






CASE REPORT

Successful Treatment of Mixed Amblyopia with Optic Nerve Hypoplasia (ONH) in an Adult Indonesian Patient

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Abstract

Introduction: Amblyopia significantly contributes to low vision and blindness in adults in an Indonesian rural setting. The treatment of amblyopia, particularly anisometropic and/or strabismic amblyopia, has long been challenging for many clinicians. This study aims to report a promising result of refractive correction, occlusion therapy, and oral citicoline on mixed amblyopia with optic nerve hypoplasia in adult Indonesian patients.

Case Presentation: A 20-year-old male with a chief complaint of blurry right eye since one year ago, becoming more severe lately. The patient had been strabismic since his childhood. History of using a -5 concave spherical lens on his RE, with the normal eye on his LE. Visual acuity (VA) of his RE was 3/60 and his LE was 6/30. The RE was deviated, with 30° of exotropia. Nystagmus was also found. Optical coherence tomography (OCT) examination found maculopathy and optic nerve hypoplasia in both eyes. We treated the patient with spectacles to correct the refractive error, occluded his fixing eye, and gave an oral citicoline. **Conclusions:** Refractive correction and occlusion therapy are still meaningful choices of therapy and have shown to be effective in treating amblyopia, combined with oral citicoline to prevent nerve cell damage. Our case of refractive correction, combined with occlusion therapy and oral citicoline on mixed amblyopia in an adult Indonesian patient, showed good results and a promising post-treatment prognosis with a decrease of exotropia degree and disappearance of nystagmus in just two months.

Keywords: mixed amblyopia; optic nerve hypoplasia; refractive correction; occlusion therapy; citicoline

Introduction

Amblyopia is the most common cause (affecting 2–4% of the population) of low visual acuity (VA) in children and adults in developed countries.^[1] In adults, the prevalence of amblyopia was 3.32% in European countries and 3.09% in The West Pacific Region countries.^[1] A study in an adult Chinese rural population showed that the prevalence of mixed amblyopia caused by anisometropia and strabismus was 4.4%.^[2] A systematic review of the global prevalence of amblyopia reported only seven studies with the mean age of the study population over 20, ranging from 29.5 to 59 years old.^[3] In Indonesia, amblyopia significantly contributes to low vision and blindness in adults in a rural settings. According to the latest study^[4] about amblyopia in the adult Indonesian population of adults 21 years or older conducted in five rural villages and one provincial town in Sumatra, amblyopia plays a major contributing cause of low bilateral vision, about 12.9% and unilateral blindness of approximately 50.0%. This study was similar to other developing rural countries in Asia.^[4] Many clinicians have long challenging difficult to manage amblyopia, especially anisometropic (difference in refractive correction) and/or strabismic (turn of one eye) amblyopia.^[5]

Amblyopia is a developmental condition that results in binocular malfunction and a severe decrease of spatial VA in the affected eye. During the essential time or phases of visual development of the postnatal windows of experience-dependent brain plasticity, the condition is caused by disruption of normal visual information.^[6] It is frequently impossible for many individuals to achieve ideal



Figure 1. (A) The patient's Hirschberg test before treatment revealed 15 degrees of exotropia and; (B) Patients became orthophoria after the treatment.

results when the amblyopic eye obtains a VA compared to the other eye.^[5] When two amblyogenic variables contribute to amblyopia, it is deemed mixed amblyopia. Particularly in partially accommodating esotropia, microtropia, and monofixation syndrome, a combination of anisometropic and strabismic amblyopia is frequent.^[7] The traditional course of treatment for amblyopia entails either surgical realignment of the eyes or optical correction of the refractive defect, followed by a period of "refractive adaptation" and long-term occlusion therapy for the good eye, usually by covering it with a patch. Adults and older children rarely receive orthodox treatment.^[6] This practice has been supported by clinical trial data showing that patching (or occlusion therapy) is mainly ineffective after ten years old.^[6] There is a strong clinical consensus that covering the other eye is effective for up to eight years during the vulnerable time. According to a sizable multicenter trial conducted by The Pediatric Eye Disease Investigator Group (PEDIG) in 2005, occlusion or atropine treatment for amblyopia proved ineffective after 12 years. However, there was a glimmer of hope that untreated kids would also make progress.^[5]

