CASE REPORT

Short-term treatment with oral amiodarone resulting in bilateral optic neuropathy and permanent blindness

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Accepted 18 December 2016

SUMMARY

A 66-year-old man was hospitalised due to worsening of his atrial fibrillation, and successfully underwent an electrocardioversion to restore sinus rhythm. He was discharged with a prescription of 600 mg amiodarone daily to retain the sinus rhythm prospectively. 3 weeks after discharge, he noticed that his vision became blurry with cloudy areas spreading throughout his field of view on both eyes simultaneously. The visual symptoms gradually worsened throughout the following 5 months, and the patient was hospitalised in the department of ophthalmology. At this point, his vision had dramatically decreased and visual acuity was measured to 0.05 (1.3 LogMAR) on both eyes. After a thorough medical examination, the patient was diagnosed with an amiodarone-induced toxic optic neuropathy. Regular follow-ups conducted throughout 7 years have shown that the patient's vision has stabilised, but remains limited to the ability of recognising hand motions on both eyes, thus characterising him as blind.

BACKGROUND

Amiodarone, a class III antiarrhythmic drug, is one of the most efficient therapy for the treatment of atrial and ventricular arrhythmias. The drug does, however, have a wide spectrum of side-effects, which can affect various organ systems. Therefore, close medical follow-up is recommended during the treatment. Eye-related side effects are very common, and usually present as epithelial micro-deposits in the cornea (>90% of patients), photo-sensitivity (25–75% of patients) and optic neuropathy with visual loss (≤ 1 –2% of patients).¹ Amiodarone-induced optic neuropathy is a rare condition, and visual loss often reverses on discontinuation of the drug. However, in some cases, the condition becomes permanent, with detrimental consequences for the affected patient, as evident in this case.

CASE PRESENTATION

The patient, a 66-year-old man, is known with a history of well-controlled essential hypertension and persistent atrial fibrillation throughout several years. He had no previous record of ocular disease. The patient was admitted to the department of cardiology because he experienced increasing physical fatigue and dyspnoea over a time course of 3–4 weeks. On examination it was found that his atrial fibrillation had worsened, and echocardiography revealed a left ventricular ejection fraction of 40%, moderate mitral valve regurgitation and mild

tricuspid valve regurgitation. The patient successfully underwent an electrocardioversion, and a daily dose of 600 mg oral amiodarone was initiated post-procedure in order to maintain the heart in sinus rhythm.

Three weeks after discharge from the hospital, the patient first noticed that his sight gradually changed: he experienced blurring vision, and reported about cloudy areas scattered throughout his field of view, on both eyes simultaneously. His vision normalised after a few hours, and he consulted his general practitioner who decided to cease amiodarone immediately.

Throughout the following 3½ months, the episodes of transient bilateral visual defects recurred with new events every 2–4 days. Then, over a time course of 4 weeks, the patient's vision rapidly deteriorated and eventually became permanently blurry and foggy. At this point, 4 months after the initial symptoms, his visual acuity was 0.32 (0.5 LogMAR) on the right eye and 0.4 (0.4 LogMAR) on the left eye. Another 3 weeks passed by before he was referred to the department of ophthalmology for evaluation.

INVESTIGATIONS

Meanwhile, his vision had decreased even further, and on admission, his visual acuity was 0.05 (1.3 LogMAR) on both eyes. Goldmann perimetry showed normal peripheral visual field borders on both eyes, and a centrocecal scotoma on the right eye. A funduscopy showed regularly shaped optic discs with sharp edges and a temporal pallor bilaterally. Intraocular pressure was normal in both eyes, and an optical coherence tomography was inapparent (figure 1). A swinging light test showed isocoric pupils with normal light reaction and no relative afferent pupillary defect. Flash visual evoked potentials (FVEPs) were prolonged bilaterally (figure 2), while an electroretinography (ERG) showed normal potentials on both eyes.

