Case report

Retinitispigmentosarevealedwithmacularedema: A case report

Abstract

The termRetinitisPigmentosaencompasses a group of hereditaryretinopathiesthatresult in progressive vision loss ; RP maybecomplicated by cystoidmacularoedema (CMO). A 40-year-old femalepresentedwithfluctuant blurred vision for 4years. Visual acuity (VA) was 20/20 in botheyes. Examination and imagingshowedsometypicalfeatures of retinitispigmentosacomplicatedwithmacularedema.Currently the patient isundermedicaltreatement. Successful management of RP-CMO shouldaim to improvebothquality and quantity of vision in the short term and mayalso slow central vision loss over time.

Keywords : retinitispigmentosa ,macularedema , carbonic anhydrase inhibitor , case report

Introduction

Retinitispigmentosa (RP) is not a single entity but rather a group of disordersthatproduce a gradualloss of vision ; there are multiple geneticallydirectedmechanisms for the progress of retinitispigmentosa. Males are affectedslightly more oftenthanfemales. The averageage of symptomonsetisdependent on the genetictype, the first symptom of RP isgenerallynyctalopia. Physical findingsinclude the "classictriad" seen on a fundoscopic exam of bony spicule pigmentation, vascularnarrowing, and abnormalpallor of the optic disc. Thesemay not beevidentearly in the disease, and the degree to whichabnormalities are seenis variable with the severity of the disease. Otherassociatedphysicalfindingsmayincludesubcapsularcataracts and cystoidmacularedema (CMO). (1) One important treatable cause of central vision lossis RP-associated CMO. (RP-CMO)

Case report

A 40-year-old womanfollowed up for RP presented to our structure for blurred visionwith no familyhistory of retinitispigmentosa. Sheismedically free with no history of bloodloss. Shehad no history of ocular inflammations, no history of ocular trauma, and no previousocularsurgeries.Her parents are not related (negativeconsanguinity), and none of her siblings isaffected.

It shouldbenotedthat the patient is a carrier of the PRPH2 mutation revealed by genetictesting 4 yearsago, in the context of rodconedystrophy. Moreover, the patient is not

a carrier of a systemicpathology;thisis a non-syndromicform of RP. The patient ispaucisymptomatic, and her main functional complaint is night blindness. This dystrophyiscomplicated by cystoidmacularedema, which causes visualdiscomfortexperienced by the patient as moderateblurring;thisiswhatinitiallyprompted the consultation and led to the diagnosis. The particularity of our case lies in the factthat the patient has been reporting an exacerbation of the symptomatology and an accentuation of the visualblurduring menstruation for severalyears.

On generalexamination, the patient was in good health, and hervisualacuitywasgenerallypreserved at 10/10 in the right and lefteyes. Intraocular pressure was normal in botheyes.

Slitlampexaminationshowed a normal anterior segment with no cataract . Fundus examinationrevealed a slightintraretinal pigment migration in the midperiphery, no waxy disc pallor, and no vesselattenuation. The fundus appearance of the right and lefteyeisshown in Figure 1.
FAF of the right eyerevealeddecrease AF signal in the midperipheryassociatedwith an abnormalparafoveal ring or curvilinear arc of increased AF [Figure 2]. Retinal structure wasanalyzedqualitativelywithtransfoveal horizontal spectral domainopticalcoherencetomography scans (OCT, Heidelberg Engineering, Inc., Heidelberg, Germany). OCT of the right eyeshowedcystoidmacularedema. The left macula appearedabnormalwithslightintraretinalfluid[Figure 3].Severaltherapeuticmethods have been introduced , the patient
iscurrentlystable on carbonic anhydrase inhibitorCAI per os, half a tablet 2 times a day.