Reduced optic nerve axon density is a hallmark of optic nerve hypoplasia (ONH). Bilaterally or unilaterally, it may manifest.^[6] It can appear as an individual anomaly or in conjunction with other midline brain anatomical problems such as septum pellucidum absence, corpus callosum agenesis, cerebral hemisphere abnormalities, or pituitary gland abnormalities. A substantial number of ONH patients have concurrent structural central nervous system abnormalities (90%) and neuro-developmental handicaps (70%).^[6] ONH can develop bilaterally symmetrically, bilaterally asymmetrically, or unilaterally. Relative afferent pupillary abnormalities can also be detected in unilateral and asymmetric bilateral ONH. Congenital sensory nystagmus frequently manifests at 1-3 months of age in cases of bilateral ONH, and by the age of one, strabismus, typically esotropia, has developed. Most often, strabismus occurs in situations that are clearly unilateral or asymmetrical.^[6]

Studies regarding the treatment of mixed amblyopia in adults or any case reports of mixed amblyopia and other ocular problem and its management in Indonesian patients are still minimal. This study intended to report a successful case of mixed amblyopia and ONH management in adults with refractive correction and occlusion therapy in an Indonesian patient. Hopefully, this case report can give another perspective on alternative treatment for mixed amblyopia patients, especially in Indonesia, where eye healthcare facilities are minimal.

Case presentation

A 20-year-old male presented to our hospital with a chief complaint of blurry right eye since one year ago, with the blurry becoming more severe lately. The parents reported that the patient had been strabismus since childhood, which has become more severe lately. The patient did not get any treatment for his strabismus other than spectacles; however, according to his mother, the patient rarely used his spectacles until now. History of using a -5 concave spherical lens on his right eye, with the normal eye on his left eye. He has a twin; however, the twin's eyes are normal. His mother, uncle, and grandmother have myopia; however, there was no family history of strabismus. He was born at nine months, with a low birth weight of 1.500 g. He was placed in an incubator for 13 days and used an oxygen aid when he was three days old. He got seizures when he was three months old. The patient had normal growth and development.

His RE VA was 3/60, and his LE VA was 6/30. The right eye was deviated, with 15 degrees of exotropia on the Hirschberg test, as shown in Figure 1. There was also nystagmus. From the direct ophthalmoscope examination, his optic nerves looked normal. The patient underwent an optical coherence tomography (OCT) examination to look for other abnormalities on his optic nerve. A maculopathy and ONH were found in both eyes (Figure 2). There were no other abnormalities on both eyes or other parts of the body.

On the day of admission, we gave the patient spectacles to treat the amblyopia and improve the patient's VA. On his RE, his VA before the correction was 3/60 and became 6/30 after cycloplegic refraction with the correction of S -6.50 C -0.50 A 180° lens. On his LE, his VA before the correction was 6/30 and became 6/8 after cycloplegic refraction with the correction of the S -3.50 lens. We also gave the patient citicoline 1.000 mg once daily. One month after the first treatment, the exotropia degrees became less than ten prism diopters, and the nystagmus was minimal. We decided to continue the spectacles, patched his left eye for one hour, and citicoline 1.000 mg once daily. One month after the second treatment, the

exotropia degrees diminished and became orthophoria, and the nystagmus disappeared. We decided to continue the spectacles, patched his right or left eye for two hours, and citicoline 1.000 mg once daily.

Discussion and conclusions

Mixed amblyopia is a significant disease that can lead to low vision and blindness if not treated early. However, the treatments remained challenging, especially in adults. The 16 persons with strabismic or mixed amblyopia studied in the rural adult Chinese population, esotropia was detected in eight (50%), exotropia was detected in seven (43.8%), and exophoria was detected in one (6.3%).^[2] According to the same study^[2], females also had a significantly higher prevalence of mixed amblyopia than males, with 50%. Our case was contrary to this study.

We reported a case of mixed amblyopia with onset at 20 years old with a chief complaint of blurry right eye since one year ago, which became more severe lately. Clinically, the patient's right eye showed deprived exotropia. These symptoms elucidated with the patient's history that he has been strabismic since childhood and left untreated. This condition is worsened with anisometropia (OD -5, OS plano). Typical signs of amblyopia such as an eye that wanders outward, eyes that do not work together, and abnormal results of vision screening tests were also found in the patient. Mixed amblyopia should be distinguished from other deprivation disorders which may be associated with amblyopia, such as blepharoptosis, congenital cataract, congenital corneal opacities, hemangioma, optic nerve coloboma, persistent fetal vasculature, and other retinal diseases.^[8] Another study showed that if amblyopia is suspected, visual impairment can lead to ONH. Retinal changes in amblyopic patients have been investigated in several studies through OCT examination. Both retinal nerve fiber layer (RNFL) and macular thickness were evaluated, and different results were obtained from these studies. RNFL thickness in

amblyopic patients was found to be thicker, thinner, or unchanged compared to control groups in some studies.^[9] In our study, OCT examination revealed the typical abnormality of the macula that followed amblyopia in the affected and fellow eye, in which maculopathy (decrease of both RNFL and macular thickness) and ONH diagnosis were confirmed, with the average of RNFL thickness in both his RE and LE were 68 μm , the average macular thickness in his RE was 257 μm and 250 μm in his LE, the average C/D ratio in his right eye is 0.79 and 0.77 in his LE.

