Fundus autofluorescence and optical coherence tomography in the management of progressive outer retinal necrosis

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Abstract

A 41 year-old female patient with acquired immune deficiency syndrome (AIDS) presented with progressive nasal visual field loss in her right eye. Ophthalmic exam revealed widespread areas of retinal opacification with hemorrhage consistent with progressive outer retinal necrosis (PORN), which was confirmed by polymerase chain reaction (PCR) for varicella zoster virus (VZV) DNA. The patient was treated with intravenous and intravitreal foscarnet and ganciclovir with a resultant improvement clinically. Optical coherence tomography (OCT) and fundus autofluorescence (FAF) imaging revealed progressive changes indicative of widespread retinal pigment epithelial (RPE) and outer retinal dysfunction. OCT was useful in documenting progressive changes in macular architecture during therapy including neurosensory elevation, cystoid macular edema, and severe outer retinal necrosis, at initial exam, 1 week, and 1 month follow-up. Fundus autofluorescence revealed areas of stippled, hyperfluorescence within extensive zones of hypofluorescence, which progressed during the follow-up period. These areas appeared to represent lipofuscin or its photoreactive components within larger regions of RPE loss. The combination of OCT and FAF was useful in the characterization of the RPE and retinal anatomy in this patient with PORN.

Keywords

Progressive outer retinal necrosis; varicella zoster virus; fundus autofluorescence; optical coherence tomography

Introduction

Progressive outer retinal necrosis (PORN) is a clinical entity in the spectrum of herpetic viral retinitides. Initially described by Forster et al in two AIDS patients, PORN is primarily found in immunosuppressed individuals¹, but has been rarely reported in immunocompetent patients.² Clinical features of PORN include multiple areas of yellow-white, deep retinal opacification, which become confluent. Following acute infection, large areas of outer retinal necrosis predispose patients to rhegmatogenous retinal detachment in up to 70% of cases.³ One prior report described the utility of OCT for the diagnosis of PORN. In this report, an area of decreased reflectivity within the outer retina was suggestive of outer retinal necrosis in the acute phase of the disease.⁴ Subsequent reports on OCT findings in PORN have described retina edema in the acute phase of disease with diffuse retinal

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thinning observed later in the clinical course.⁵⁻⁶ We report the OCT and fundus autofluorescence (FAF) findings in a patient with PORN, both in the acute phase of disease and following therapy, and correlate anatomic findings on OCT with FAF abnormalities.

Case report

A 41 year-old African-American female with a history of HIV/AIDS and oral candidiasis presented with a 3-day history of decreasing visual field in her right eye. CD4 count was 14 cells/ μ L. She was not on highly active anti-retroviral therapy (HAART).

Visual acuity was 20/20 OD and 20/16 OS. Pupillary examination revealed sluggish light reactivity OD, brisk reactivity OS, and a 1+ relative afferent pupillary defect OD. Humphrey visual field (HVF) 24-2 testing OD revealed a dense superior and inferior nasal visual field defect, which extended to involve the superotemporal quadrant. Slit lamp examination showed 1+ anterior chamber inflammation with trace anterior vitreous cells OD. Fundus exam OD revealed mild optic disc edema and multiple, deep white retinal opacities involving the posterior pole and retinal periphery. In the temporal retina, the areas of retinal opacification were confluent, and associated with areas of perivascular hemorrhage. In the perifoveal region, a crescent-shaped band of retinal opacification extended from the inferonasal to the superotemporal perifoveal retina, sparing the central fovea (Figure 1A and 2). Fundus exam OS was normal. OCT in a vertical plane demonstrated increased thickness corresponding to the area of perifoveal opacification (Figure 1B). Inner retinal hyper-reflectivity in the region of perifoveal opacification and decreased reflectivity in the outer retina, suggestive of outer retinal edema, were also seen. PORN was confirmed with PCR of an aqueous specimen, which was positive for VZV DNA.

The patient was started on intravenous acyclovir and ganciclovir induction therapy. Intravitreal ganciclovir therapy was also instituted biweekly (2 mg/0.05 mL/injection). At 1 week, intravitreal foscarnet (1.25 mg/0.05 mL/injection) was added because of disease progression. The patient's IV regimen was changed to ganciclovir and foscarnet following consultation with the Infectious Disease service.

At 1 week, visual acuity OD was 20/32. Areas of retinal opacification were more prominent both peripherally and in the perifoveal region (Figure 1D). OCT through the fovea showed increased foveal thickness with cystoid spaces of low reflectivity in the outer retina (Figure 1E). At 1 month follow-up, visual acuity was 20/40 OD. In the inferior perifoveal region, the area of previous retinal opacification had progressed to an atrophic, translucent, schisis-like cavity (Figure 1G). On OCT, loss of reflectivity of both middle and outer retinal lamina was observed inferiorly, consistent with the atrophic changes appreciated clinically. In addition, the hyper-reflective outer retinal band, corresponding to the retinal pigment epithelial (RPE) layer appeared discontinuous and irregular (Figure 1H).

