A Case of Acute Zonal Occult Outer Retinopathy which was Initially Diagnosed as Retrobulbar Optic Neuritis

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ABSTRACT

Acute zonal occult outer retinopathy (AZOOR) is a disease characterized by visual impairment without prominent fundus findings at the beginning. Therefore, AZOOR can be initially diagnosed as retrobulbar optic neuritis (ON), which causes unilateral visual impairment in a young patient. In this report, a case of AZOOR initially diagnosed as retrobulbar ON is presented with multimodal imaging findings. The aim of this report is to emphasize that AZOOR is a clinical condition that should be kept in mind in the differential diagnosis of retrobulbar ON. Although its clinical diagnosis is difficult, optic coherence tomography and electroretinography findings are very useful in diagnosing.

Keywords: Acute zonal occult outer retinopathy, ERG, multimodal imaging, OCT, retrobulbar optic neuritis.

INTRODUCTION

Acute zonal occult outer retinopathy (AZOOR), first defined by Gass in 1992, is a disorder with unclear etiology which is caused by dysfunction of outer retina.[1-3] It generally presents with unilateral visual complaints in young adults and it may evolve to bilateral disorder over time; it may show recurrence by 30%. Although marked findings may not always present in fundus examination, imaging techniques may be helpful for diagnosis. Here, a case of AZOOR together with multimodal imaging findings was presented, which was initially diagnosed as retrobulbar optic neuritis (ON).

CASE REPORT

A 29-years old male patient presented to our clinic with photopsia and impaired vision over one week. In his history, there was strabismic amblyopia in left eye. It was also found out that the patient had influenza 3 weeks ago and that he subsequently presented to ophthalmologist with disturbed vision and referred to a neurologists where he was diagnosed as optic neuritis (ON) and received systemic steroid therapy over 4 days (1 g intravenous methyl prednisolone for 3 days; followed by 1 mg/kg oral methyl prednisolone). In the ophthalmologic examination, best-corrected visual acuity was 20/25 in the right eye and 20/50 in the left eye and intraocular pressure was normal in both eyes. Anterior segment examination was normal in the right eye while there was exotropia in the left eye. In the fundus examination, a well-defined retinal fading involving superior and temporal foveal regions in the right eye was observed while fundus examination was normal in the left eye (Figure 1). No inflammatory finding was detected in anterior segment and fundus examination. On spectral-domain optical coherence tomography (SD-OCT, Spectralis, Heidelberg Engineering, Germany), a trizonal appearance was observed in the sections corresponding to areas with fading in the right eye. The SD-OCT was normal beyond demarcation line (zone 1) while multi-focal hyper-reflective material (zone 2), resembling subretinal drusenoid deposits, was observed within demarcation line. It was seen that external limitane membrane was faded and ellipsoid zone could not be tracked (zone 3) on sections extending temporal areas (Figure 2a). On fundus autoflorescence (FAF) imaging, retinal atrophic lesion had well-defined margins and hyper-autoflorescence appearance (Figure 3a). On fluorescein angiography (FA), this area was observed as fenestral defect (Figure 3b). On OCT- angiography (OCTA, Optovue, Fremont, California, USA), retinal and choriocapillaris vascularization were observed on 6x6 mm section centered to fovea while

