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Case Report / *Olgu Sunumu*

Ocular Problems in Triple-A Syndrome and Their Management

Triple A Sendromlu Bir Olgudaki Göz Problemleri ve Tedavi Yaklaşımı

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Summary

Triple-A syndrome (Allgrove syndrome), is a rare autosomal recessive syndrome that is characterized by adrenal insufficiency, alacrimia and achalasia. In this report, we present a case of triple-A syndrome and discuss the ocular manifestations of the diseases along with evaluation of the therapeutic options. In addition to the classic triad of triple-A syndrome, our patient had intermittent exotropia. The patient was receiving oral steroids for adrenal insufficiency and artificial tear drops for eye dryness. Surgery was planned for exotropia. Punctum plug insertion was made simultaneously with bilateral lateral rectus recessions. Postoperative follow-up revealed near and distant horizontal deviation at the interval of ±10 PD. The patient's complaints about eyes regressed significantly as well. Triple-A syndrome is a life threatening and rare disorder that could be fatal when undiagnosed. Punctum plugs are convenient therapy option for the treatment of xerophthalmia encountered in triple-A syndrome. With strabismus surgery including punctum plug insertion, any other surgery can be simultaneously carried out during a single session of general anesthesia. *(Turk J Ophthalmol 2012; 42: 492-4)*

Key Words: Tripple A syndrome, exotropia, dry eye

Özet

Triple A (Allgrove sendromu) nadir rastlanan, otozomal resesif olarak kalıtım gösteren ve adrenal yetmezlik, alakrima ve akalazya ile karakterize bir sendromdur. Bu olgu sunumunda bir Triple A sendromu vakası sunuyor ve hastalığın göz bulguları ile tedavi seçeneklerini tartışıyoruz. Klasik Triple A üçlemesine ek olarak, hastamızda geniş açılı intermitan ekzotropya mevcut idi. Adrenal yetmezlik için oral steroid ve kuru göz için suni gözyaşı kullanmakta idi. Ameliyat ekzotropya nedeni ile planlandı. Punktum plak yerleştirilmesi, iki taraflı dış rektus geriletmesi ile beraber gerçekleştirildi. Postoperatif takipte tatmin edici seviyede füzyonal konverjans gözlendi, yakın ve uzak kayma açıları ±10 prizm dioptri (PD) aralığında idi. Hastanın kuru göz şikayetlerinde önemli derecede azalma oldu. Triple A (Allgrove sendromu) eğer teşhis edilmez ise ölümcül olan nadir rastlanan bir sendromdur. Triple A'da görülen kseroftalmi tedavisinde punktum plakları uygun seçenektir. Ekzotropya ameliyatı ve punktumlara plak yerleştirilmesi cerrahi gereken olgularda genel anestezi altında eşzamanlı olarak yapılabilir. *(Turk J Ophthalmol 2012; 42: 492-4)*

Anahtar Kelimeler: Tripple A sendromu, ekzotropya, kuru göz

Introduction

Triple-A syndrome (Allgrove syndrome), is a rare autosomal recessive syndrome that is characterized by adrenal insufficiency, alacrimia and achalasia. In this report, we present a case of triple-A syndrome and discuss the ocular manifestations of the diseases along with evaluation of the therapeutic options. In addition to the classic triad of triple-A syndrome, our patient had intermittent exotropia. The patient was receiving oral steroids for adrenal insufficiency and artificial tear drops for eye dryness. Surgery was planned for exotropia. Punctal plugs insertion was made simultaneously with bilateral lateral rectus recessions. Postoperative follow-up revealed near and distant horizontal deviation at the interval of ±10 PD. The patient's complaints about eyes regressed significantly as well. Triple-A syndrome is a life threatening and rare disorder that could be fatal when

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Case Report

A six-year-old girl was admitted to ophthalmology outpatient service with a history of stinging eye, periorbital redness, intermittent strabismus, and the patient was experiencing difficulty when staring at light. The patient had normal mental and motor abilities. Best-corrected visual acuity was 20/20 (with -1.00 diopter) in the right eye and 20/20 (with -1.25 diopter) in the left eye. Intraocular pressures were within normal limits. Biomicroscopic evaluation revealed superficial punctate fluorescein dye retention (Figure 1). Schirmer test performed under topical anesthesia demonstrated wetting of 4 mm in the right eye and 2 mm in the left eye after five minutes. Tear osmolarity value was detected by using OSMOMAT 030-D device (Gonetec GmbH, Germany) and the osmolarity scores were 321 mosmol/l, which is beyond the normal range (normal value <310 mosmol/l). Pupilla and fundus examinations were within normal limits. Central cornea thicknesses were approximately 560 microns in right and 556 microns in left. The patient successfully showed all 38 plates in Ishiara color vision test.

