

CASE REPORT

**USHER SYNDROME WITH POSTERIOR
SUBCAPSULAR CATARACT****Bramantya Surya Pratama¹, Nadia Artha Dewi¹**¹Department of Ophthalmology, Faculty of Medicine, Universitas Brawijaya – Saiful Anwar General HospitalEmail: bramantyaspr@yahoo.com**ABSTRACT**

Introduction: Usher Syndrome (USH) is an autosomal recessive disorder characterized by congenital sensorineural deafness and progressive loss of vision due to retinitis pigmentosa. The aim of this report is to report rare cases of USH by performing diagnostic steps based on clinical examination and family history with expectations that if a similar case is found, an earlier diagnosis and rehabilitation can be done.

Methods: Diagnosis is based on history taking, ophthalmologic examination, followed with ear, nose, and throat (ENT) examination.

Results: A 23-year-old man came to the Ophthalmology Outpatient Department with complaints of having bilateral blurred vision especially during nighttime and visual field constriction starting 12 years prior to the visit. The patient experienced gradual vision deterioration followed by whitish spot in his left eye. Patient is deaf and mute since birth. Three family members of the paternal line exhibit the same symptoms. Patient's best corrected visual acuity was right eye 6/15 and left eye hand movement. Anterior segment examination showed bilateral cataract while posterior segment examination revealed peripheral bone spicules appearance and waxy pallor optic disc bilaterally. Loss of neurosensory layer, worse in the left eye, was discovered through Optical Coherence Tomography (OCT). Humphrey perimetry of the right eye indicated tunnel vision. Examination by otorhinolaryngologist revealed a sensorineural hearing loss. In this patient, there is no management for the disorders due to the poor prognosis of visual acuity. What can be done to improve the patient's quality of life is supportive therapy. It is important to screen and educate families suffering from the same disorder for early diagnosis & rehabilitation.

Conclusion: Clinical examination and family history confirm the diagnosis of USH. Early diagnosis and early rehabilitation are essential to improve patient's quality of life. In this case, no management was carried out for the cataracts because the visual acuity of both eyes did not match the cloudiness of the lens so there is possibility that the visual acuity could not improve. Rehabilitations that can be done for the patients are visual and social rehabilitation to improve quality of life.

Keywords: usher syndrome, retinitis pigmentosa, posterior subcapsular cataract, sensorineural hearing loss

PRELIMINARY

Usher syndrome (USH) is an autosomal recessive disorder characterized by congenital sensorineural hearing loss and progressive loss of vision due to retinitis pigmentosa. This syndrome is divided into three subtypes; Type I, Type II, and Type III. Usher syndrome

contributes to 3-6% of the total deaf population, 8-33% of individuals with retinitis pigmentosa and, 50% of the deaf-blindness population¹⁻⁴.

One of the comorbidities that appear in patients with USH is cataract. Cataracts that accompany USH usually occur at a relatively young age. The most common type of cataract in USH is the Posterior Subcapsular Cataract (PSC). This causes the patients vision to greatly decrease because the cloudiness of the lens, though mild, can make it difficult for light to reach the retina. This syndrome is very rare with incidence of 3 to 4.4 per 100,000 people. The purpose of this case report is to find out how to establish a clinical diagnosis of USH from clinical symptoms, clinical examination, and family history so that education related to prognosis and genetic counseling of patients can be done⁵⁻⁷.

CASE ILLUSTRATION

A 23-year-old man came to the outpatient clinic with complaints of decreased vision & hearing, mute since childhood, and cataracts in his left eye. The patient's mother said the patient is deaf and blind since childhood. History of drug use was denied. The patient complained that both eyes got blurry especially during nighttime, vision was narrowing, and getting blurry especially the left eye for the last 12 years. The patient also complained of clouding lens in both eyes that appeared from 5 years old especially in the left eye.