Fundus autofluorescence (FAF) images using a Topcon fundus camera (excitation filter 580 nm, barrier filter of 695 nm) were also obtained during follow-up. At the initial visit, subtle areas of hypofluorescence were observed in the posterior pole (Figure 1C). At 1 week follow-up, FAF images showed a region of hypofluorescence with interspersed stippled, hyperfluorescent signal in the superotemporal macula, which had not been appreciated initially (Figure 1F). This region corresponded to an area of retina in which confluent opacification was appreciated. At 1 month follow-up, an additional area of similarly stippled, hyperfluorescent signal was also observed inferior to the fovea, corresponding to the translucent area of outer retinal necrosis and schisis seen clinically and by OCT (Figure 1I). In addition, widespread regions of hypofluorescence with interspersed, stippled hyperfluorescent signal appeared throughout the retinal periphery (Figure 2C). These

findings corresponded to areas of previous peripheral retinal opacification, which appeared atrophic at 1 month post-treatment.

2 months after the initiation of therapy, the patient returned for follow-up with a visual acuity of hand motions and a macula-off rhegmatogenous retinal detachment with multiple retinal breaks. Following pars plana vitrectomy, retinectomy, and silicone oil tamponade, retinal attachment was achieved. Visual acuity at 10-month follow-up remained finger counting at 1 foot despite anatomic reattachment.

Discussion

Our case report demonstrates the progression of structural changes of the retina by OCT and FAF during the management of PORN. In the early stages of PORN, areas of retinal opacification were increased in overall thickness. At this stage, the inner retina appeared hyper-reflective while the outer retina showed mild decreased reflectivity and disorganization, indicative of early inflammation and tissue damage. Following therapy, OCT showed an overall reduction in retinal thickness; clinically, large atrophic areas of retina were observed. In some areas (e.g. foveal center), cystoid macular edema had resolved with restoration of normal architecture. However, in adjacent areas where atrophy could be seen clinically, prominent tissue disorganization and loss, greater in the outer than the inner retina, were observed on OCT.

The staged progression of FAF changes was also observed in this patient. Early in the course of disease, when retinal opacification was first observed, abnormalities in fundus FAF were subtle and limited in extent. Changes in FAF appeared to follow retinal opacification and were correlated with areas where retinal necrosis and tissue breakdown were seen on OCT. It is possible that these FAF changes occur subsequent to photoreceptor death and outer retinal injury and inflammation by VZV. The subsequent accumulation of lipofuscin or its photoreactive degradative components from tissue breakdown by RPE cells may then give rise to the appearance of multiple areas of stippled hyper- and hypofluorescence.

This case of PCR-confirmed PORN correlates early and subacute clinical changes to the progression of OCT appearance and FAF imaging. Although late histological changes of PORN have been described as a full-thickness breakdown of the retina,⁷ the sequence of pathological events in different levels of the retina in PORN is still incompletely understood. The observations in this case indicate that the early events in PORN take the form of outer retinal inflammation, opacification and swelling. With continuing tissue breakdown and necrosis in outer retina, lipofuscin from cellular debris accumulates in the RPE, resulting in patchy stippled FAF patterns. In the late phase, recovery of normal retinal thickness and lamination is seen in less affected areas, while full-thickness loss of retinal tissue is seen in other more affected areas, resulting in atrophy, formation of schisis cavities in some areas, and eventually, attenuation and loss of the RPE layer. Future concurrent use of OCT and FAF imaging modalities with clinical examination may provide further insight into the nature of progression of PORN and the effect of intervention in the course of the disease.

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Figure 1.

At initial presentation fundus photo OD shows widespread retinal opacification and heme (A). Corresponding OCT (B) shows hyper-reflectivity of inner retina (asterisk) and outer retinal edema (arrows) while FAF (C) shows subtle hypofluorescence (arrows). At 1 week, fundus lesions remain prominent (D) and OCT shows outer retinal disorganization (arrow) with persistent inner retinal hyper-reflectivity (asterisk, E). FAF now shows area of stippled hyperfluorescence in an area of hypofluorescence (F). At 1 month, atrophic changes are seen with resolution of opacities (G) but OCT shows schisis cavity (asterisk) and irregular RPE (arrows, H). FAF shows multiple areas of hypo- and hyperfluorescence (black arrows, white arrow), which correspond to large areas of RPE atrophy and necrosis (I).

Figure 2.

Photo montage demonstrating widespread retinal opacification and perivascular hemorrhage at initial visit (A). Widespread RPE atrophy and necrosis is seen at 1 month follow-up (B) with multiple regions of stippled hyper/hypofluorescence on the FAF image corresponding to widespread RPE atrophy (C).