A full neurological evaluation was performed, and with exception of the optic nerve, all were found normal. An MRI of the cerebrum was, along with an EEG, inapparent. A serological screening for rheumatic diseases (antinuclear antibodies, double stranded DNA antibodies, antineutrophil cytoplasmic antibodies, antimitochondrial antibodies, anticardiolipin, lupus anticoagulant, and C reactive protein) was negative.

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To cite: Knudsen A. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-217436

Figure 1 Ocular coherence tomography images of the right (A) and left (B) eye. Both eyes display a normal retinal profile with no signs of oedema, epithelial detachment or other macular pathologies.

DIFFERENTIAL DIAGNOSIS

In this case major cerebral vascular lesions, such as a cerebral apoplexy or transient ischemic attack, present as important differential diagnosis entities, considering the patient's history of atrial fibrillation and hypertension. He was, however, on anticoagulation therapy at the time, and MRI of his cerebrum showed no signs of cerebrovascular events or obstructing tumours.

Ischaemic optic neuropathies affect the smaller blood vessels supplying the optic nerve, and are a common cause of visual loss. Arteritic anterior ischaemic optic neuropathy (AAION) is a complication of temporal arteritis, and characterised by vascular inflammation, resulting in occlusion of the ophthalmic artery and subsequent ocular ischaemia. However, the patient's serology screening was negative, and treatment attempted with 100 mg prednisolone daily for 3 days did not stop the patient's visual deterioration, thus ruling out AAION as the cause. Non-arteritic anterior ischaemic optic neuropathy (NAION) presents as sudden unilateral visual loss and is caused by ischaemia of the optic nerve due to infarcts or circulatory insufficiencies. In this case, the inapparent MRI and the slow symptomatic progression rule out NAION since symptoms evolving for several months deem a cerebrovascular accident unlikely.

Toxic optic neuropathies are a collection of relatively rare conditions, where the optic nerve is damaged by exposure to a neurotoxic substance. Amiodarone is a known cause of toxic optic neuropathy.² Since patients treated with amiodarone have pre-existing cardiovascular risk factors, it can be challenging to

determine whether the affected individuals develop a toxic optic neuropathy due to amiodarone exposure, or rather NAION due to circulatory events.³ The symptomatic onset gives valuable information when distinguishing one condition from the other: NAION usually presents as acute unilateral visual loss, while amiodarone-induced optic neuropathy most often manifests as insidious bilateral vision loss.⁴ The normal ERG rules out a retinal/macular dysfunction, while the FVEPs with prolonged latency indicate a delay through the visual pathway, as is usually the case in toxic optic neuropathies.⁵ Considering the clinical presentation as a whole, the patient was diagnosed with an irreversible toxic optic neuropathy, induced by amiodarone.

OUTCOME AND FOLLOW-UP

A medical follow-up 3 months after the initial investigations showed a further decrease of the patient's vision. At this point, visual acuity was limited to the recognition of hand motions on the right eye, and finger counting on the left eye. A funduscopy revealed pale, atrophic optic discs on both eyes. FVEPs were barely detectable or completely absent, while ERG potentials remained normal on both eyes.

Regular follow-ups have since been conducted throughout a total of 7 years. The appearance and state of the optic discs has not changed since the diagnosis was made (figure 3). The patient's vision has stabilised, but remains limited to the ability of recognising hand motions on both eyes. According to the WHO ICD-10 classification, he is thus characterised as blind.

Figure 2 Flash visual evoked potentials from stimulation of both eyes. The signals are derived midoccipital to midfrontal (Oz-Fz) and show prolonged P100 peak times bilaterally. Right eye: A1=112.2 ms. B1=108.6 ms. Left eye: C1=126.6 ms. D1=121.8 ms.

Figure 3 Colour fundus images of the right (A) and left (B) eye, respectively, taken at one of the patient's regular follow-ups. The optic discs of both eyes appear to be pale and atrophic with no observable changes compared to previous examinations. On the left eye, signs of a non-diabetic retinopathy are visible with retinal haemorrhages and an area of hard exudates. The retinopathy arose after the initial diagnosis and is not related to the patient's toxic optic neuropathy.

