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Case Report

The Anatomical and Functional Response to a Combination of Oral and Topical Carbonic Anhydrase Inhibitors in a Patient with Foveoschisis

Burak Turgut* and Tamer Demir

Department of Ophthalmology, Faculty of Medicine, Fırat University, Elazig, Turkey

***Corresponding author:** Burak Turgut, Department of Ophthalmology, Faculty of Medicine, Fırat University, 23119, Elazig, Turkey, Tel: +90 4242333555; Fax: +90 4242388096; E-mail: drburakturgut@gmail.com

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Abstract

We report the anatomical and functional responses to a combination of oral and topical Carbonic Anhydrase Inhibitor (CAI) for foveoschisis in a case of X-Linked Juvenile Retinoschisis (XLRS). A 26 years old man having the visual impairment in both eyes since his childhood was admitted to the ophthalmology clinic in our university hospital. He had diagnosed the XLRS in several hospitals and any medical treatment had not recommended for foveoschisis causing the visual impairment. His systemically history was including bronchial asthma. The Visual Acuity (VA) of both eyes was 3/10 according to Snellen charts. Fundus examination revealed radial cystoid appearance in the petaloid configuration in fovea and retina pigment epithelium alterations at superior mid-peripheral retinae in both eyes. Optical coherence tomography showed the foveal cystoid structures and the loss of foveal depression and the splitting at inner retinal layers in the macula. An oral CAI for seven days and then a topical CAI were used. A significant reduction in foveal cystoid structures size and some improvement in visual acuities in both eyes was observed in 10 days following the treatment initiation. At the 10th week, VA was measured as 6/10 and 5/10 in right and left eyes, respectively. The combination of oral and topical carbonic anhydrase inhibitors should be considered for anatomical and functional improvements in the patient with foveoschisis.

Keywords

Carbonic anhydrase inhibitors; Foveoschisis; Oral; Topical; X-linked juvenile retinoschisis

Introduction

The X-Linked Juvenile Retinoschisis (XLRS) is the most common juvenile macular degeneration in males. The females are carriers for this disease. Its prevalence among males has been estimated as 1/15000-1/30000 [1-3]. Characteristic features of the disease are mild to severe central visual loss, radial streaks arising from foveoschisis, splitting at inner layers in the peripheral retina, and a negative electroretinogram due to a significant reduction of b-wave amplitude [1-4]. Fovealschisis or foveoschisis (retinal splitting in the fovea) in the petaloid pattern of folds radiating out from the fovea is the characteristic finding of XLRS. Foveoschisis is present in about 100% of cases and it is not only pathognomonic but also essential for the XLRS diagnosis [1-4]. In the previous reports, it has been demonstrated that both oral and topical forms of Carbonic Anhydrase Inhibitor (CAI) are successful in the medical treatment of the foveoschisis and peripheral retinoschisis in XLRS [5-11].

We aimed to report the anatomical and functional responses to a combination of oral and topical CAIs in a case of XLRS.

Case Presentation

A 26 years old man admitted to our clinic with the complaint of the visual impairment in his both eyes since childhood. He had diagnosed the XLRS in several hospitals and any medical treatment had not recommended for foveoschisis causing the visual impairment. His systemically history was including bronchial asthma. The Visual Acuity (VA) of both eyes was 3/10 according to Snellen charts. His intraocular pressure was 16 mmHg in both eyes. Direct and indirect light reflexes were intact in both eyes, without a relative afferent pupillary defect. The anterior segment examination and extraocular movements were normal. Fundus examination with ophthalmoscopy using a +90 diopter noncontact lens, red-free and color fundus photography revealed radial cystoid appearance in the petaloid configuration in fovea and Retina Pigment Epithelium (RPE) alterations at superior mid-peripheral retinae in both eyes. Optical Coherence Tomography (OCT) (Zeiss Cirrus HD-OCT 5000, Carl Zeiss Meditec Inc., Dublin, CA, USA) showed the foveal cystoid structures and the loss of foveal depression and the splitting at inner retinal layers in the macula. Central Foveal Thicknesses (CFT) in the right and left eye were 391 and 388 micrometers, respectively (Figure 1A and B). An oral CAI (totally 750 mg acetazolamide per a day in three tablets of each containing 250 mg acetazolamide) for seven days was used and then treatment was continued with a topical CAI (dorzolamide in three drops per a day). During treatment with oral CAI, the patient experienced the side effects such as fatigue, and numbness in his fingers and lips due to systemically usage of the CAI. He did not experience any side effects due to topical CAI. The usage of topical CAI was recommended for at least of six months.