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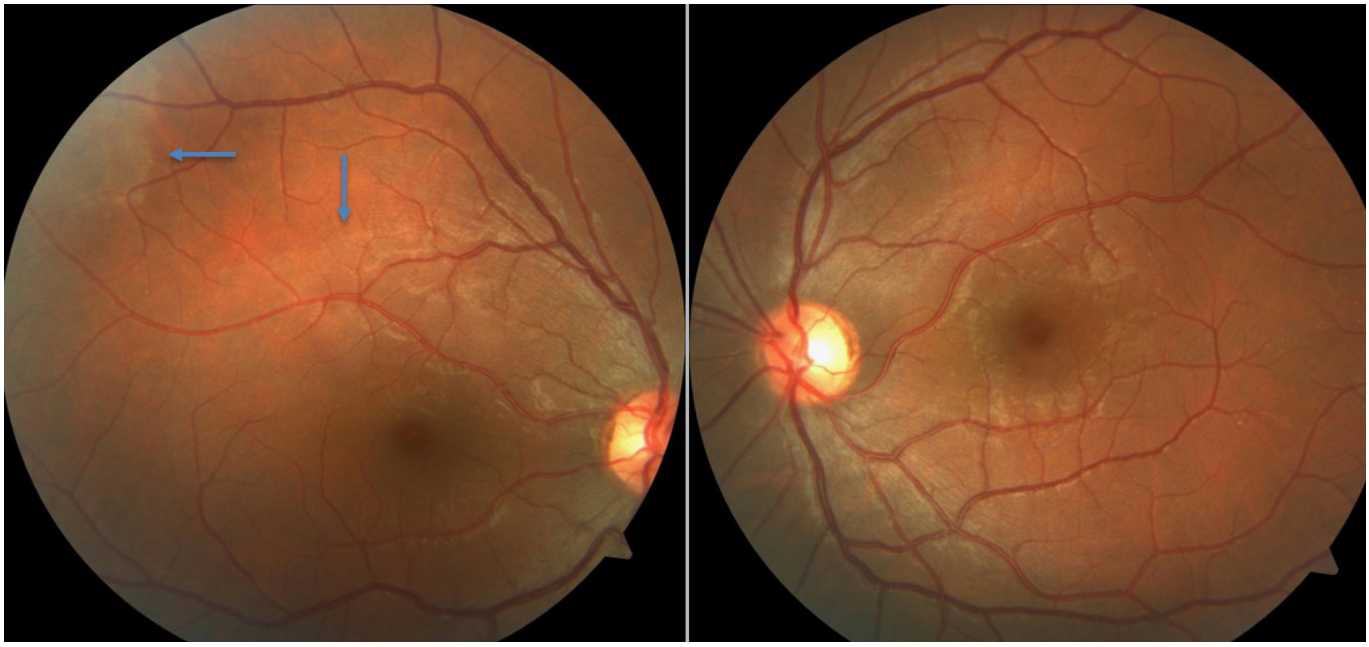

Figure 1: *On color fundus figure of right eye, well-defined retinal fading are seen at superior and temporal to fovea (blue arrows). Color fundus figure of left eye was normal.*