The patient is the eldest of two. The patient's brother had no complaints of hearing loss or blurred vision. During pregnancy, the mother had no history of illness, no vaginal bleeding, and no attempt to abort. The baby was delivered normally by midwife and started crying immediately. There is no history of disease or congenital abnormalities. His weight was normal (3500 grams). The child's growth and development were relatively late; the child lifts his head at 7 months old, and started to prone and sit alone at 1 years old. The patient was finally able to walk at the age of 3 years. The patient never babbled and uttered a single word. Several families of his father suffered from the same condition, like his grandfather, his uncle from grandfather's younger brother, his cousin from father's younger brother, all of whom suffered from muteness, deafness, and eyes problems.

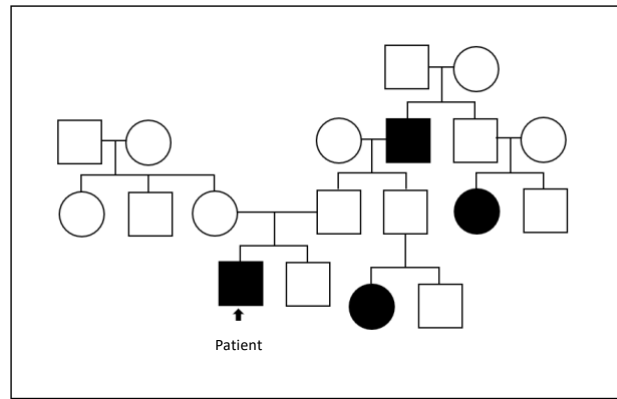
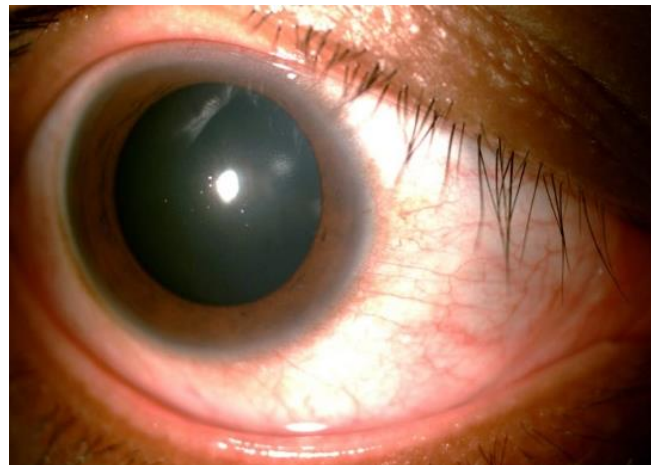


Image 1. Family tree. Several family members of the father suffer from the same condition, like his grandfather, his uncle from the grandfather's younger brother, and his cousin from the father's younger brother.

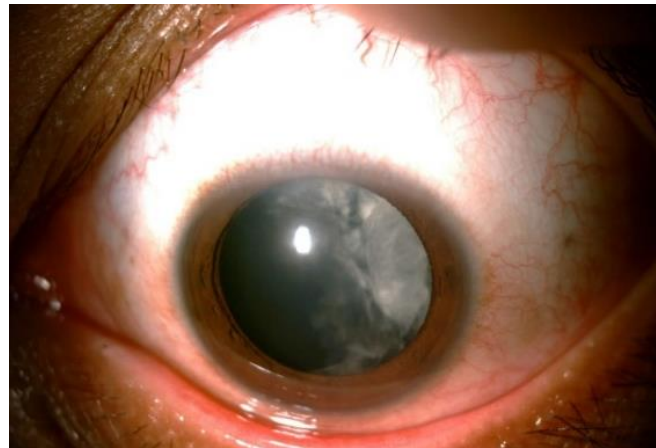
On ophthalmologic examination, visual acuity of the right eye was 6/30 with correction S-3.50 C-2.00 x5 → 6/15 and the left eye was hand movement. Anterior segment examination showed a thin PSC in the right eye, and the left lens showed a thick cortical cataract and PSC. Examination of the eyeball position revealed sensory exotropia (XT) of the left eye and eccentric fixation of the right eye.