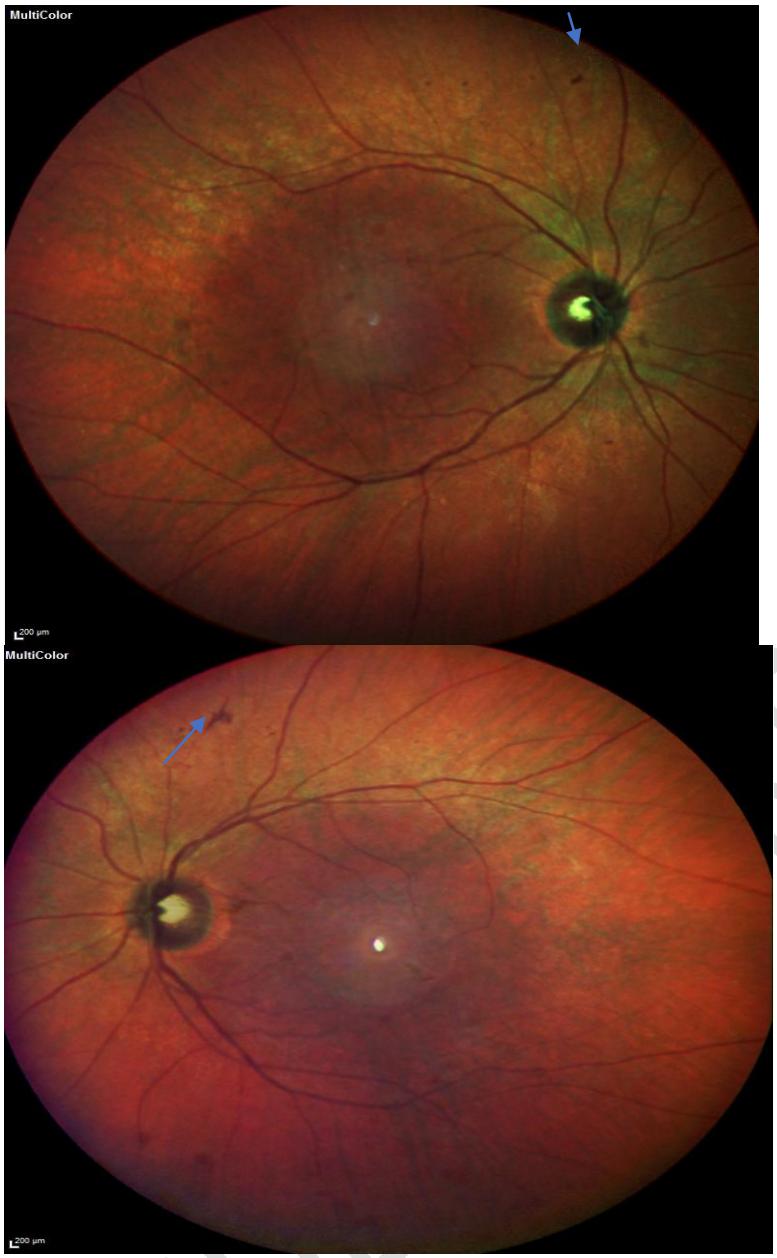

Figure 1 : Color fundus photographs of right thenlefteyesshowingslightintraretinal pigment migration in the midperiphery

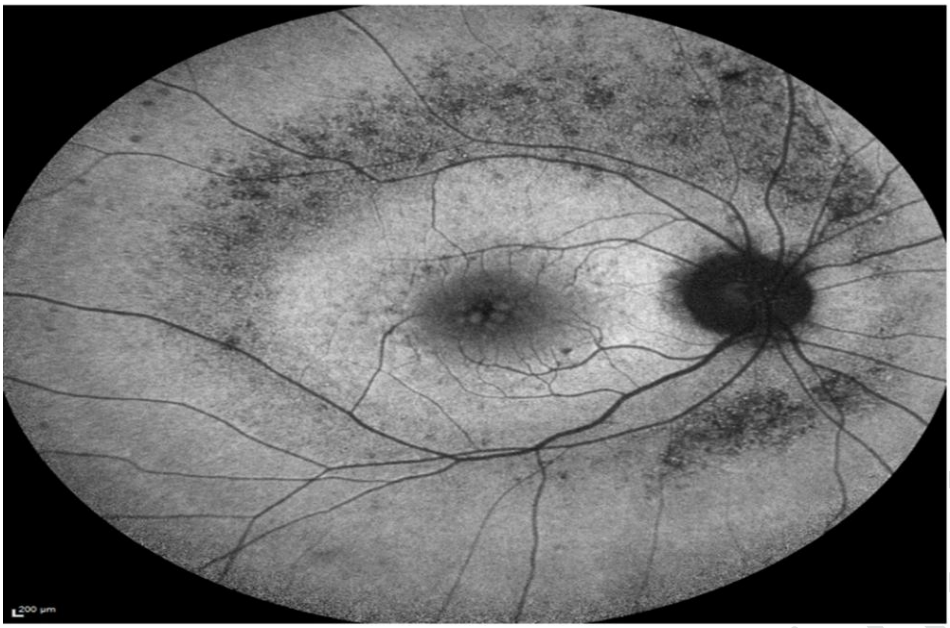

Figure 2 : Fundus autofluorescence (FAF) imagingshowingdecrease AF signal in the midperipheryassociatedwith an abnormalparafoveal ring or curvilinear arc of increased AF