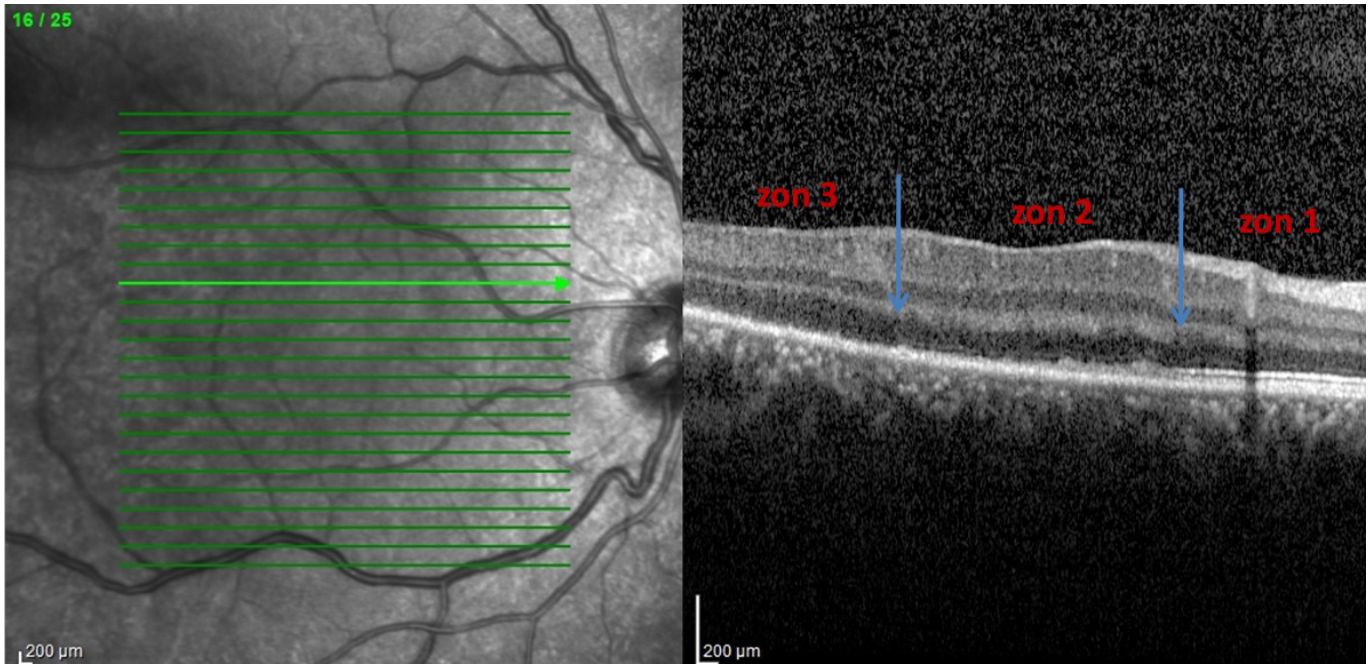

Figure 2: *On optical coherence tomography (OCT) of right eye at presentation, trizonal appearance is seen on sections corresponding to faded area. The SD-OCT is normal beyond demarcation line (zone 1) while multi-focal hyper-refl ective material (zone 2), resembling subretinal drusenoid deposits, is observed within demarcation line. It is seen that external limiting membrane was faded and ellipsoid zone cannot be tracked (zone 3) on sections extending temporal areas.*

en face images were found to be normal (Figure 4). In electroretinography (ERG, MonPack One Visual Stimulator, Metrovision, France), there was reduction in scotopic responses of right eye when compared to left eye (Figure 5). In visual field testing, arcuate scotoma was detected inferior nasal region of right eye. Cerebral magnetic resonance imaging (MRI) was normal. Again, color vision examination and visual evoked potential (VEP) testing was normal. Moreover, biochemistry, complete blood count, ESR and CRP were also normal. The patient was diagnosed as AZOOR and systemic steroid therapy was tapered (8 mg per week) over 3 months. On month 6, it was found that BCVA was improved up to 20/20 and that fundus findings were completely resolved (Figure 6a).