a



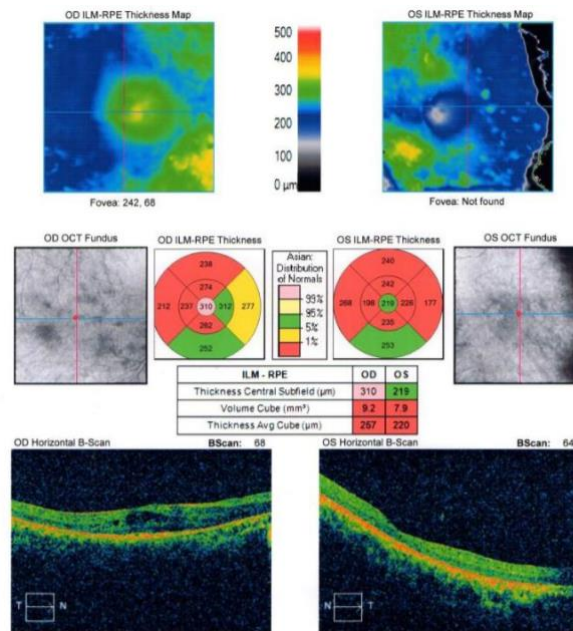
b



c

Figure 2. Anterior segment photo. There were cloudiness in both eyes. ; a. Photograph of both eyes showed XT Sensory of the left eye and eccentric fixation of the right eye; b. PSC in the right eye is mild; c. Left eye has thick cortical cataract and PSC

Examination of the posterior segment revealed bone spicules on the peripheral area and waxy pallor optic disc in both eyes. Left eye the examination was slightly obstructed by the cataract. Other examinations were within normal limits. From the macular OCT examination, it was found outer retinal thinning in both eyes where there was still a little Outer Nuclear Layer (ONL) and neurosensory layer in the right eye and there was thinning of the ONL and no neurosensory layer was seen the left eye. Macular edema was found in the right eye.



a

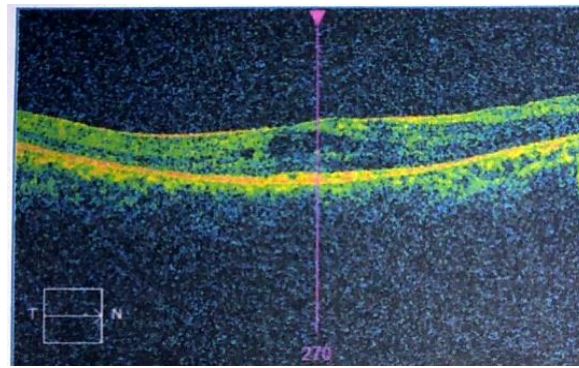
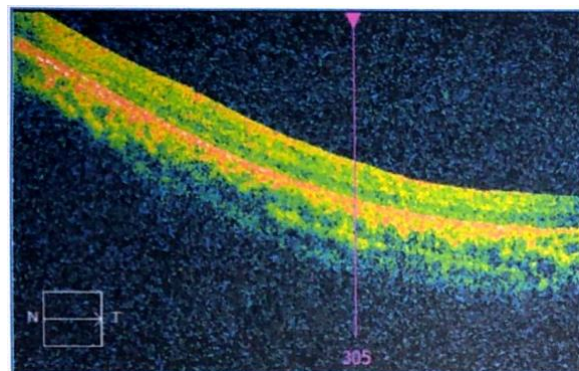
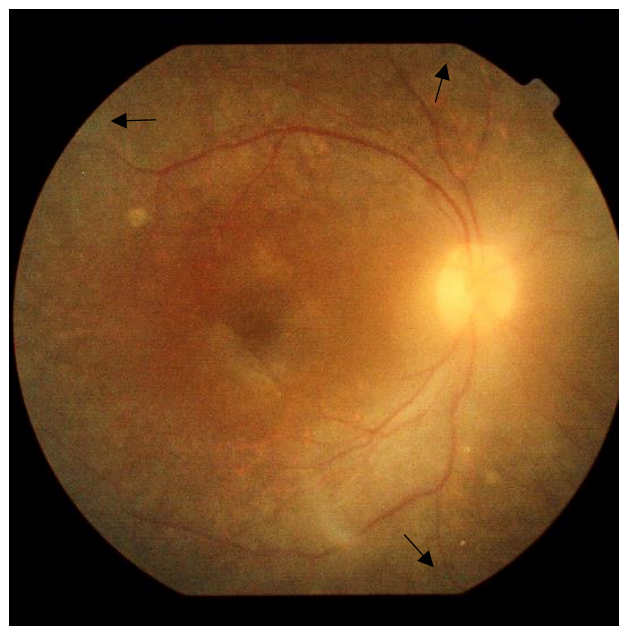
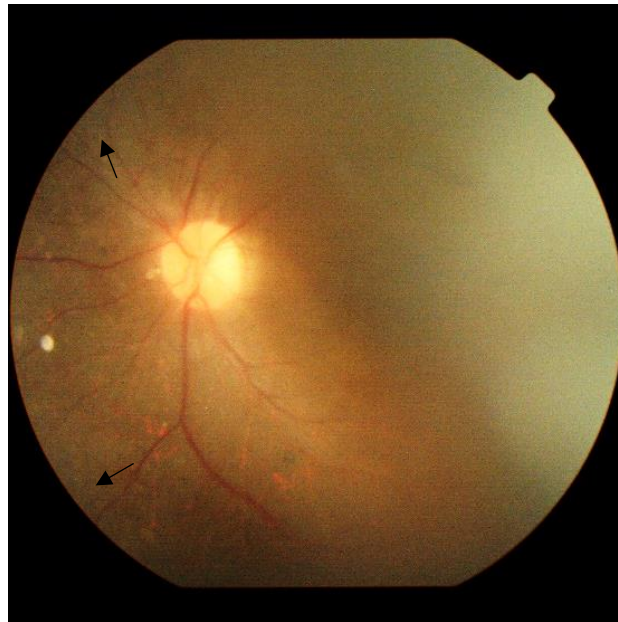
**b****c**

