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CASE REPORT

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Rapid myopization of the fellow eye in anisometropic amblyopia treated with 1% atropine: a case report

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Abstract

Background High anisometropia is often accompanied by amblyopia. One percent atropine penalization is an important treatment for anisometropic amblyopia and is as effective as occlusion therapy. On the other hand, 1% atropine had the strongest effect on controlling refractive error and axial length (AL) changes in myopic patients.

Case presentation A female child was diagnosed with anisometropia at the age of two. Cycloplegic retinoscopy examination revealed refraction of + 2.5 diopters the right eye and -8.5/-1.5 × 120 diopters the left eye, and full correction spectacles and patching therapy were prescribed for the child. Anisometropic amblyopia was then diagnosed because the best corrected vision acuity in highly myopic eyes is 20/100. Owing to poor compliance, visual acuity recovery in the amblyopic eye was unsatisfactory, and 1% atropine was applied two times per week for the fellow (right) eye. Since then, the fellow eye has experienced rapid myopization, with the refractive error increasing to -7.5/-1.25 × 15 diopterswithin five years. In addition, the visual acuity of the amblyopic (left) eye has improved gradually to 20/20, although the refraction status has remained stable.

Conclusions In this report, a high anisometropic amblyopia patient underwent rapid myopization in the fellow eye with constant use of 1% atropine, in contrast to the stable refraction status of the amblyopic eye.

Keywords Anisometropia, Amblyopia, Myopization, Atropine

Background

High anisometropia is a unique refraction state in which an individual's two eyes have a spherical equivalent difference greater than 3D [1]. Previous studies have reported that the prevalence of anisometropia ranges from 1.27% to 25.6% in different populations and ages; however, high anisometropia is rare [2–6]. Anisometropia is an important cause of amblyopia, which defined as a condition in which the best-corrected visual acuity of one or both eyes is lower than normal, or there is a difference of two or more lines between the visual acuities of the two eyes [7, 8]. Amblyopia therapy options may often involve penalization of the nonamblyopic eye using either occlusion or atropine [9]. Atropine penalization, which involves the administration of 1% atropine to the fellow eye once or twice a week, is as effective as occlusion in amblyopia treatment and is an important therapy on the basis of solid evidence from the Paediatric Eye Disease Investigator Group [7, 10, 11].

On the other hand, atropine has been widely recognized as one of the most effective strategies for slowing myopia progression [12]. Various concentrations of equal or less than 1% atropine are able to effectively control refraction and axial length (AL) growth in myopia in a dose-dependent manner and 1% atropine has

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the strongest effect [12–14]. This case report describes a child with anisometropic amblyopia whose fellow eye experienced rapid myopic growth with consistent 1% atropine use, whereas the amblyopic eye remained stable.