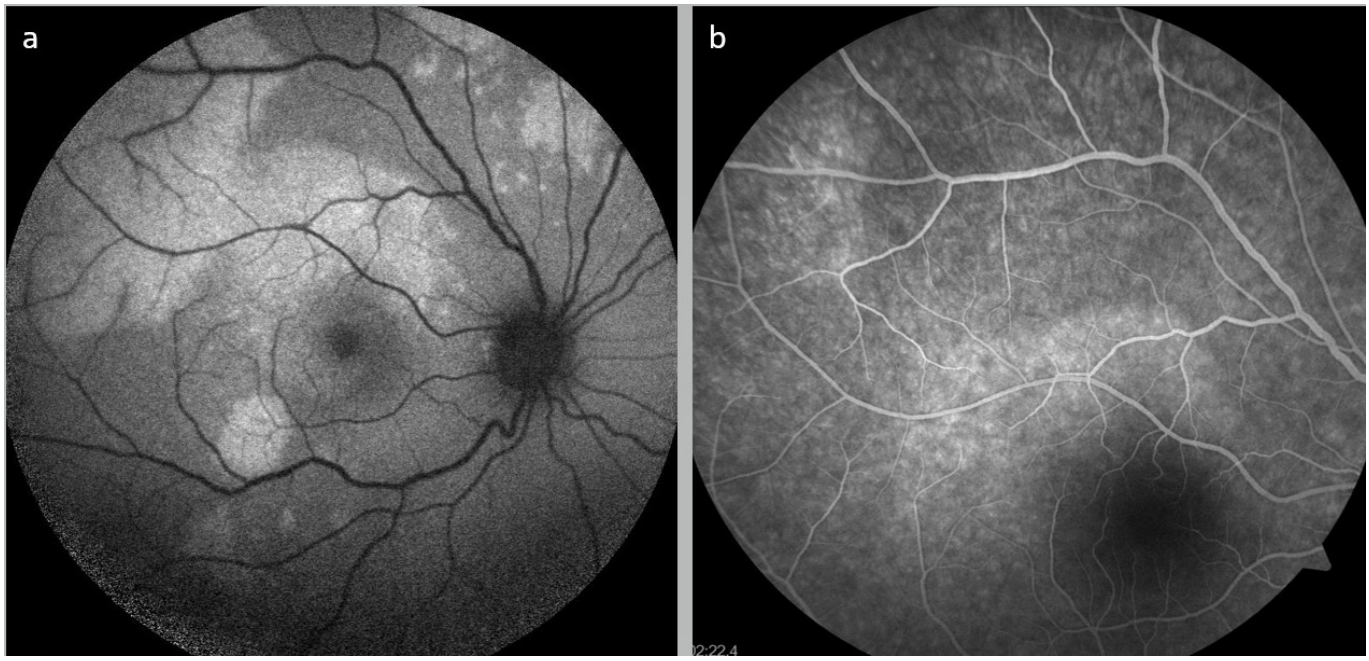

Figure 3: *a) Retinal atrophic lesion shows a well-defined hyper autoflorescence on fundus autoflorescence imaging. b) On fluorescein angiography, this area is seen as fenestral defect.*

