Amblyopia is a frequent cause of monocular visual impairment in children. Large-scale studies report a prevalence of 1.6–3.6% of the population.\[1\] The most common cause of amblyopia is anisometropia, a refractive imbalance between the eyes. Anisometropia is the sole identifiable amblyogenic factor in 37% of cases, and concomitantly with strabismus, in an additional 24% of cases.\[2,3\]

Anisometropic amblyopia ordinarily develops in the more ametropic eye. The severity of the amblyopia is generally believed to be related to the degree and type of anisometropia, although this is still controversial.\[4-6\] Among the anisometropias, hyperopic anisometropia is the most common amblyogenic cause of refractive amblyopia. Affected children have a more severe form of amblyopia at lower levels of anisometropia. They ostensibly use the less hyperopic eye for both near and distance fixation because it requires less accommodation. Therefore, the more hyperopic eye constantly receives a blurred image, resulting in amblyopia.\[7\] Myopic anisometropia is less common and usually develops at a higher level of asymmetric refractive error.
since in mild-to-moderate anisomyopia, the more myopic eye can still be used for near fixation and the less myopic eye is favored for distance fixation, with possible consequent diminished binocular vision (monovision). Astigmatic anisometropia is another potential reason for refractive amblyopia.

Treatment of anisometropic amblyopia is challenging, and several different approaches are available. The mainstay of treatment is the correction of the refractive error with spectacles accompanied, when indicated, by patching or pharmacologic penalization of the preferred eye.

The aim of this report was to describe a case series of children with anisometropic amblyopia, without any additional ocular pathology or strabismus, who were diagnosed relatively late with amblyopia and preferred the hyperopic eye. This phenomenon seems to be unpredicted and contrary to expectations and poses a challenge for glasses prescription.

Methods

A retrospective cohort design was used. The clinical database of a tertiary medical center was reviewed for all children with anisometric amblyopia diagnosed and treated during 2014–2016. Children, in whom the amblyopia was diagnosed in the more emmetropic or myopic eye rather than the hyperopic eye, were identified. Exclusion criteria were the presence of any other amblyogenic factor (strabismus, structural defect, and deprivation amblyopia) or neurological impairment. Data were collected from the medical records of the eligible patients, as follows: Demographic parameters, best-corrected visual acuity (BCVA) for each eye, refraction, treatment, glasses prescription, follow-up, and final BCVA.

The study protocol was approved by the local ethics committee.

Results

Four children met the study criteria out of 327 children (0.01%) followed for anisometric amblyopia in a large tertiary center over a 3-year period. An additional child with strabismus in addition to anisometric amblyopia and two children with borderline anisometric amblyopia (preference for the hyperopic eye but no deterioration in BCVA in the other eye) were excluded from the study.

The cohort included two girls and two boys of mean age 6.8 years (range 4–8 years) at diagnosis. Mean follow-up time was 2.6 months. One child was lost to follow-up. Clinical profiles of the patients are shown in Table 1. In all four patients, the right eye was amblyopic. Refraction range in the amblyopic eyes was 0–(−4.5) sphere with 0–(−0.75) cylinder, and in the preferred (non-amblyopic) eyes, +1–(+3.25) diopters sphere with 0–(−0.75) diopters cylinder. Mean BCVA in the right amblyopic eyes was LogMAR 0.46 (0.3–0.7), and in the left preferred eyes, LogMAR 0.02 (0–0.07). The mean spherical difference was 4 (1–6.5) diopters.

All patients underwent complete ocular and neuro-opthalmologic examinations, including color test, visual field at confrontation, pupillary response to light, fundus and disc examination, and eye motility. None was found to have any additional pathology contributing to the amblyopia or decreased acuity besides the anisometropia itself.

Treatment for the amblyopic eye consisted of full cycloplegic spherical refractive correction or the closest possible while maintaining BCVA, with mild modified subjective correction of the cylinder. Three patients were also initially treated with patching of the better-seeing eye for 2–6 h/day. Mean BCVA after treatment was 0.20 (0.07–0.3), with an improvement of more than 3 lines in two children.

Discussion

This study describes a unique phenomenon of anisometric amblyopia, in which the amblyopia is unexpectedly diagnosed in the mildly myopic or emmetropic eye rather than the hyperopic eye. In our experience, this is an uncommon finding, and many ophthalmologists need to be alerted to it.