Case presentation

In 2014, a female child born in January 2012 was brought to the Lixiang Eye Hospital of Soochow University by her parents due to exotropia of the left eye. The patient had never previously undergone a medical consultation. The mother has a −3 diopters myopia and the father is emmetropic. Premature birth and history of oxygen therapy were denied. The Hirschberg test indicated exotropia at approximately 15° in the left eye, but the simultaneous prism and cover test could not be performed. After 5 days of treatment with a 1% atropine agent to paralyze the ciliary muscle, the child's retinoscopy examination revealed refractive error of +2.5 diopters the right eye and −8.5/−1.5×120 diopters the left eye. However, the visual acuity test could not be performed due to a lack of cooperation by the patient. A full correction spectacle for the left eye with plane glass for the right eye was prescribed to the patient, and patching therapy of 6 h per day was also prescribed. Three months after the visit, the girl was brought in for a follow-up check. The refractive status was the same as that at the last examination. The visual acuity testing was performed by Log Mar visual acuity charts with E label, which is more convenient for children to learn and in order to communicate more easily, we converted to the Snellen expression. The uncorrected visual acuity (UCVA) was 20/33 in the right eye and 20/400 in the left eye, and the BCVA was 20/25 in the right eye and 20/100 in the left eye. Therefore, anisometropic amblyopia was then diagnosed. The same treatment strategy was continued. After 7 months, the refraction and visual acuity were almost the same as those at the last follow-up due to poor compliance. The importance of treatment was re-emphasized to parents, and Bangerter foil was applied to suppress the fellow eye. Ten months later, the BCVA of amblyopic eye was improved, with the refractive status unchanged. Moreover, the ocular alignment improved to orthotropia. After one year, the refractive error of +1.00 diopters for the fellow eye, while the amblyopic eye remained stable. However, the BCVA had not improved since the last visit. Therefore, 1% atropine was prescribed two times per week for the right eye because of unsatisfactory compliance. Six months after atropine was used, the BCVA of the amblyopic eye improved, and hyperopia of the fellow eye decreased. After half a year, the BCVA of the amblyopic eye reached 20/25, and the fellow eye gained plain refraction. One year later, the BCVA reached 20/20 in the fellow eye and 20/25 in the amblyopic eye, with a refractive error of −1.00 diopters in the right eye. Over the next nine months, myopia progression in the fellow eye seemed to occur even faster, and the refractive error increased to −3.25/−0.5×10 diopters. The rate of increase in myopia of the fellow eye was almost the same in the next two years. The refractive status was −5.5/−1.0×15 diopters in the first year and −7.5/−1.25×15 diopters in the second year, whereas the refraction of the amblyopic eye remained stable. The BCVA of the amblyopic eye reached 20/20 in the second year, so the use of 1% atropine was discontinued. During the next two years, the refraction of both eyes remained stable, and the BCVA of the amblyopic eye decreased slightly (20/22). The flow chart shows the main process of patient follow-up and treatment (Fig. 1).

A comprehensive examination was conducted when the child was eleven years old. The central corneal thickness of the fellow eye was 483 μm and that of the amblyopic eye was 494 μm. The intraocular pressure measured with Icare in both eyes was 13 mmHg and 14 mmHg, respectively. Dilated fundus examination revealed no obvious lesions (Fig. 2). The mean choroidal thickness within a 1 mm-diameter circle centred on the macular fovea was 241 μm in the fellow eye and 325 μm in the amblyopic eye (Fig. 3).

Discussion

The mechanism of anisometropia is not entirely clear, but current studies suggest that both environmental factors and genetics play roles in its development [15–18]. With respect to the changes in anisometropia with age, some controversies exist. Deng et al. [3]. reported that the prevalence of anisometropia decreased in a US-based cohort study in which refraction was measured via noncycloplegic retinoscopy. Similarly, a study of 46 anisomyopic subjects demonstrated that the less myopic eye tended to become more myopic, whereas the more ametropic eye showed more stable refraction [19]. Lin and colleagues suggested that the development of anisometropia varies across ages and refractive conditions [20]. These researchers specifically reported that anisometropia increases in magnitude in myopic and antimetropic children aged < 6 years, and the mean anisometropia is similar in these groups after the age of 6 years. However, for hyperopic children, anisometropia remains similar between the ages of 3 and 13 years [20]. In this report, the hyperopic eye experienced rapid and constant myopization, whereas the highly myopic eye remained stable until anisometropia eventually disappeared.

In this case, due to poor compliance, the child received 1% atropine penalization therapy from the age of 5 years, and the visual acuity of the amblyopic eye recovered well. Interestingly, with the improvement in visual acuity of the

