxicity

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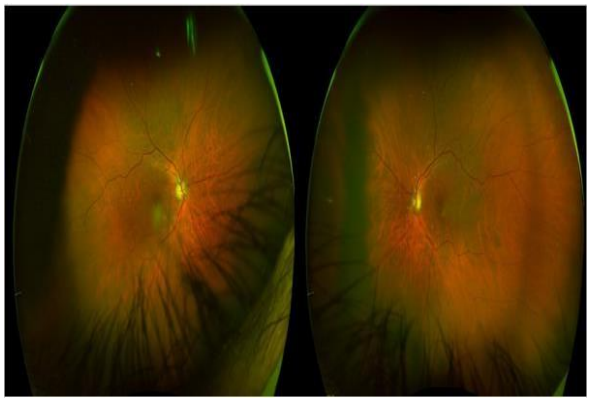

FIGURE1 Initial fundus of both eyes, shows bilateral papillary edema predominantly on the right

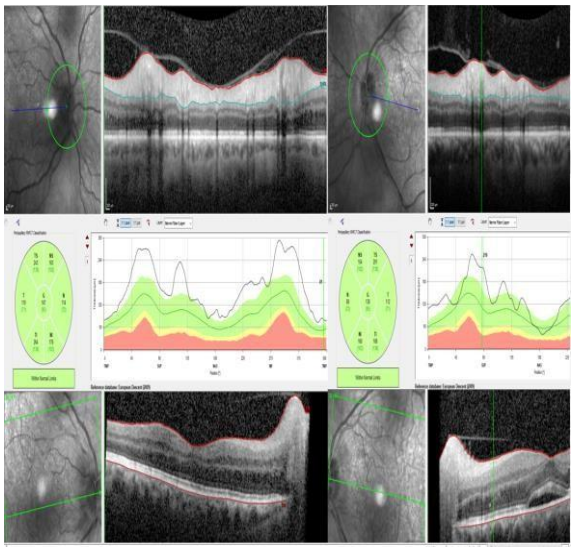

FIGURE 2Initial papillary and macular OCT in the right and left eye shows bilateral papillary edema predominantly on the right with a serous retinal detachment at the retrofoveolar area in the left eye

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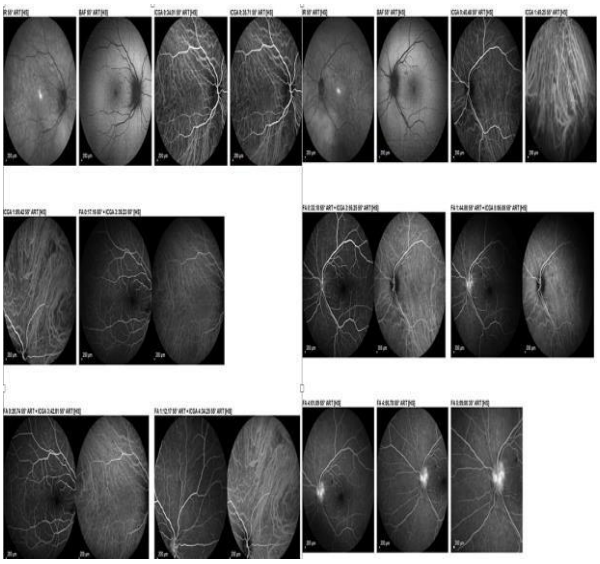

FIGURE 3Fluorescein and indocyanine green (ICG) angiography confirms bilateral papillary edema and the absence of signs of vasculitis or granuloma

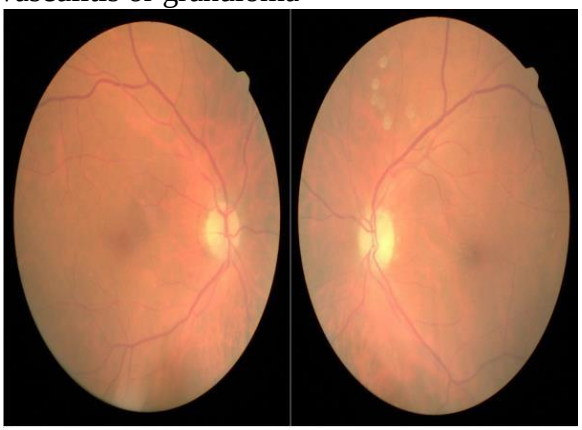

FIGURE 4Photographs of left and right optic discs 8-week follow-up after discontinuation of amiodarone demonstrating resolution of disk edema and hemorrhages and development of temporal disk pallor in both eyes .

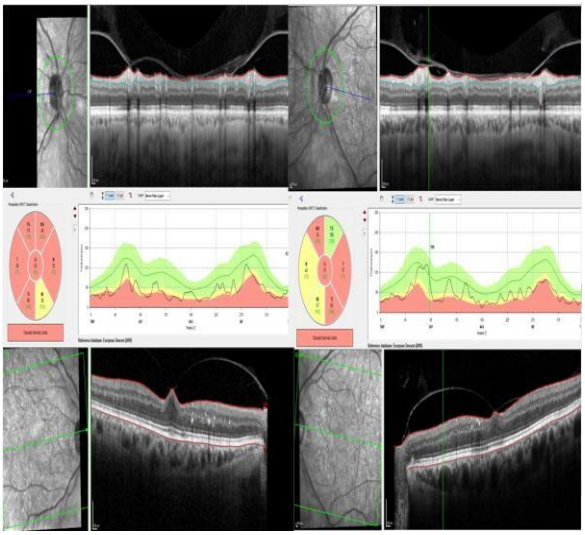

FIGURE 5Macular and papillary OCT 2 months after discontunaiting amiodarone.

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