This group of children was first evaluated at a mean age of 6.8 years, with a wide variation. Because the amblyopia was

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BCVA: Best-corrected visual acuity, FU: Follow-up, LE: Left eye, LogMAR: Logarithm of the minimum angle of resolution, N/A: Not applicable, RE: Right eye, Tx: Treatment
not severe and was diagnosed late, we can only assume that it either developed with time or went “below the radar.” The lack of previous records makes the explanation of this phenomenon difficult.

Anisohyperopia is a significant and well-known amblyogenic risk factor. Children with a mild or even moderate myopic refractive error have good vision at near, with full visual potential in the myopic eye along with proper cortical visual development, without signs of amblyopia. However, the presence of a hyperopic refractive error always demands accommodation to improve vision when this is compounded by anisohyperopia, there remains a constant monocular blur in the more ametropic eye since with details clearly focused on the fovea of the better eye, no stimulus is provided for the further accommodative effort required to produce a clear image in the fovea of the more hypermetropic eye.[5]

It is not clear why in our patients the hyperopic eye was preferred, as the natural preference in young children is to develop an excellent vision in the eye that sees better at near, which usually is the emmetropic or myopic eye, with consequent amblyopia of the contralateral eye.

A mild chronic form of accommodation spasm or over accommodation could be the underlying mechanism for this type of unpredicted eye preference. This would shift the more emmetropic eye to become myopic, whereas the more hyperopic eye would become the more emmetropic and thus preferred eye. The dry refraction of patient 3 supports this possible etiology.

A second theory is that the amblyopia we detected was actually long standing and had preceded by far the development of the anisometropia. There could have been a third amblyogenic factor in the non-hyperopic eye that had since resolved, leaving the amblyopia. As some claim, the anisometropia could have developed as a consequence of the amblyopia and its possible effect on the emmetropization process,[5,11,13] or it could have developed as the natural course in these children, unrelated to the amblyopia.[14,15]

Furthermore, changes in refraction in the young age group can be substantial. It is possible that before the current presentation, some of the children had an amblyogenic refractive error in the non-hyperopic eye, such as a larger astigmatism. This refractive error may have caused the amblyopia in the non-hyperopic eye and naturally changed to its present form with time.

Another theory is based on the assumption that the dominant eye is preferred regardless of its refraction. Eye dominance is independent of refractive error (myopia or hyperopia) and, according to several studies, is determined very early in infancy.[16] This process could, perhaps, result in our patients preferring the dominant eye even though it eventually became the eye with greater ametropia.

Alternatively, the non-hyperopic eye may have a subclinical organic abnormality in the optic nerve, retinal ganglion cells, or retinal nerve fiber layer, causing poorer vision. However, a complete examination of optic nerve function was normal. Unfortunately, optical coherence tomography, which could theoretically detect such an abnormality, was not performed in our patients. Be that as it may, an organic abnormality seems less likely given the improvement in BCVA after treatment, which would not be expected under these circumstances.

Three patients were treated with full or near full refractive correction to the preferred eye, with reduced correction or even myopic biased correction to the amblyopic eye. One patient (that was lost to follow-up) refused to wear glasses or patch. The other three also needed patching of the non-amblyopic eye initially, to improve acceptance of the glasses. Full correction glasses according to cycloplegic refraction were not accepted by all these patients.

The underlying pathophysiology of this clinical presentation is not completely understood. It might be more common than expected. We found only a single similar case report in literature, in which a patient with anisometropic amblyopia showed a preference for the best visual development in the more hyperopic eye.[17] We have put forth a few simple theories to try and explain this phenomenon. However, the older age of some of the children at diagnosis and the absence of previous eye examinations or documentations limit our ability to fully characterize it.

Conclusion

This study describes the phenomenon of anisometropic amblyopia in the non-hyperopic eye, with the counterintuitive hyperopic eye being the one with better vision. This was unique and rare finding. We suggest a treatment approach consisting of complete correction of only the amblyopic eye, while correcting the preferred eye only to the level that vision is not blurred. When the amblyopia is only partially corrected, patching is added. Compliance is very important, as affected children are diagnosed relatively late and will not accept any correction. It is important that clinicians be aware of this phenomenon, as it requires some modification of conventional glasses prescription. Further longitudinal studies are needed to shed light on the underlying pathophysiological mechanism.

Financial Disclosures

This study was partially supported by the Zanvyl and Isabelle Krieger Fund, Baltimore, Maryland, USA. The funding organization had no role in the design or conduct of this research.

Authors’ Contributions

Design of the study (NG-C and RS.); conduct of the study (AS, RS, and NG-C); preparation of the manuscript (AS, NG-C, and MA); and review and approval of the manuscript (AS, RS, MA, and NG-C).

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