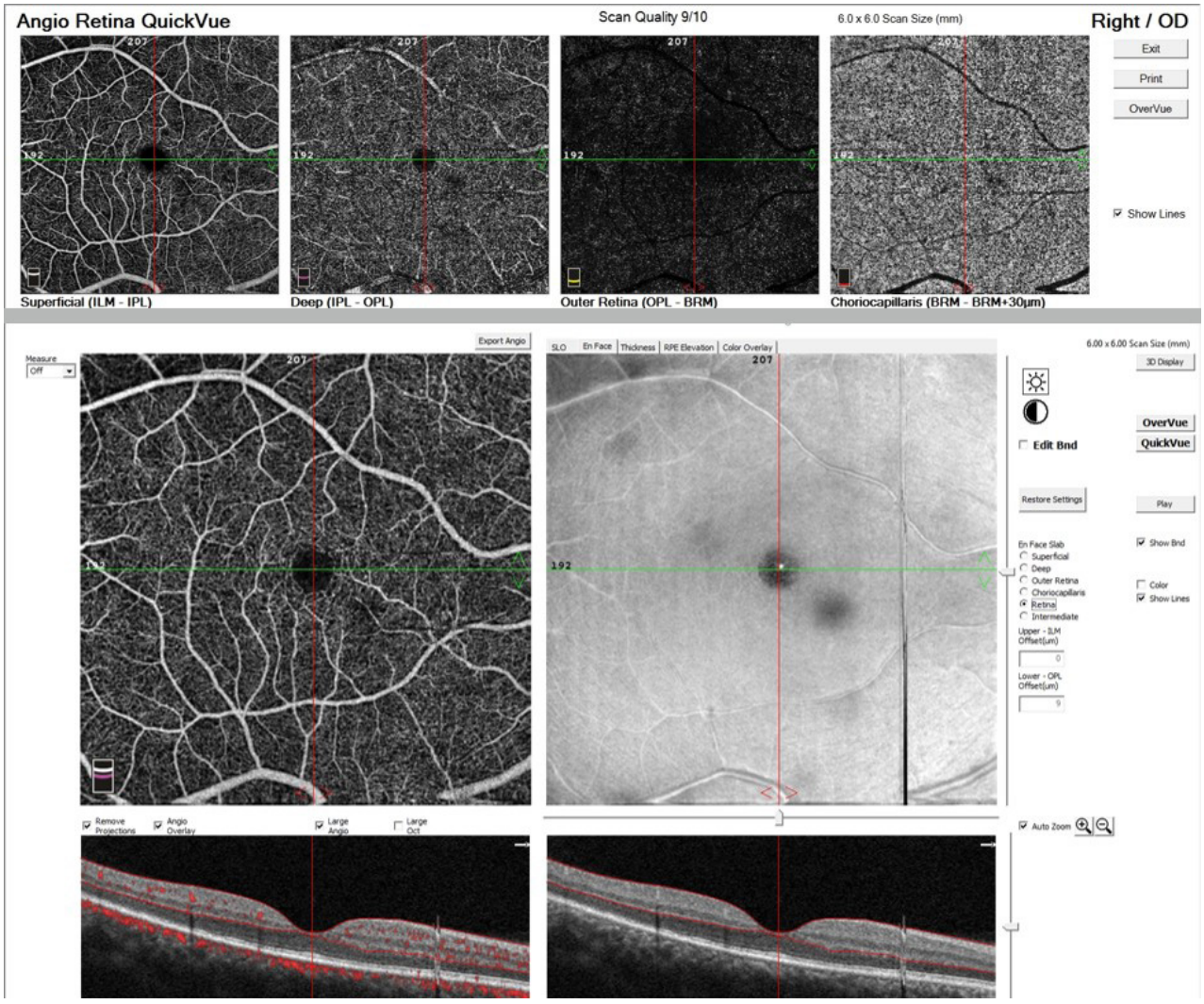

Figure 4: *On optical coherence tomography angiography of right eye, retinal and choriocapillaris vascularization (upper image) are seen while en face images are normal.*