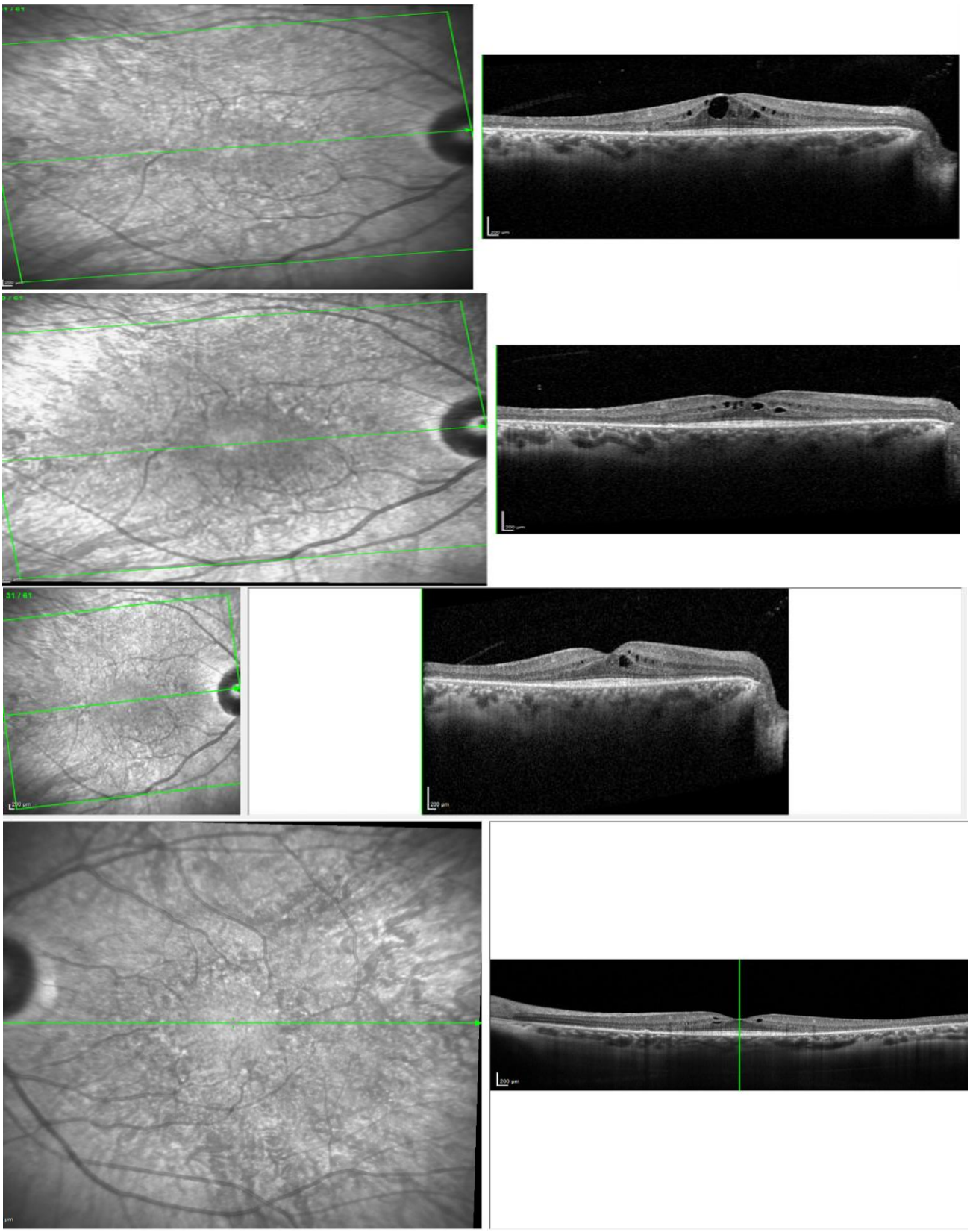

Figure 3 : spectral domainopticalcoherencetomography scans of the right eyeshowingcystoidmacularedema in different stages of the follow up . The left macula appearedwithslightintraretinalfluid

Discussion

RetinitispigmentosaRP isalsoknown as hereditaryretinaldystrophy, itis themostcommoninheriteddisease of the retina. usuallybilateral,. RP maypresent and progresswith a variety of clinical manifestations, , mainlyloss of night vision, whichisfollowed by a gradualnarrowing of the visualfields. Over time, depending on the severity and rate of progression of the disease, tunnel vision or complete vision loss can be the result.