Strabismological exam revealed no restriction and excess muscle movements. Distant angle deviation was 40 PD exotropia and near angle of deviation was 30 PD exotropia. After all these evaluations, the patient was diagnosed with keratoconjunctivitis sicca and intermittent exotropia (Figure 2).

Dermatological evaluation revealed generalized hyperpigmentation, which was more prominent on the lips, gums, buccal and genital mucosae, palmoplantar regions with accentuation at the palmar creases, as well as on knees and elbows. She had also recurrent angular cheilitis (Figure 3). Patient's history revealed that skin darkening progressed within the last 2 years. Respiratory and cardiovascular system examinations did not demonstrate any pathological results. In her biochemical analysis, early morning cortisol levels were 0.223 ug/dl and 0.294 ug/dl (N: 5-25 ug/dl), which were extremely low. Thyroid function tests, anti-thyroid peroxidase, as well as biochemical parameters including fasting serum glucose, serum Na and serum K were within normal limits.

Barium swallow test revealed uncoordinated peristalsis. On the barium-filled esophagus, images resembling that of achalasia could be observed. Brain and orbital magnetic resonance imaging revealed normal brain tissue but lacrimal glands were bilaterally missing (Figure 4). In the light of these laboratory and clinical findings, the patient was diagnosed to have triple-A syndrome.

Investigations of the other possible autonomic defects revealed hearing loss of the right ear, while bilateral outer ear canals and tympanic membranes were normal. The patient was diagnosed with mixed type hearing loss. Hearing aid was recommended for her right ear.

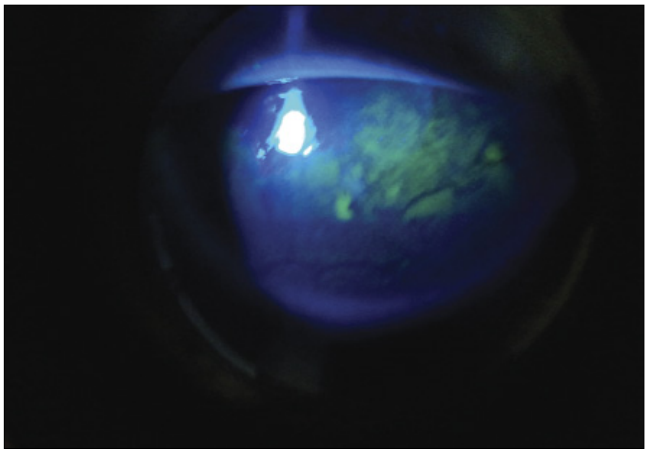

Figure 1. Biomicroscopic evaluation revealed superficial punctate fluorescein dye retention

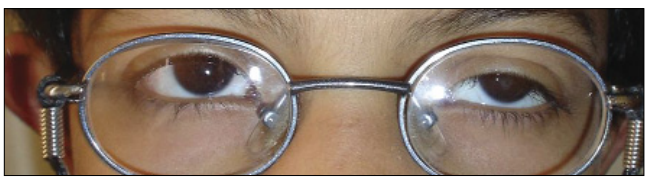

Figure 2. Patient's pre-operative image

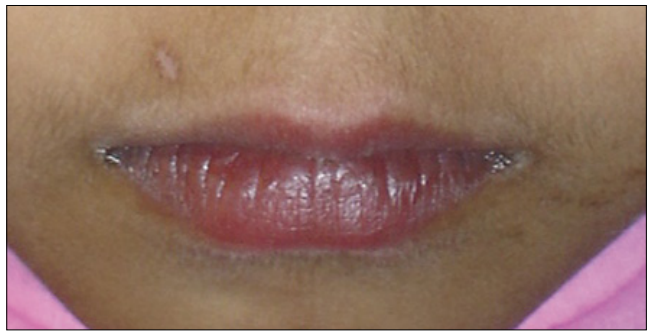

Figure 3. The patient had generalized hyper-pigmentation and angular cheilitis

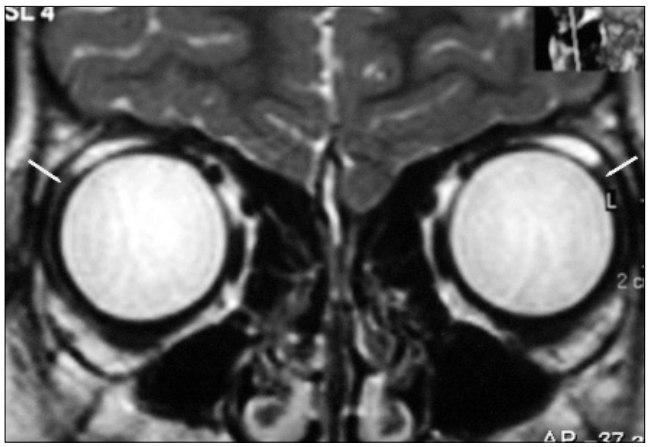

Figure 4. Magnetic resonance imaging show absence of both lacrymal glands

The patient was treated with oral steroids by pediatric endocrinology. Topical artificial tears were administered. The bilateral inferior punctal plugs were inserted (Figure 5) and in the same session bilateral 8 mm lateral rectus recessions were performed. Following the surgery, near and distant horizontal deviation was less than 10PD (Figure 6) and photophobia complaints were diminished gradually. In the follow-up visits, we are using preservative-free artificial tears like poliviniyl alcohol (Refresh®). Her Schirmer test scores are between 5-7 mm in 5 minutes. There is no epiphora, but sometimes, we observe superficial punctate epitheliopathy recurrences.