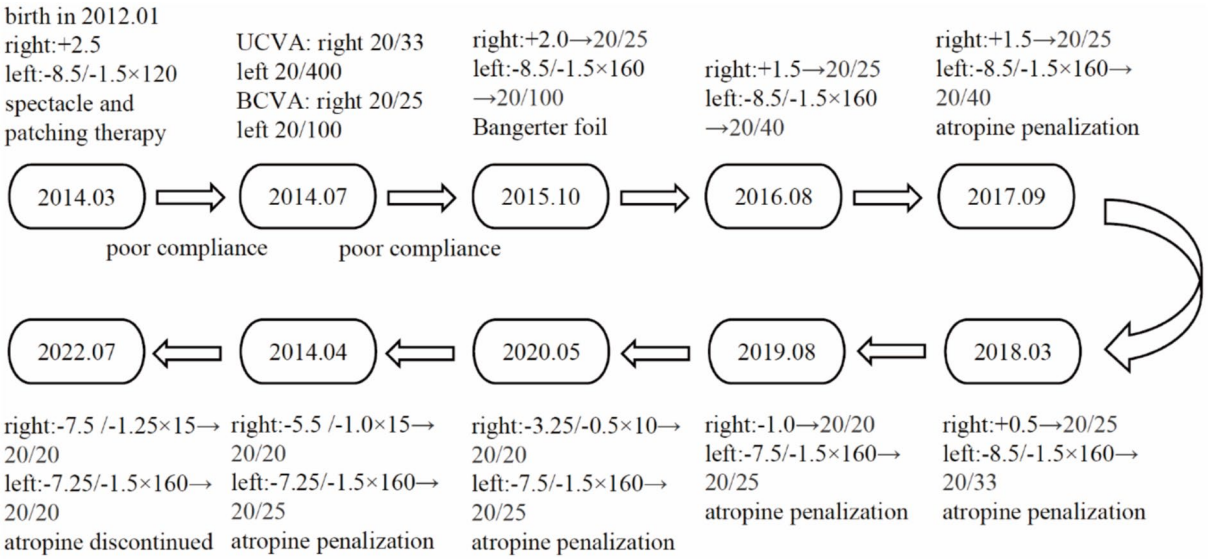

Fig. 1 Patient follow-up and therapy flow chart

Fig. 2 Fundal photograph of the patient

amblyopic eye, the myopia of the fellow eye developed rapidly, whereas the refraction of the amblyopic eye was relatively stable. Notably, this process occurs in amblyopic eyes with continuous administration of 1% atropine, which is considered to be the most effective method for delaying the progression of myopia [13, 14, 21, 22].

The efficacy of atropine in slowing myopia progression was officially reported as early as 1979 [23]. Since then, numerous studies and reports have been published on the effects of atropine on myopia; however, the exact mechanisms remain largely unknown. Huang et al. [21] reported the efficacy of sixteen interventions for myopia control in children. They proposed that the efficacy of atropine for myopia control increased with increasing concentration and that 1% atropine had the strongest myopia control effect, which was even greater than that of orthokeratology [21]. The same conclusion was further confirmed in numerous subsequent studies [12–14].