Figure 3. Macular OCT examination results. a. There is a difference in thickness and contour of the fovea in the right eye and left eye b. There is macular edema and thinning of the neurosensory layer in the right eye c. There is a thinning ONL and no neurosensory layer in the left eye.

**a**



b

Figure 4. Funduscopy examination results. a. right eye, b. left eye. Bone spicules are visible on the periphery of both eyes (arrows) & there is a waxy pallor optic disc in the both eyes.

From the perimetry examination, there was *tunnel vision* in the right eye, while the left eye cannot be evaluated. A severe sensorineural deafness with negative acoustic reflex was found in both ears on audiometry examination.

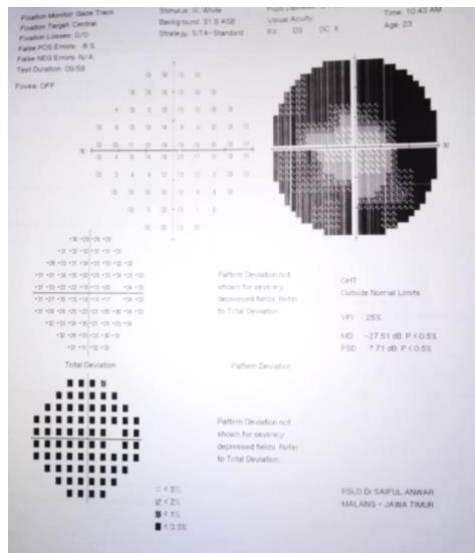


Figure 5. Perimetry test results. There was tunnel vision in the right eye. The left eye could not be examined because the visual acuity was 1/300.