DISCUSSION

Toxic optic neuropathies most often have optic disc swelling as a key feature, which can persist for several months, before progressing to optic nerve atrophy with visible pallor of the disc. The patient in this case did not show any signs of optic disc swelling when examined, but a temporal pallor of his optic discs was in fact observed. Since the examination took place 5 months after the first symptoms, the optic disc swelling may have progressed to pallor in the time window before the examination was performed. A previous study found the median resolving time of disc swelling to be 3 months.⁶

Patient's perspective

- ▶ Anyone can end in a situation similar to mine. It is a fact that my vision declined and eventually disappeared completely, after I was treated with amiodarone. Until this day my condition remains with no therapy option.
- ▶ My unexpected blindness has unwillingly torn me out of my regular active life, and I face the consequences on a daily base. The social decline was preprogrammed when I became blind, and my social status has dramatically decreased over the past years. I am increasingly isolated from former relations and my quality of life is practically zero. My girlfriend of nearly 10 years ended our relationship because of my blindness, and I remain alone with no help to master my life. My current situation is a constant struggle, and I am forced to adapt to the new challenges that I face on a daily base. The only way I still endure my situation is because of strict planning and rigorous discipline in every aspect of my life.
- ▶ My advice to anyone in a similar situation is to always prepare and inform yourself minutely in relation to hospitalisation and offered treatments: Read the leaflet of any medication prescribed several times and always insist on a second opinion if in doubt. Medical doctors are obliged to inform their patients, so demand thorough information and clarification of any risks related to your treatment. This is the only way that we as patients can make a qualified decision about our own health and well-being.

Amiodarone is highly lipophilic and has a large distribution volume, which leads to deposits in multiple tissues throughout the body. The terminal half-life varies substantially inter-individually and ranges between 13 and 142 days.¹ These pharmacokinetic properties suggest that the patient may have been exposed to amiodarone for several months, before the drug was completely eliminated, despite discontinuation after only 3 weeks of treatment. Long-term exposure could explain the progressive decrease of the patient's visual function over a prolonged time period, before stabilising at the current level.

Several case reports describing visual loss and optic neuropathy after treatment with amiodarone have been published

throughout the past few years. A review from 2012 includes 296 cases with mean therapy duration of 9 months before onset of visual loss. 20% of patients were noted as having a visual acuity of <20/200 (>1.0 LogMAR) in at least one eye, and 58% of patients experienced an improvement of their visual function after cessation of amiodarone.⁷ What makes this current case extraordinary is the fact that the patient experienced the first visual symptoms after only 3 weeks of daily treatment with 600 mg of orally administered amiodarone. Similar cases with such rapid onset of visual loss are extremely rare, and have thus far only been observed in patients treated with intravenous amiodarone.^{8,9} This case is, therefore, the first description of how an amiodarone-induced toxic optic neuropathy can occur after only 3 weeks of treatment, with orally administered amiodarone. This proves as a strong reminder of the risks related to the treatment with amiodarone, and stresses the importance of thoughtful use of the drug.

Learning points

- ▶ Amiodarone is one of the most efficient antiarrhythmic drugs, but with its efficacy comes a broad range of side effects, including optic neuropathy. If a patient experiences visual impairment due to optic neuropathy while treated with amiodarone, immediate cessation of the drug may reverse the symptoms. In some cases, the visual loss does, however, become permanent, with detrimental consequences for the affected individual's quality of life.
- ▶ Whenever amiodarone is prescribed, the physician is obliged to inform the patient about the potentially severe side effects, and must emphasise the importance of regular medical examinations in order to minimise the risk of their occurrence. If serious side effects should occur, the patient must be subjected to immediate medical attention.
- ▶ The differential diagnosis of patients with visual loss can be challenging, but valuable information is provided in the clinical presentation and time course of symptom development; ischaemic optic neuropathies usually manifest as sudden unilateral visual loss, while toxic optic neuropathies most often present as insidious bilateral visual loss.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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