Recent investigations questioned and offered solid evidence that different tactics can promote brain plasticity in adulthood and recover visual function in amblyopic individuals, contrary to the clinical notion that amblyopia is an incurable illness.^[10] The definitive management of amblyopia is correct for any factor degrading the quality of the visual image (e.g. infantile cataract extraction, ptosis repair), refractive correction, and occlusion therapy. It has long been established that treating an underlying refractive defect is essential in the management of amblyopia. Prior to occlusion therapy, refractive correction alone can have a number of substantial advantages and significantly enhance amblyopic visual acuity. The most traditional, straightforward, and efficient approach of treating amblyopia is occlusion. It works to both increase visual acuity in the amblyopic eye and remove distracting factors from the fixing eye in the opposite eye. Its favorable characteristics make it the preferred amblyopia treatment.^[10] In studies conducted in children aged 7-12 years, part-time occlusion is comparable to full-time occlusion in the effectiveness of treatment for mild to moderate amblyopia, unlike in severe amblyopia, where six hours and full-time occlusion were more effective than two hours occlusion therapy.^[11] Several studies suggest that drug therapy such as oral administration of citicoline in combination with patches helps to achieve more stable effects in the treatment of amblyopia than

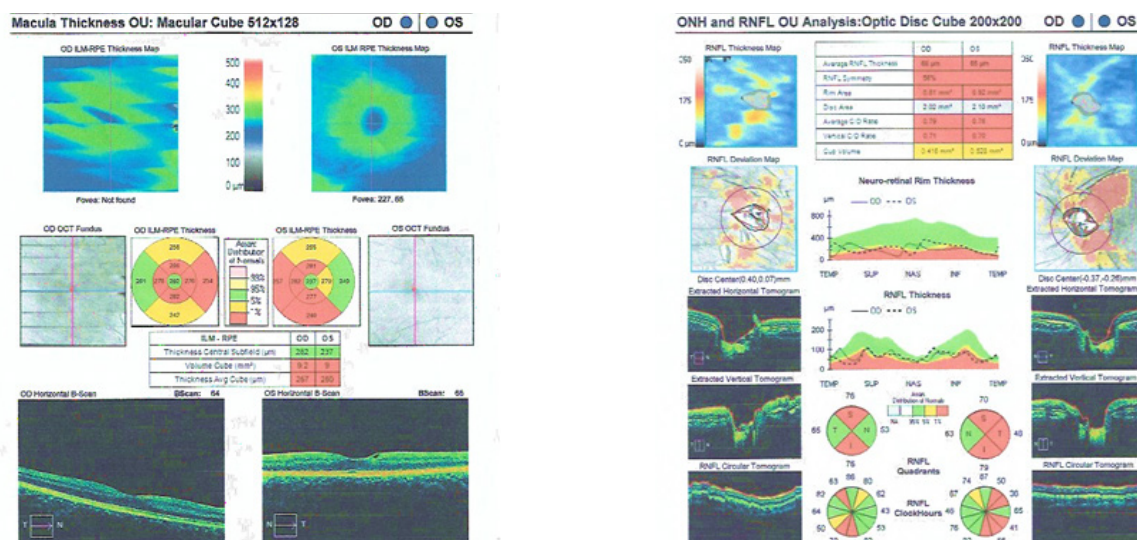


Figure 2. The OCT examination of patients revealed maculopathy and optic nerve hypoplasia.

the administration of patches alone.^[10] Our case was a bit different because we gave treatment to an adult patient. We found that there was a significant result with decreased degrees of exotropia and the disappearance of nystagmus after the refractive correction was given, one-hour occlusion therapy followed by two-hour occlusion therapy on his fixing eye, and oral citicoline 1.000 mg once daily in just two months. Citicoline is the generic name of cytidine-5'-diphosphocholine (CDP-choline), an endogenous compound that is able to increase the levels of neurotransmitters in the central nervous system by interacting with the synthesis of cellular membranes phospholipids, mainly phosphatidylcholine.^[12] Exogenous citicoline, administered by ingestion or injection, is hydrolyzed and dephosphorylated in order to form cytidine and choline, which resynthesize CDP-choline inside brain cells and proven to have neuroprotective effects in amblyopia. The condition of exotropia and nystagmus improved because the amblyopia condition improved. According to a study^[13], there will be a significant visual improvement after 18 weeks of occlusion therapy. So that, continuing of occlusion therapy and further follow up of the visual improvement need to be done.