The diseasemayinvolve vision lossalone and, in thisevent, isreferred to as "nonsyndromic" RP. The majority of RP cases, about 70% to 80%, fallinto the nonsyndromiccategory. When RP occurs in conjunctionwithsystemicdisease, itistermed "syndromic" RP. The mostcommonform of syndromic RP is Usher syndrome, whichinvolvesneurosensoryhearingloss in association with vision loss. (2)

Genetic mutations responsible for retinitispigmentosaproducebiochemicaldysfunction, specificallyaffectingrodphotoreceptors in the retina. Defectsmaybeassociatedwith multiple pathways of injury, includingapoptosis, light damage, ciliary transport dysfunction, and endoplasmicreticulum stress. The commonresult of all the possible pathwaysis the death of the rodphotoreceptors.(3) Since the rods are responsible for low-light vision, the ever-increasingloss of thesecellsproduces the characteristic night blindnessassociatedwith RP and a gradual diminution of peripheral vision. Eventually, the destruction of large numbers of rods has a deleteriouseffect on the retinal pigment epithelium (RPE) and begins to affect conephotoreceptors as well (4).

More than 100 geneticloci on 50 differentgenes have been found to cause multiple patterns of inheritance and expression for retinitispigmentosa ..Approximately 20% of RP cases are autosomal recessive, with 10 to 20% autosomal dominant and 10% X-linkedrecessive. The remaining cases are termedsporadic, and no familyhistory or knownmolecular basis isfound.

The autosomal recessiveformwilldevelopsymptoms in the earlyteenyears, but thoseaffectedwith autosomal dominant RP willlikely not have symptomsuntilwellintotheir 20s. More thanthree-quarters of individualswith RP willbesymptomatic and present for clinicalevaluation and diagnosis of the disease by the time they are 30 years of age.

Threeclinicalfindingstypical of retinitispigmentosa are the presence of bone spicule pigmentation, vascularnarrowing, and optic nerve pallor (5).

Macularoedema (MO), the accumulation of intraretinalfluid in the macula, is a commonsightaffectingsequelae of retinitispigmentosa (RP). However, itisunclearwhysome patients develop ME, and others do not. (6)Cystoidmacularoedema (CMO) has been reported to occurin 10%–50% of patients.(7)RP-CMO is not alwaysassociatedwith a reduction in visualacuity (VA) ; somestudiesfound no correlationbetween total maculararthickness and VA.

There are no standard treatments for patients withretinitispigmentosa. The mostwidelyrecommendedtreatment for manyyears has been supplementationwithvitamin A, whichsomestudies have shown to slow the rate of retinaldeterioration.However, a recentreviewfound no significantbenefit to vitamin A for RP. (8,9)

In recentyears,genetic causes of RP have been betterunderstood, and gene-specific or mutation-specific investigations point to the possibilitythatgene augmentation therapymightbedesigned to restore normal gene expression in photoreceptors. Otherresearchinvolvescell replacement therapy, whichinvolvestransplantingretinalprogenitorcells (or non-ocular stem cells) into the eye to repopulate the retinawithfunctionalphotoreceptors.

Multiple types of electronicretinal implants exist and have showngreat promise in restoring partial vision in patients with end-stage disease (10) .Whilethese avenues are verypromising for vision restoration and preservation, there are complicated issues for rehabilitation management of these patients, as well as device-specific challenges, such as functionallongevity. (11)

Severalstudies have shown RP-CMO improvementfollowingtreatmentwith CA inhibitors (CAIs)oral, or topical.(12)

Oral, periocular and intravitrealSteroidsreduce the synthesis and release of pro-inflammatorycytokines,togetherwith suppression of inflammatorycellproliferation and migration whichcontributes to reduction of CMO. Steroids have been observed to improvevisualacuityVA and/or central macularthickness CMT in RP-CMO

While no studies have assessedvitreouslevels of VEGF in patients with RP or RP-CMO, anatomical and/or functionalimprovement of RP-CMO has been observedfollowingintravitreal anti-VEGF medication (13,14)

Oral luteinwasfound to have no statisticallysignificanteffect on CMT in patients with RP with or without CMO. While oral iodine has not been trialledspecifically for RP-CMO, higherurinary iodine concentration has been observed to besignificantlyassociatedwithreduced CMT in non-smoking adultswith RP-CMO .

grid laser photocoagulationwasundertaken in one eye of 16 patients withbilateral RP-CMO. Six treatedeyesgained one or more lines of vision, while none of the untreatedeyesdid. Seven untreatedeyeslost one or more lines of vision, while none of the treatedeyesdid. Thirteen of 16 eyesshoweddecreasedfluoresceinleakageaftertreatment. Laser mayremovehypoxicdegeneratingretina, thusreducing VEGF production. (13)

Conclusion

This case highlights the importance of investigatingmacularabnormalities in cases of RP. This is to detecttreatable pathologies such as FTMH and CME. Treatingthesemacular pathologies helpsmaintain central vision in RP cases.RP-CMO commonlycomplicates RP, however, its exact underlyingpathogenesisremainsuncertain. Proposedmechanismsthat are mostlikely to beinvolvedinclude breakdown of the BRB and/or RPE pumpmechanismfailure and/or Müller celloedema and dysfunction. When CS are presentthey are mostcommonlylocated in the INL, suggestingthatinner BRB dysfunctionmay have a greaterrolethan the outer BRB, in development of RP-CMO. A betterunderstanding of thesemechanismswillfacilitatebettertargeted and likely more efficacious and durable therapies.