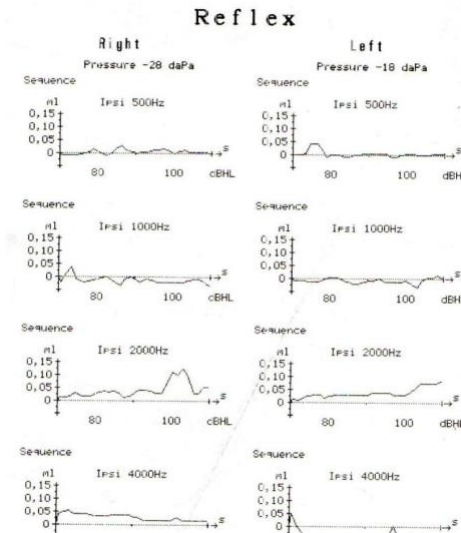


Figure 5. Result of acoustic reflex examination. The acoustic reflex in both ears was negative.

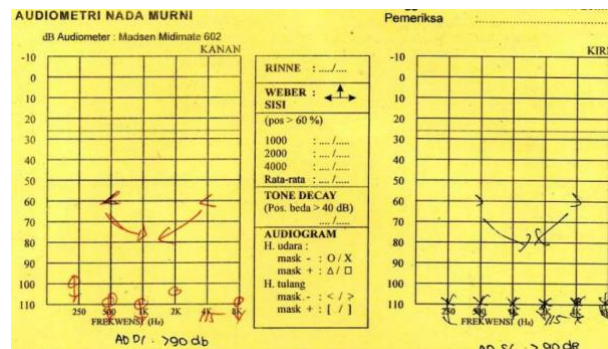


Figure 6. Audiometric examination results. Severe sensorineural deafness was found in both ears.

DISCUSSION

Based on the history taking and the examinations, the patient is deaf and blind since childhood. Both eyes are blurred especially at night and have narrowed vision since the patient was 12 years old. Patient still can see when he was little but as time goes by, the patient shows signs and symptoms of USH which is characterized by congenital sensorineural hearing loss and progressive loss of vision due to retinitis pigmentosa. The symptoms are combination of hearing loss and vision loss, and sometimes balance problem. The patient's family also had the same condition, whom were mute, deaf, and have eyes problems. This finding is suitable with the autosomal recessive pattern of USH⁷⁻¹⁰.

Complaints of narrowed vision were confirmed by the presence of tunnel vision on primary examination. Funduscopic examination of the patient revealed bone spicules & waxy pallor discs which are characteristic of retinitis pigmentosa. Patients with USH experience eye disorders, namely retinitis pigmentosa which is a group of hereditary retinal degeneration characterized by progressive photoreceptor dysfunction and accompanied by progressive cell

loss and eventually atrophy of several layers of the retina leading to progressive loss of visual acuity, visual field defects, and night blindness¹².

OCT examination of the macula revealed thinning of the outer layer of the retina. There were few neurosensory cells left in the right eye but no neurosensory layer was found in the left eye. The loss of the neurosensory layer on the retina causes a progressive decrease in vision. On OCT examination, macular edema was also found in the right eye. The pathogenesis underlying the association between retinitis pigmentosa and macular edema remains uncertain. Macular edema often occurs in retinitis pigmentosa due to several mechanisms, including damage to the blood-retinal barrier, damage or dysfunction of the pumping mechanism in the retinal pigment epithelium, edema and dysfunction of the Muller cell, antiretinal antibodies and traction on the vitreous. An electroretinogram (ERG) should be performed to confirm the retinitis pigmentosa. In USH patients, ERG showed negative results. ERG was not performed in this patient due to unavailability of equipment. In addition to ERG, genetic testing is a supporting examination to help establish a diagnosis. Based on research from Abdelkader (2018), it shows that severe retinal degeneration in USH patients is caused by mutations in the MYO7A gene^{13,14}.

The patient cataracts appeared from 5 years old, there was a thin PSC in the right eye and there was a cortical and PSC in the left eye. Cataract is one of the most common USH comorbid. David et al. (1986) stated that the prevalence of pediatric cataracts in USH patients was 53%. Patients with retinitis pigmentosa usually have a combination of posterior cortical cataract and PSC. These conditions, when combined with a limited central visual field, can cause significant visual abnormalities even when the opacities are relatively mild^{6, 13, 15, 16}.