Mixed amblyopia, especially in an adult, is considered a rare condition that can lead to low vision and blindness without prompt treatment. Refractive correction and occlusion therapy are still a significant choice of therapy and have shown to be effective in the treatment of amblyopia, combined with oral citicoline as prevention from nerve cell damage. Our case of refractive correction, combined with occlusion therapy and oral citicoline on mixed amblyopia with ONH in an adult Indonesian patient, showed good results and a promising prognosis after treatment. One of the limitations of our study was not obtaining OCT data from the patient after the visual acuity improved. However, continuous monitoring and evaluation are required to ensure and maintain a good prognosis for the patient's vision.

Prompt treatment strategies can increase brain plasticity in adulthood and restore visual function in adult patients with mixed amblyopia and ONH.

References

- [1] Hashemi H, Pakzad RMs, Yekta A, Bostamzad P, Aghamirsalim M, Sardari SMs, et al. Global and regional estimates of prevalence of amblyopia: A systematic review and meta-analysis. *Strabismus* 2018;26:168–183. <https://doi.org/10.1080/09273972.2018.1500618>.
- [2] Wang Y, Liang YB, Sun LP, Duan XR, Yuan RZ, Wong TY, et al. Prevalence and causes of amblyopia in a rural adult population of Chinese the Handan Eye Study. *Ophthalmology* 2011;118:279–283. <https://doi.org/10.1016/j.ophtha.2010.05.026>.
- [3] Fu Z, Hong H, Su Z, Lou B, Pan C-W, Liu H. Global prevalence of amblyopia and disease burden projections through 2040: A systematic review and meta-analysis. *Br J Ophthalmol* 2020;104:1164–1170. <https://doi.org/10.1136/bjophthalmol-2019-314759>.
- [4] Saw S-M, Husain R, Gazzard GM, Koh D, Widjaja D, Tan DTH. Causes of low vision and blindness in rural Indonesia. *Br J Ophthalmol* 2003;87:1075–1078. <https://doi.org/10.1136/bjo.87.9.1075>.
- [5] Maconachie GDE, Gottlob I. The challenges of amblyopia treatment. *Biomed J* 2015;38:510–516. <https://doi.org/10.1016/j.bj.2015.06.001>.
- [6] Dahl S, Pettersson M, Eisfeldt J, Schröder AK, Wickström R, Teär Fahnehjelm K, et al. Whole genome sequencing unveils genetic heterogeneity in optic nerve hypoplasia. *PLoS One* 2020;15:e0228622. <https://doi.org/10.1371/journal.pone.0228622>.
- [7] Astle AT, McGraw P V, Webb BS. Can human amblyopia be treated in adulthood? *Strabismus* 2011;19:99–109. <https://doi.org/10.3109/09273972.2011.600420>.
- [8] Milla M, Piñero DP. Characterization, passive and active treatment in strabismic amblyopia: A narrative review. *Int J Ophthalmol* 2020;13:1132–1147. <https://doi.org/10.18240/ijo.2020.07.18>.
- [9] Zagui RMB. Amblyopia: Types, Diagnosis, Treatment, and New Perspectives. *Am Acad Ophthalmol* 2019. <https://www.aao.org/disease-review/amblyopia-types-diagnosis-treatment-new-perspectiv> (accessed February 7, 2022).
- [10] Atakan M, Culfa S, Calli U, Penbe AD, Atakan TG, Ozerturk Y. Evaluation of retinal nerve fiber layer and macular thickness in amblyopia. *J Clin Exp Ophthalmol* 2015;6:1–4. <https://doi.org/10.4172/2155-9570.1000437>.
- [11] Pescosolido N, Stefanucci A, Buomprisco G, Fazio S. Amblyopia treatment strategies and new drug therapies. *J Pediatr Ophthalmol Strabismus* 2014;51:78–86. <https://doi.org/10.3928/01913913-20130107-01>.
- [12] Iulia C, Ruxandra T, Costin L-B, Liliana-Mary V. Citicoline - A neuroprotector with proven effects on glaucomatous disease. *Rom J Ophthalmol* 2017;61:152–158. <https://doi.org/10.22336/rjo.2017.29>.
- [13] Singh I, Sachdev N, Brar GS, Kaushik S. Part-time occlusion therapy for amblyopia in older children. *Indian J Ophthalmol* 2008;56:459–463.