A significant reduction in the size of foveal cystoid structures and some improvement in VA in both eyes were observed at the 10th day following the treatment initiation. OCT in this examination revealed that the foveal depression re-formed partially and that foveal cystoid structures were reduced significantly. CFT in the right and left eye were 278 and 307 micrometers at this examination (Figure 1C and D). In the follow-up examination at 17th day, VAs was 5/10 in both eyes and foveoschisis had more improved (Figure 1E and F). At the 5th week (Figure 1G and H) and 10th week (Figure 1I and J), VA was measured as 6/10 and 5/10 in right and left eyes, respectively. OCT findings were similar to those on the 10th day and CFT in the right and left eye were 300 and 292 micrometers (Figure 1I and J).

In the follow-up examination at 3th month following the treatment, there was no significant difference in fundus and OCT findings than those at 10th week and the patient was continuing to use the topical CAI.

Discussion

X-linked juvenile retinoschisis is a bilateral macular degeneration presenting usually in the middle of the first decade of life or the age of early elementary school. Other synonyms of XLRS are juvenile retinoschisis, congenital retinoschisis, and juvenile macular degeneration/dystrophy. At the first presentation, VAs of affected males are typically at the level of 2/10-4/10. However, the loss in VA may progress to the level of legal blindness (VA <20/200) at the 6th or 7th decade [1,2].

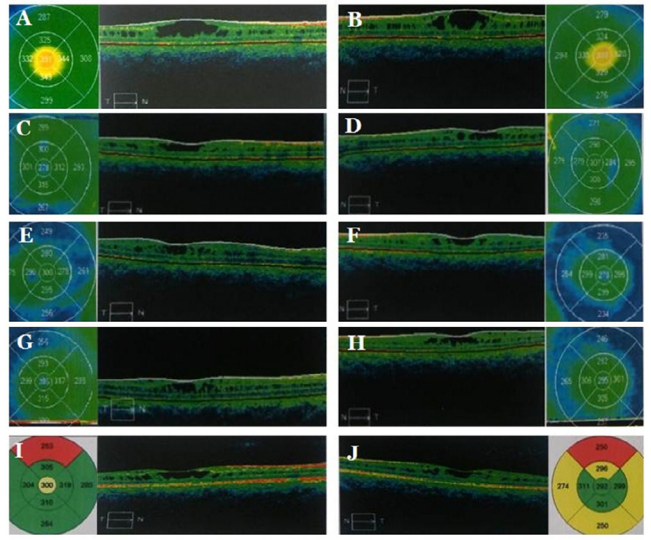

Figure 1: Horizontal OCT scans and macular thickness maps of both eyes at the initial examination (A,B), 10th day (C,D), 17th day (E,F), 5th week (G,H) and 10th week (I,J) of the treatment.

Carrier females are usually asymptomatic. Foveoschisis or fovealschisis is retinal splitting in the fovea and it is present in about 100% of the cases with XLRS. Thus, foveoschisis is not only pathognomonic but also essential for the XLRS diagnosis. The retinal splitting is at the nerve fiber layer and the ganglion cell layer in XLRS whereas degenerative or age-related peripheral retinoschisis, splitting are located in the outer retina through the outer nuclear layer and plexiform layer [1,2].

The characteristic finding of foveoschisis is cystoid lesions with a radial pattern around foveola. Cystoid lesions may be disappearing at an advanced age, or a large cavity (cystoid foveal degeneration) may occur with emerging of the cyst walls [1,2].