Research from Jackson et.al. (2001) stated that in patients with retinitis pigmentosa without other retinal abnormalities, cataract surgery was beneficial for them and most of the patients showed subjective visual improvement. However, this patient had significant neurosensory tissue dystrophy and the vision did not match the thickness of the cataract so the visual prognosis after cataract surgery was poor. In addition, there is strabismus in this patient which indicates that the decrease in vision has occurred since the patient was little. Research from Jasdeep et al (2019) showed that patients with rod-cone dystrophy showed a poor prognosis of visual acuity so the cataract surgery was not performed in these patients^{15, 17, 18}.

On the hearing examination, the acoustic reflex examination found negative acoustic reflexes in both ears and the audiometric examination showed severe sensorineural hearing loss was found in both ears. Deafness or hearing loss in USH is caused by the abnormal development of hair cells. Most of the children with USH are born with moderate to severe hearing loss,

depending on the type. Very rarely hearing loss occurs during adolescence or old adulthood. The patient has been deaf mute since childhood. Audiometric examination showed severe sensorineural hearing loss on both ears. USH can also cause balance problems due to the abnormal development of vestibular hair cells, the sensory cells that detect gravity and head movement. In some cases, vestibular dysfunction was found but no balance problems occurs^{19, 20}.

There are three types of USH with different characteristics. In America, type 1 and 2 are the most common. The clinical findings of this patient were consistent with USH type 2, with moderate to severe hearing loss from birth, progressive decrease in night vision especially during adolescence, and normal balance function¹⁰.

Table 1. USH type table. Clinical Features by Type and Subtype of USH10

Clinical	Sub-type	Gene Location	Type 1	Type 2	Type 3
Hearing	Ia	14q	Severe hearing loss or deafness at birth	Moderate to severe, hearing loss at birth	Progressive hearing loss as a child or adolescent
	Ib	11q			
	Ic	11p			
	Id	10p			
	Ie	21q			
	If	10q			
Vision	IIa	1q41	Decreased night vision by age 10, and progressive loss of vision in young adulthood	Decreased night vision in adolescence, and progressive loss of vision in young adulthood	Varies; Decreased night vision often begins in adolescence and worsens in young adulthood
	IIb	3p			
	IIc	5q			
Vestibular function (balance)	III	3q	Balance disorders at birth	Normal balance	Normal to close to normal, when the child has the possibility of having problems

Early diagnosis can reduce the damage caused by this syndrome. Examination and screening of families who suffer from the same complaint can strengthen the diagnosis. Education to the family regarding genetic factors in this case is important in order to avoid marriage of relatives which can increase the incidence of this case. Management involves approaching hearing, vision, and balance problems. This patient was not treated for abnormalities found such as cataracts, macular edema, and strabismus due to poor visual acuity prognosis so what can be done to improve patient's quality of life is supportive therapy. In this patient, supportive therapy including visual and social rehabilitation can be given. Rehabilitation that can be done by training in reading Braille letter, using glasses to improve

visual acuity and use hearing aids as a social function.

CONCLUSION

Based on the patient's history taking, family history, eye examination, and ENT examination, the diagnosis of USH can be established. Management of USH depends on the patient's prognosis. In this case, no treatment was carried out for cataracts because the visual acuity of both eyes did not match the cloudiness of the lens so there is possibility that visual acuity would not improve. In the case of USH, it is important to do early diagnosis and early rehabilitation to improve patient's quality of life. The options are visual rehabilitation to improve visual acuity by using glasses and social rehabilitation by using hearing aids to improve patient's quality of life. Educating the family members regarding genetic factors in this case is also important so that early detection of other members suffering from the same condition can be done immediately.