Discussion

In order to facilitate the diagnosis, after the first report of triple-A syndrome, cases with typical triad (adrenal insufficiency, alacrimia and achalasia) were described. Alacrimia is the early and one of the cardinal features of the syndrome.[1] Other features of the syndrome such as achalasia and adrenal insufficiency may be observed in further stages of the diseases.[2] Of the approximately 100 cases reported so far, some have autonomic disorders dominating the clinical phenotype. Osteoporosis, xerostomia, accommodative exotropia are examples of these disorders.[3,4] Babu et al.[5] have evaluated the ocular manifestations of two affected siblings, and in addition to dry eyes, they have observed diminished pupillary light reflex. They have suggested that this was due to autonomic disregulation that could be seen in patients affected with the syndrome.

In addition to the classic triad of the syndrome, our case had large-angle divergence excess type of intermittent exotropia, normal mental and motor abilities, generalized and progressive hyperpigmentation of the skin and mucosa, and hearing loss. Although most of the published cases in literature are children, el-Rayyes et al.[6] have reported a 24-year-old case with hypoglycemia in whom the diagnosis was made by means of an adrenocorticotropic hormone (ACTH) stimulation test. However, the authors believe that the diagnosis should depend on genetic testing.

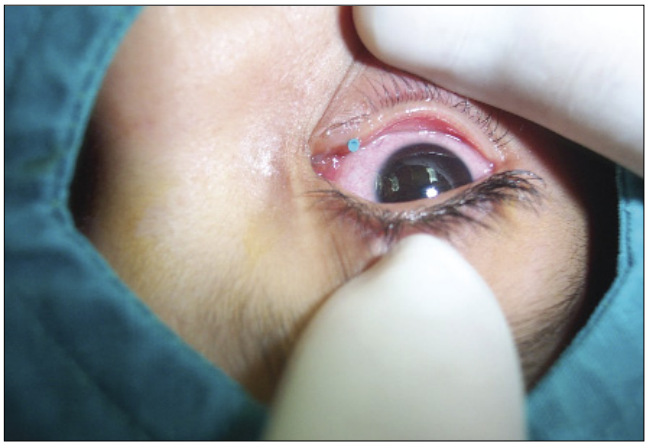

Figure 5. Insertion of bilateral superior and inferior punctal plugs

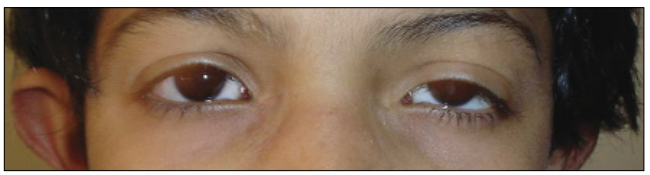

Figure 6. Patient's post-operative image

Up-to-date, the genetic studies demonstrated two leading mutations related to triple-A syndrome: an IVSC14+1 G–A mutation and a R155P mutation in exon 6. It is believed that the existence of R155P mutation in triple-A gene (ALADIN) is more valuable than stimulation tests in adults.[3] Younger cases, however, presented with hypoglycemic crisis. Moreover, there is emphasis on mental retardation in both reports.[7,8] Due to lack of consent by the patient's parents, we were unable to held genetic analysis.

In our case, there was no mental or motor retardation. This may point out to a large phenotypic spectrum among the patients reported. On the other hand, these cases might have been diagnosed in the advanced stages of the disease. In pediatric cases, placing punctal plugs is a good option to resolve dry eye symptoms. Moreover, if a strabismus surgery for any kind of tropia was planned, both procedures can be done simultaneously, which will reduce the total time spent under general anesthesia.

Triple-A syndrome, also known as achalasia-addisonianism-alacrimia syndrome or Allgrove syndrome, is a rare autosomal and life-threatening congenital progressive disorder. The affected patients typically have adrenal insufficiency due to ACTH resistance. The importance of this case is her having large-angle intermittent exotropia and the usage of punctal plugs in treatment of dry eye. In these cases, which generally concerns pediatric ophthalmology, a detailed neurological exam and hearing test are warranted in addition to a detailed ophthalmologic examination.

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