Foveal lesions in XLRS may include single or a combination of largely radial striations, microcystic lesions (most commonly), honeycomb-like cysts, RPE mottling/alterations, loss of the foveal reflex, or foveal atrophy [12,13].

Peripheral retinoschisis is present in a half of the cases and is not essential for diagnosis. However, it is responsible from Retinal Detachment (RD) and Vitreous Hemorrhage (VH). The most common localization of peripheral retinoschisis is inferotemporal peripheral quadrant. Thus, XLRS may cause to rhegmatogenous RD in the 5-22% and VH in the 4-40% of the cases. The avoidance of head trauma and high-contact sports is recommended to the patients with XLRS [1,2].

The fundus findings to be observed except retinoschisis and Foveoschisis are grayish-white dendritic lesions, perivascular white sheathing, vitreous veils/nets, pseudo- papillitis, anterior/posterior vitreous detachment, syneresis and grayish-white spots like chorioretinitis scars [1-4].

The differential diagnosis of XLRS should be done from Cystoid Macular Edema (CME), Goldmann-Favre Syndrome, enhanced S-cone syndrome, retinitis pigmentosa, VCAN-related vitreoretinopathy and degenerative or age-related retinoschisis. Foveoschisis commonly mimics CME and it is the one of the most common causes of pseudo-CME. However, in fundus fluorescein angiography of an eye with foveoschisis, any leakage the late phases are not observed [1,2].

XLRS is caused by the mutation in the Retinoschisin gene (RS1) on chromosome Xp22.2. Retinoschisin, also known as XLRS protein is a peptide providing the structural and functional integrity of the retina released by bipolar cells and photoreceptors and which is synthesized by RS1 gene. It is composed of an N-terminal leader sequence, RS1 domain, discoidin domain, and C-terminal segment, each of which has been found to contain disease-causing mutations in XLRS patients [2-4]. It has been demonstrated histopathologically that, in the case of the existence of RS1 gene mutation or defective retinoschisin gene, abnormal retinoschisin causes dysfunction of Müller cells, and subsequently the splitting at retinal nerve fiber layer [1-4]. In recent genetical studies, it has been detected that The RS1 gene mutation over 125 at the different locations are related with XLRS [2-4].

Although there is no approved treatment for XLRS, since it is a recessive disease caused by the loss of retinoschisin function, it has been considered that gene replacement therapy is a potential treatment option for patients with XLRS. In this treatment modality, it is purposed that the introduction of a functional copy of a gene into a patient's own cells using a delivery system such as adeno-associated viral vectors expressing the human RS1 gene [14-16].

Pars-Planavitrectomy (PPV) is indicated when the severe complications such as VH and RD occur. If the VH or RD occurs in childhood age, PPV should be performed to avoid amblyopia. The prophylactic treatment of retinoschisis by laser photocoagulation or vitreoretinal surgery is generally not being recommended [1-4].

In most cases, treatment of XLRS is limited to the prescription of low-vision aids. In recent case series and reports, it has been demonstrated that topical or oral CAI provided a significantly reduction in foveoschisis with an improvement of visual acuity in about a half of cases. However, the anatomical and visual improvements are not correlated with each other [5-11].

It has been considered that CAIs might act via the increased fluid outflow from RPE due to inhibition of CA in the RPE cells containing higher levels of CA, active ionic transport of intraretinal fluid, a pH alteration to be cause secondary fluid transport in the retina or the enhancement of retinoschisin production [5-11].

Conclusion

Carbonic anhydrase inhibitors in both oral and topical forms may provide both anatomically and functionally improvement in the patients with foveoschisis. However, the patients should be cautioned about the adverse effects and rebound phenomenon of the drugs and the recurrence possibility of the foveoschisis.

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Authorship and contribution

All authors listed on the title page made significant contributions to this manuscript.

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Competing interest

The authors have no conflict of interest or financial relationships related to this manuscript.

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