REFERENCES

1. Sahu S, Singh SK. Usher syndrome Type I in an adult Nepalese male: a rare case report. *Nepalese Journal of Ophthalmology*. 2017; 9(2):203-205.
2. Yan D, Liu XZ. Genetics and pathological mechanisms of Usher syndrome. *Journal of human genetics*. 2010; 55(6):327.
3. Millan JM, Aller E, Jaijo T, Blanco-Kelly F, Gimenez-Pardo A, Ayuso C. An Update on the Genetics of Usher Syndrome. *Journal of Ophthalmology*. 2011; 2011.
4. Kristiyan T, Dewi NA, Refa S. Usher Syndrome in Two Siblings, A Case Report. *International Journal of Retina (IJRETINA)*. 2019; 02(01).
5. Liu Y-C, Wilkins M, Kim T, Malyugin B, Mehta JS. Cataracts. *The Lancet*. 2017; 390(10094):600-612.
6. David A. Newsome MWJS, Jr, MD; Irene H. Maumenee, MD. Cataract Extraction and Intraocular Lens Implantation in Patients With Retinitis Pigmentosa or Usher's Syndrome. *Archives of Ophthalmology*. 1986; 104(6):852-854.
7. Du W. Genetic analysis of a family with Usher syndrome. *J International Eye Science*. 2018; 18(10):1880-1882.
8. Mathur P, Yang J. Usher syndrome: hearing loss, retinal degeneration and associated abnormalities. *Biochimica et Biophysica Acta -Molecular Basis of Disease*. 2015; 1852(3):406-420.
9. Schietroma C, Parain K, Estivalet A, Aghaie A, de Monvel JB, Picaud S, et al. Usher syndrome type 1-associated cadherins shape the photoreceptor outer segment. 2017; 216(6):1849-1864.
10. Kimberling WJ, Hildebrand MS, Shearer AE, Jensen ML, Halder JA, Trzuppek K, et al. Frequency of Usher syndrome in two pediatric populations: Implications for genetic screening of deaf and hard of hearing children. *Genetics in Medicine*. 2010; 12(8):512.
11. Creel DJ. Electroretinograms. In: *Handbook of clinical neurology*: Elsevier; 2019. p. 481-493.
12. Sun LW, Johnson RD, Langlo CS, Cooper RF, Razeen MM, Russillo MC, et al. Assessing photoreceptor structure in retinitis pigmentosa and Usher syndrome. *Investigative ophthalmology visual science*. 2016; 57(6):2428-2442.
13. Abdelkader E, Enani L, Schatz P, Safieh L. Severe retinal degeneration at an early age in Usher syndrome type 1B associated with homozygous splice site mutations in MYO7A gene. *Saudi Journal of Ophthalmology*. 2018; 32(2):119-125.
14. Strong S, Liew G, Michaelides MJB. Retinitis pigmentosa-associated cystoid macular oedema: pathogenesis and avenues of intervention. 2017; 101(1):31-37.
15. H Jackson DG-H, P Rosen, A C Bird, S J Tuft. Outcome of cataract surgery in patients with retinitis pigmentosa. *British Journal of Ophthalmology* 2001; 85:936-938.
16. Jacobson SG, Aleman TS, Sumaroka A, Cideciyan AV, Roman AJ, Windsor EA, et al. Disease boundaries in the retina of patients with Usher syndrome caused by MYO7A gene mutations. *Investigative ophthalmology visual science*. 2009; 50(4):1886-1894.
17. Pierrache LH, Hartel BP, Van Wijk E, Meester-Smoor MA, Cremers FP, De Baere E, et al. Visual

- prognosis in USH2A-associated retinitis Pigmentosa is worse for patients with usher syndrome type IIa than for those with nonsyndromic retinitis Pigmentosa. *Ophthalmology*. 2016; 123(5):1151-1160.
18. Gill JS, Georgiou M, Kalitzeos A, Moore AT, Michaelides M. Progressive cone and cone-rod dystrophies: clinical features, molecular genetics and prospects for therapy. 2019; 103(5):711-720.
 19. Ebermann I, Scholl HP, Issa PC, Becirovic E, Lamprecht J, Jurklies B, et al. A novel gene for Usher syndrome type 2: mutations in the long isoform of whirlin are associated with retinitis pigmentosa and sensorineural hearing loss. 2007; 121(2):203-211.
 20. Smith R, Berlin C, Hejtmancik J, Keats B, Kimberling WJ, Lewis R, et al. Clinical diagnosis of the Usher syndromes. 1994; 50(1):32-38.