Setting up clinical trials for RP-CMO, however, remains a challenge due to itslowprevalence, the highly variable course of disease progression, significantgenetic and allelicheterogeneity and very slow progression to visualloss.

theevidencecurrentlyavailablesuggeststhattopicalCAIsmaybeused as a first-line approach. Considerationshouldbegiven to the possibility of sideeffects and potential for rebound CMO. Oral CAIsmaybe a second-line agent, but thereis the risk of more sideeffects.

As there are currently no treatments for the underlyingretinaldegeneration in RP and given the potentiallyreversible nature of RP-CMO, thereis a real need to betterunderstanddiseasemechanisms and undertake prospective clinical trials of therapeutic agents to provide the evidence base to improvetreatment of RP-CMO. Successful management of CMO shouldaim to bothimprovequality and quantity of vision in the short term and slow the rate of vision loss over time.

Refrencens

1. 1 Verbakel SK, van Huet RAC, Boon CJF, den Hollander AI, Collin RWJ, Klaver CCW, Hoyng CB, Roepman R, Klevering BJ. Non-syndromicretinitispigmentosa. Prog Retin Eye Res. 2018 Sep;66:157-186.
2. 2 Wolfrum U, Nagel-Wolfrum K. [The Usher Syndrome, a Human Ciliopathy]. Klin MonblAugenheilkd. 2018 Mar;235(3):273-280.
3. 3 Yang YJ, Peng J, Ying D, Peng QH. A Brief Review on the PathologicalRole of Decreased Blood Flow Affected in RetinitisPigmentosa. J Ophthalmol. 2018;2018:3249064.
4. 4 Xu H, Chen M, Forrester JV. Para-inflammation in the agingretina. Prog Retin Eye Res. 2009 Sep;28(5):348-68.
5. 5 Shintani K, Shechtman DL, Gurwood AS. Review and update:currenttreatment trends for patients withretinitispigmentosa. Optometry. 2009 Jul;80(7):384-401.
6. Arias, J.D., Kalaw, F.G.P., Alex, V. et al. Investigating the associations of macularedema in retinitispigmentosa. Sci Rep 13, 14187 (2023)
7. S Strong, G Liew,and M MichaelidesRetinitispigmentosa-associatedcystoidmacularoedema: pathogenesis and avenues of interventionBr J Ophthalmol. 2017 Jan; 101(1): 31–37
8. 6 Rayapudi S, Schwartz SG, Wang X, Chavis P. Vitamin A and fishoils for retinitispigmentosa. Cochrane DatabaseSystRev. 2013 Dec19;2013(12):CD008428.
9. 7 Schwartz SG, Wang X, Chavis P, Kuriyan AE, Abariga SA. Vitamin A and fishoils for preventing the progression of retinitispigmentosa. Cochrane DatabaseSystRev. 2020 Jun 18;6(6):CD008428.
10. 8 Ward J, Meijer P. Visual experiences in the blind induced by an auditorysensory substitution device. ConsciousCogn. 2010 Mar;19(1):492-500.

11. 9 Anil K, Garip G. Coping strategies, vision-relatedquality of life, and emotionalhealth in managingretinitispigmentosa:asurveystudy. BMC Ophthalmol. 2018 Jan 30;18(1):21.
12. Pacella E, Arrico L, Santamaria V, et al..Dorzolamide chlorhydrate versus acetazolamide in the management of chronicmacularedema in patients withretinitispigmentosa: description of three case reports. Ophthalmol Eye Dis. 2014;6:21–6.
13. Ahn SJ, Kim KE, Woo SJ, et al.. The effect of an intravitrealdexamethasone implant for cystoidmacularedema in retinitispigmentosa:a case report and literaturereview. OphthalmicSurg Lasers Imaging Retina2014;45:160–4.
14. Schaal Y, Hondur AM, Tezel TH. Subtenon triamcinolone for cystoidmacularedema due to retinitispigmentosaunresponsive to oral acetazolamide. Can J Ophthalmol2016;51:e113–5.