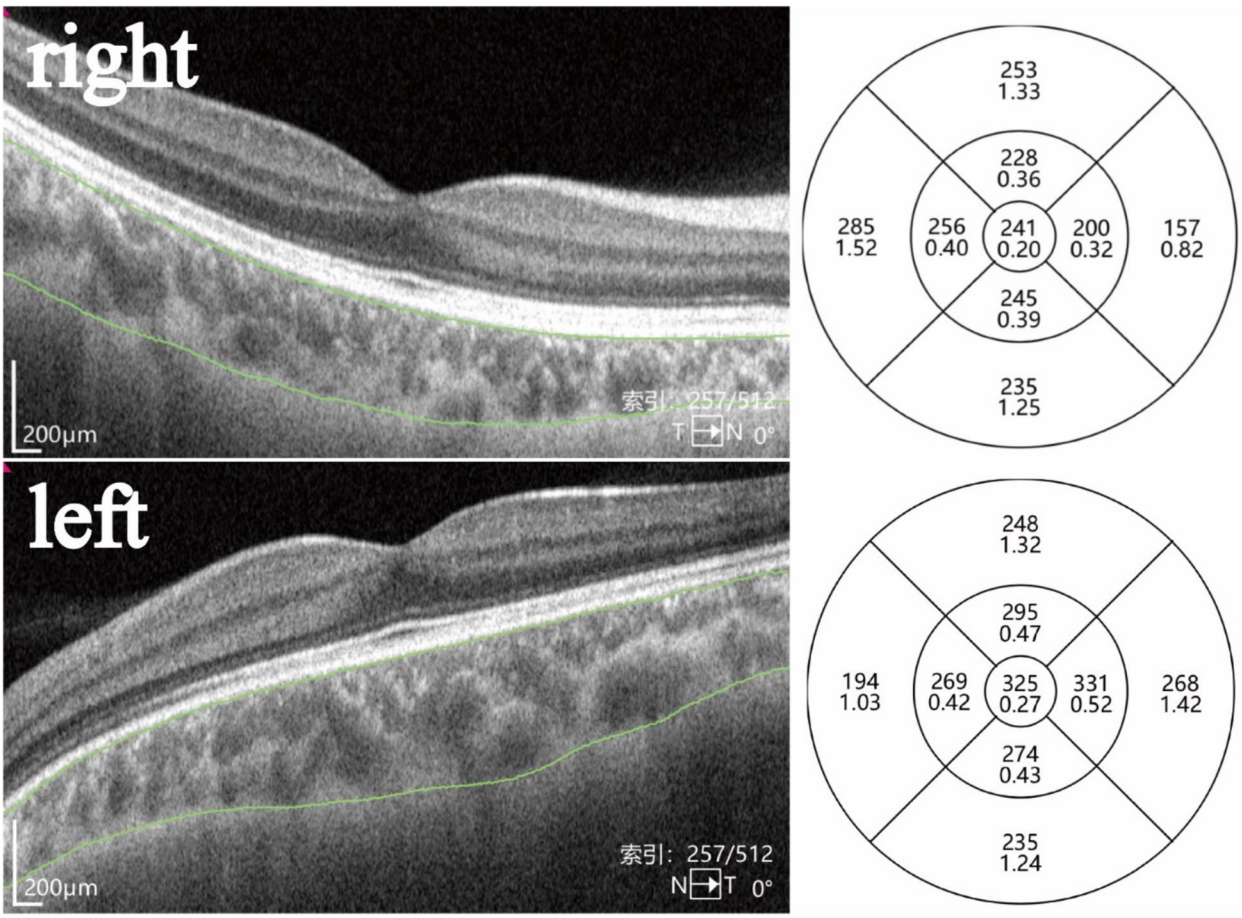

Fig. 3 Optical coherence tomography image of both eyes. The left column shows the choroid automatically recognized by the instrument, and the right column shows the values of choroidal thickness in different regions

In this report, the fellow eye experienced rapid and sustained myopization of approximately 1D per year with 1% atropine treatment. Similarly, Shih et al. [1] investigated refractive changes in amblyopic children with high anisometropia and reported that the fellow eye underwent a greater degree of myopia (- 4.83 ± 2.53 D) compared with the amblyopic eye (- 1.63 ± 1.57 D) in the myopic group. Moreover, 5 subjects received 0.1% or 0.3% atropine treatment, and the myopia progression (yearly change) of fellow eyes was −0.80 ± 0.21 D, which was similar to that of those without atropine treatment (−0.89 ± 0.56 D) [1]. This result was consistent with our findings, which potentially suggests that atropine is ineffective for anisometropia-related myopization, even at high concentrations.

The mechanism of the antimyopic effects of atropine remains unknown. Given that atropine has been reported to stimulate the release of dopamine (DA) into the extracellular space and vitreous space, the role of DA in myopia progression has received increasing attention [24]. Zhou et al. [25] and Chen et al. [26] demonstrated that dopamine D1 receptor activation has an inhibitory effect on myopia progression and axial elongation. Another study also revealed the anti-myopic effects of dopamine D2 and D4 receptors in tree shrew models [27]. In addition, a previous study reported that atropine induces the synthesis of the extracellular matrix in scleral fibroblasts, thereby thickening the scleral tissue and reducing its elasticity and elongation, thus decreasing myopia progression [28]. Moreover, some scholars believe that atropine can increase choroidal thickness and relieve hyperopic defocus, which is an important theory that causes myopia [29, 30]. Unfortunately, none of these theories can explain myopia progression in our case.

Notably, the mean choroidal thickness within a 1 mm-diameter circle centred on the macular fovea was 241 μm in the fellow eye and 325 μm in the amblyopic eye in our study. Scholars believe that the choroidal thickness in amblyopic eyes is greater than that in fellow and normal eyes [31–33]. On the other hand, the choroidal thickness was thinner in the more myopic eyes of patients with

anisometropia and was negatively correlated with axial length [34, 35]. Wan et al. [36] reported that the subfoveal choroid thickness in high myopia amblyopia patients was 177.79 ± 64.46 μm and was significantly thinner than that in patients with a normal thickness (330.20 ± 89.38 μm), low myopia (305.54 ± 70.75 μm) and moderate myopia (297.68 ± 63.82 μm). However, in our case, the choroidal thickness was greater in the high myopic amblyopia eye than in the fellow eye, which was the opposite of Wan's conclusion, and the choroidal thickness of the fellow eye was thinner than that of the normal eye. Thickness of the choroid is associated with the development of myopia and axial elongation [37–39]. This may partly explain the rapid development of myopia in the healthy eye.