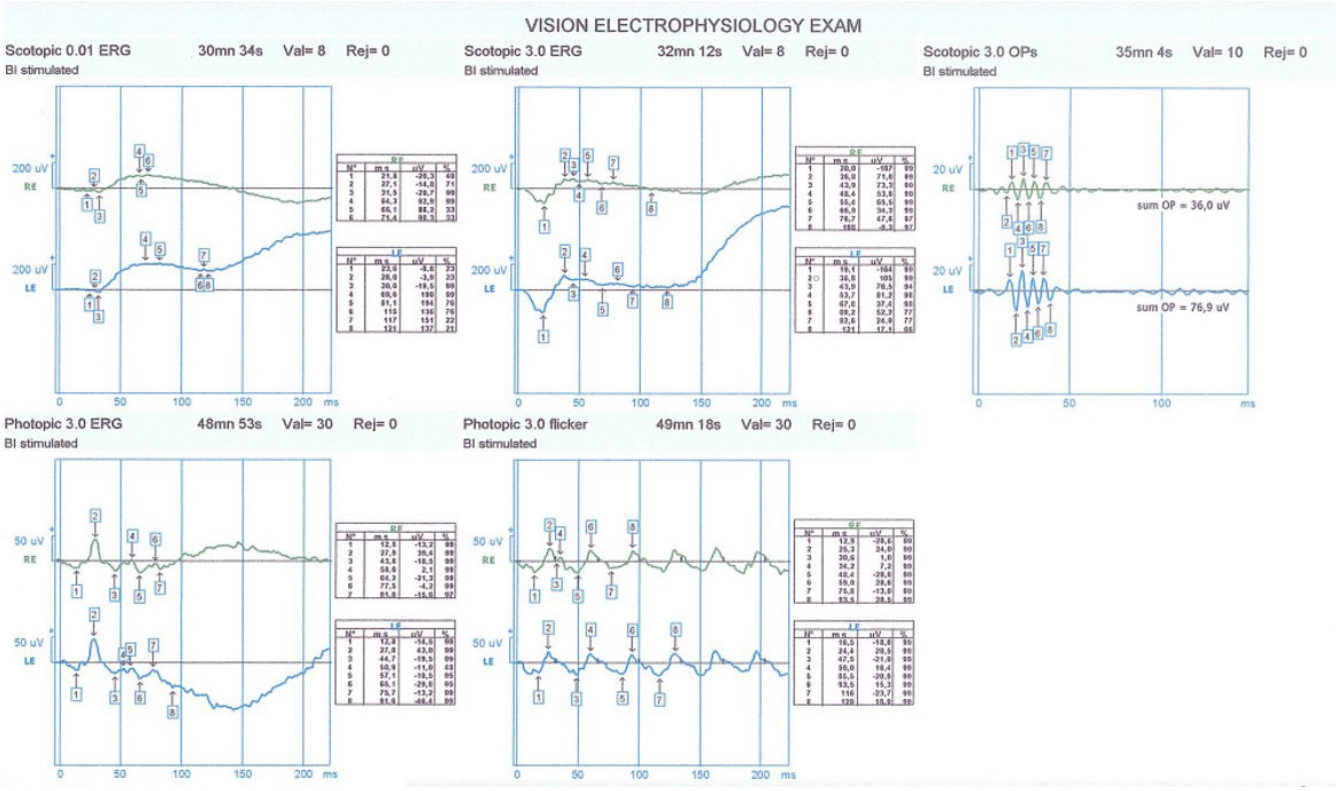

Figure 5: *It is striking that scotopic responses in right eye was decreased when compared to left eye on ERG.*