Interestingly, we noticed that the myopization of the fellow eye seemed to begin with the improvement in visual acuity of the amblyopic eye in our patient. Shih et al. [1] and Caputo et al. [19] reported that high myopic anisometropia gradually decreases with faster myopization in less myopic eyes. However, Zedan et al. [40] came to an opposite conclusion, observing that anisometropic myopia increased rapidly in the first few years of life and stabilized thereafter. We hypothesize that the reason for this result is the difference in the study subjects. Although the subjects in Caputo's study all had high myopic anisometropia with or without amblyopia, 86.9% of participants exhibited improved visual acuity at the end of the follow-up, 58.69% had the same best corrected visual acuity in both eyes, and 58.7% had recovered stereopsis. Moreover, Shih excluded subjects whose final visual acuity did not reach 20/30 at the 2-year follow-up. In contrast, in Zedan's study population, the best corrected visual acuity of the more myopic eyes was only 0.47 ± 0.31 (range: 1.00 to 0.10) at the end of the study, which was much worse than the 0.02 ± 0.04 (range: 0.10 to 0.00) of the less myopic eyes, and 68% of the eyes were still amblyopic. Therefore, we hypothesize that, in individuals with high myopic anisometropia, improvements in visual acuity in amblyopic eyes and the recovery of binocular vision may play critical roles in the myopization of less myopic eyes. These two factors are the key goals of amblyopia treatment, presenting a challenge for the management of high myopic anisometropic amblyopia. Myopia progression is often accompanied by thinning and stretching of the sclera, choroid, and retina, increasing the risk of irreversible vision-threatening impairment such as choroidal neovascularization, retinal and choroidal atrophy, posterior scleral staphyloma, lacquer crack formation and macular degeneration [41–43]. Although reducing the magnitude of anisometropia is a goal in the treatment of anisometropic amblyopia, it is equally important to prevent the onset and delay the progression of myopia in the fellow eyes. However, it appears that there are certain contradictions in these aspects, so how to balance it needs further study.

This case report has several limitations. First, we merely observed the phenomenon of rapid myopia progression in the fellow eye in spite 1% atropine instillation. There indeed exist documented cases where myopia continues to progress despite atropine use, while the possibility cannot be ruled out that myopia progression might have been even faster without atropine intervention. Second, choroidal thickness measurements were only performed at ages 12 and 13 (two results consistent), with no assessments conducted during the rapid myopia progression phase. Therefore, the findings only demonstrate that the fellow eye's choroidal thickness was thinner than that of the amblyopic eye, but cannot provide conclusive evidence whether choroidal thinning occurred during the rapid progression period.

Conclusions

In conclusion, this case report presents the treatment of a patient with high anisometropic amblyopia (9D), whose fellow eye underwent rapid myopization with constant use of 1% atropine in contrast to the stable refraction status of the amblyopic eye. These findings suggest that the mechanism of myopia progression in anisometropic amblyopia patients is unique and atropine appear to have insignificant control effects on this type of myopia progression. The recovery of visual acuity in amblyopic eyes may play a critical role in myopia progression in fellow eyes. It poses a challenge to the management of high myopic anisometropic amblyopia: vision improvement or myopia controlment.

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Authors' contributions
QJZ wrote the main manuscript text; XQC revised and re-edited the manuscript; SCY modified the first manuscript version; GFM collected the data; and LJN provided the case. All the authors read, reviewed and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This prospective study was approved by the Lixiang Eye Hospital of Soochow University Institutional Review Board and adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from the patient's parents.

Consent for publication
Written informed consent was obtained from the patient's parents for the publication of clinical details and clinical images.

Competing interests
The authors declare no competing interests.

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