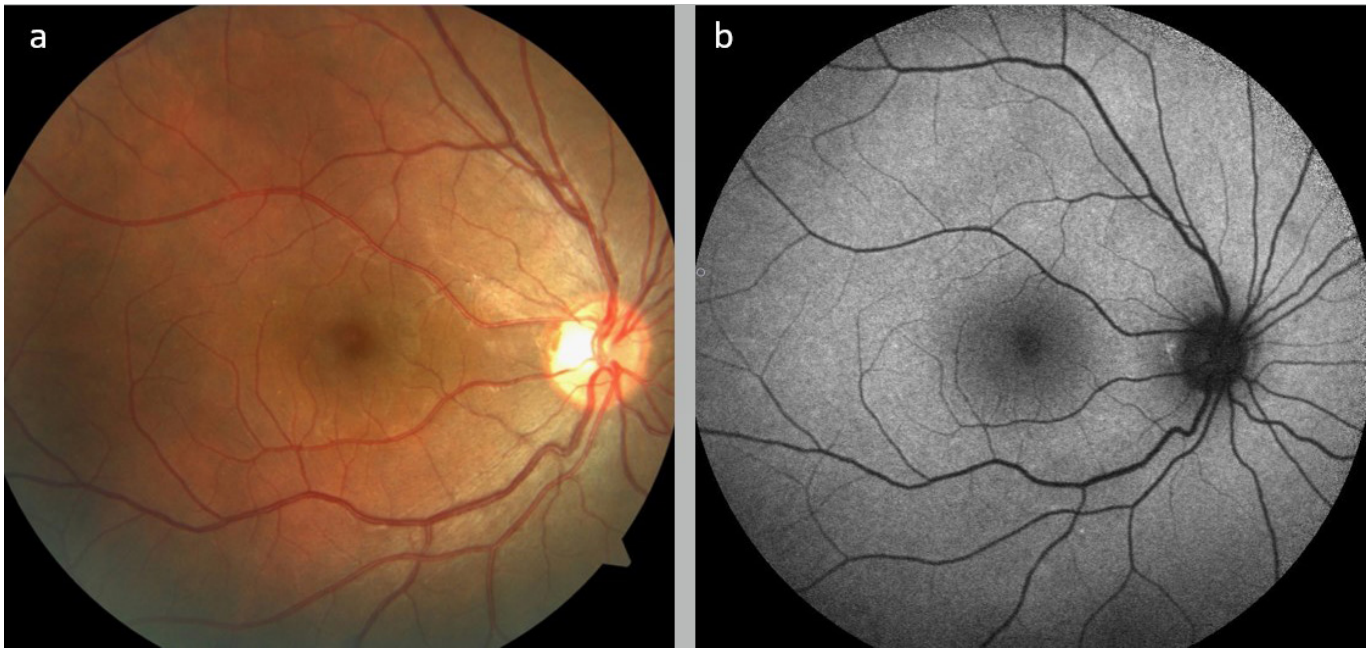

Figure 6: *a) Color fundus figure of right eye is normal on month 6 after presentation. b) fundus autoflorescence image of right eye is normal on month 6.*

It was also observed that fundus autoflorescence (Figure 6b) and SD-OCT findings (Figure 2b) were completely recovered.

DISCUSSION

The AZOOR is a disorder with unclear etiology in which underlying infections and immune system disorders are implied; cases with preceeding influenza-like clinical presentations have been reported. Given the unclear etiology and non-specific findings, AZOOR can be confused with several disorders including optic neuropathy, paraneoplastic retinopathy, autoimmune retinopathy, toxic retinopathy, lymphoma and retinitis pigmentosa.[1-3] However, understanding the imaging findings facilitates

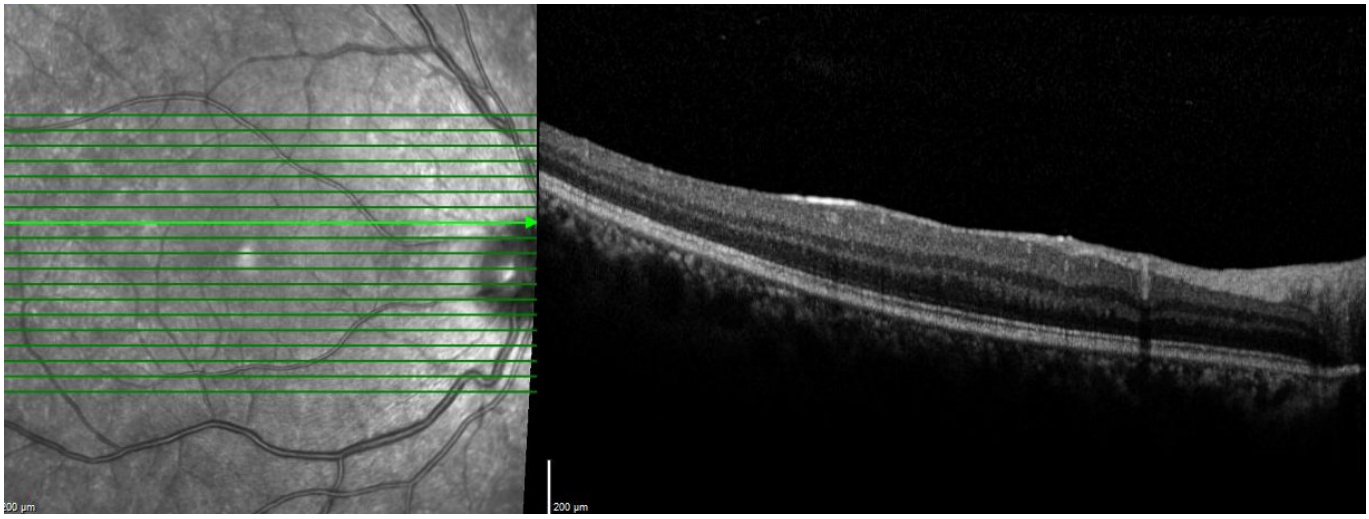

Figure 7: *OCT imaging of right eye is normal on month 6 after presentation.*

the diagnosis in AZOOR. In fundus examination, a grey-white demarcation line separating normal and involved areas can be observed in early phases. Over time, the involved retinal region evolves to an appearance of well-defined RPE depigmentation area as similar to sector RP. The posterior pole and peripheral retina can also be involved although peripapillary area is generally involved.[1-3] On SD-OCT images, there was thinning in outer retinal layers with atrophy and ellipsoid zone impairment in general. The trizonal appearance, which is defined in some patients, is SD-OCT finding considered as pathognomonic for AZOOR.[4] In trizonal appearance, sections out of demarcation line is normal in zone 1 while multi-focal hyper-reflective material resembling subretinal drusenoid deposits are observed within demarcation line in zone 2 and there is no external limiting membrane in zone 3.

FAF imaging is highly valuable in the diagnosis of AZOOR. In the literature, it has been reported that there is abnormal FOF finding in approximately 90% of patients with AZOOR[1-3] although it may variable. The lesion can either be completely hyper-autofloresence or hypo- and hyper-autofloresence in center and hyper-autofloresence at periphery.[1-3] Enlarged blind spot is most common finding while scotoma compatible with lesion and narrowed peripheral visual field can be observed. Scotoma may also be enlarged over time. Electroretinography is an important test which confirms diagnosis in case of suspected AZOOR. ERG abnormalities are observed in almost all cases while normal ERG excludes the diagnosis of AZOOR. Decreased scotopic and/or photopic responses are seen in ERG.[1-3,5] In AZOOR, ERG may show findings not only in symptomatic eye but also in asymptomatic eye;[6] the knowledge that there may be acute exacerbation in asymptomatic eye is important for clinical follow-up.

FA is less specific than other imaging modalities, which may be either normal or it may show hyper-fluorescein fenestral defect associated with RPE defect. On indocyanine green angiography, lesion is frequently seen as late hyper-fluorescence.[1-3] Due to recent introduction, OCTA findings are limited for AZOOR. Naik et al. reported that hyper-reflective spots were observed in a patient with AZOOR at ellipsoid zone on en face OCTA images; however, retinal and choriocapillaris vascularization was normal.[7]

In the AZOOR treatment, several treatment options including systemic corticosteroids,[8] other immunosuppressive agents[10] and anti-microbial agents[11] have been attempted; however, no definitive efficacy could be shown. It was reported that intravenous pulse methyl prednisolone followed by oral prednisolone was reported to achieve recovery of visual field.[8] However, pulse steroid therapy cannot prevent recurrence. Azathioprine[9] or mycophenolate[8] is recommended as a treatment option in reactivation. In recent years, there are publications showing that intravitreal steroid injections achieve visual and anatomic improvement in AZOOR.[12] However, the fact that there are studies indicating spontaneous recovery of visual functions in AZOOR has raised questions about efficacy of above-mentioned treatments.[9]

AZOOR is most commonly confused with retrobulbar optic neuritis. The lack of marked fundus findings at onset and presentation with unilateral visual impairment in younger individual suggest retrobulbar ON. In a study by Jiang et al., it was found that 26 patients diagnosed with retrobulbar ON were re-evaluated and it was found that 14 of 26 patients were actually AZOOR.[13] SD-OCT and ERG play important role in the differential diagnosis of these disorders. However, in the literature, there are limited number of case reports showing association of AZOOR with retrobulbar ON and multiple sclerosis.[14,15]

The underlying autoimmune etiology may be account for such associations.

The paraneoplastic retinopathies should also be considered in the differential diagnosis of AZOOR. The major paraneoplastic retinopathies include cancer-related retinopathy and melanoma-related retinopathy, which may present with bilateral loss of vision and visual field, photopsia and night blindness. ERG is highly affected in both retinopathies; in addition, negative ERG pattern in stable night blindness is characteristic in melanoma-related retinopathy. Although unilateral involvement and younger age in our patients suggested diagnosis other than paraneoplastic retinopathy, etiological work-up should be performed to establish definitive diagnosis.[16]

In conclusion, AZOOR should have to be distinguished from retrobulbar ON as it is most common condition confusing with AZOOR and may rarely show association with AZOOR. The potential pathognomonic findings on multimodal imaging play key role in distinguishing AZOOR and retrobulbar ON.

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