High-resolution adaptive optics imaging complements standard spectral domain optical coherent tomography in retinal diseases with micro-structural details

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Abstract:

Purpose: To evaluate if high-resolution adaptive optics confocal scanning laser ophthalmoscopy (AO-SLO) can be used as an adjunct complementary diagnostic tool to spectral domain optical coherent tomography (SD-OCT) in characterizing three macular diseases: cone-rod dystrophy, acute retinal pigment epitheliitis (Krill’s disease), and occult macular dystrophy.

Methods: As part of a complete clinical examination, each patient was subjected to color fundus pictures, multimodal imaging scans with Heidelberg SpectralisTM and high-resolution retinal images with a custom built adaptive optics scanning laser ophthalmoscope (AO-SLO). The registered AO-SLO images were averaged to improve the signal to noise ratio and used to generate larger photoreceptor mosaics.

Results: AO-SLO mosaics for all three conditions showed distinct, characteristic disruptions of the photoreceptors in areas that corresponded to the abnormalities observed on fundus photography and SD-OCT scans.

Conclusions: AO-SLO defined fine structural changes associated with retinal pathology at the photoreceptor level that could not be achieved using standard diagnostic methods. A combination of adaptive optics scanning laser ophthalmoscopy (AO-SLO) and SD-OCT provided views of the retina with enhanced lateral and axial resolution. High-resolution, ultra-structural details of the retina may provide additional insights into the disease etiology, progression and management of patients with vision threatening macular diseases.

Key words: Retina; optical coherence tomography; Spectral domain optical coherence tomography; diagnostic.

Introduction

Spectral domain optical coherence tomography (SD-OCT) and adaptive optics (AO) fundus imaging provide complementary strengths in resolution of the retinal tissue. SD-OCT imaging provides axial resolution, whereas AO-SLO imaging corrects for ocular aberrations and increases lateral resolution of retinal tissue.1 AO characterizes the photoreceptor mosaic’s cone photoreceptor density, cone packing geometry, and differentiates between the S-, M-, and L-cones.2,3 AO combined with OCT can also characterize retinal nerve fiber bundles and retinal capillaries that may one day replace how we detect glaucomatous damage and provide a non-invasive alternative to IVFA.1 The clinical utility of SD-OCT and AO-SLO hold promise in early detection, structure-functional analysis and monitoring retinal disease.4 We report photoreceptor mosaics of three diseases using AO-SLO correlated with standard clinical OCT imaging of: cone-rod dystrophy, Krill’s disease, and occult macular dystrophy.

Case Reports

Patient 1: A 66-year-old male presented with decreased vision (20/30 OU) and severe photophobia in both eyes. On examination, the posterior pole showed diffuse atrophy of the retinal pigment epithelial cells with...
scattered pigment clumping in the macula bilaterally. Multi-focal electroretinogram (mERG) showed misshapen or extinguished waveforms in several test locations in both eyes. The clinical findings and electrodiagnostics are consistent with a diagnosis of cone-rod dystrophy. AO-SLO imaging of three parafoveal areas demonstrated irregular photoreceptor density and drop out of cones in the pathological area (Figure 1A-C).

**Patient 2:** A 41-year-old male presented with visual acuity of 20/25 OD and 20/40 OS. Fundus examination was remarkable for a central, dark hyperpigmented RPE hyperplasia and a surrounding halo of hypopigmentation in the left eye. SD-OCT showed distortion of the outer nuclear layer and anterior elevation of IS/OS PR line. Diagnosis of acute retinal pigment epithelitis (Krill’s disease) was made based on the clinical findings. AO-SLO imaging revealed disruption of the regular cone/rod mosaic at the center of RPE hyperplasia with no apparent dropout of the photoreceptors but inflammatory exudative fluid under the RPE (Figure 2A-C).

**Patient 3:** A 46-year-old female complained of slow worsening of vision in her right eye. Her visual acuity was 20/40 OD and 20/25 OS. Fundus examination revealed a dull foveal reflex that was further characterized as a defined disruption of the IS/OS junction on OCT imaging. However, OCT of the left macula only showed disruption of outer retinal layers with intact IS/OS junction. IVFA was unremarkable and mERG showed decreased amplitude of foveal responses OD (OD > OS). She was diagnosed with occult macular dystrophy. AO-SLO imaging showed a large area of cone photoreceptor dropout at the fovea and a normal appearing mosaic in the adjacent region (Figure 3A-B).

**Discussion**

We report micro-structural retinal changes obtained by AO-SLO imaging of three retinal diseases that correlated with OCT findings. AO-SLO provided details at single cell level that were not apparent on SD-OCT imaging.

Wolfgang, et al., reported fundus photography with AO-SLO in a case of cone-rod dystrophy with bull’s-eye lesion and found a direct correlation of structures using the two imaging modalities. The regions that appeared to be relatively spared on clinical exam correlated on AO-SLO with a tilted cone mosaic with abnormally large cone cells and reduced cone density. In our patient the photoreceptor mosaic showed disruption, cone dropout, increased cone spacing in the affected area (Figure 1A). Additionally, AO-SLO imaging of three parafoveal areas demonstrated irregular photoreceptor density and drop out of cones in the pathological area (Figure 1A-C).

In Krill’s disease, the hyperpigmented RPE area showed distinct distortion of the photoreceptor cells associated with a loss of the compact cone/rod architecture that could be clearly delineated by a normal surrounding photoreceptor mosaic. This is in contrast to what we observed in the case of cone-rod dystrophy where there was no clear transition zone. The mosaic pattern seen in the patient with active Krill’s disease may have characteristics that classify it as an acute inflammatory process leading to destruction of photoreceptors above the affected RPE cells and inflammatory transudate under the RPE cells.

AO-SLO imaging of occult macular dystrophy has been recently reported. It was shown that there was foveal disruption of the IS/OS junction on OCT that corresponded with findings of patchy dark areas containing non-uniform bright spots with irregular shapes and higher brightness intensity as compared to the normal foveal mosaic. None of their patients demonstrated a sharp disruption of the foveal IS/OS junction with inner segment abnormality, as observed by OCT and AO-SLO. Our findings are consistent with the irregular and uneven photoreceptor distribution at the affected area.

In summary, direct in vivo visualization of the cone-rod mosaic may help in understanding the disease etiology. High-resolution AO-SLO can provide complementary data to standard SD-OCT imaging that may allow early detection, progression, and evaluation of treatment modalities in patients with retinal diseases.

**References**

Castleman´s disease

CASTLEMAN’S DISEASE

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Abstract:

Castleman’s disease is a rare lymphoproliferative disorder, comprising hyaline vascular elements, and plasma cells, which can be present in unicentric or multicentric forms. This disease rarely involves the orbit/eye globe. We report the case of a 55-year old patient who was found to have a focal lesion in the orbit. Histopathology studies revealed features consistent with Castleman’s disease. The patient was treated with surgical resection and radiotherapy and was free of disease recurrence at 16-months follow up.

Keywords: Castleman disease, orbit, interleukinas, lymphoproliferative, unicentric.

Introduction

Castleman’s disease (CD) is an atypical lymphoproliferative disorder, rare and non-neoplastic, which cause is unknown.

In 1956, Benjamin Castleman presented a series of 13 cases involving a node-like lesion featuring lymphoproliferative B-cells surrounding a capillary in the mediatinum.1 Based on clinical presentation, this disease may be classified as unicentric or multicentric. From the histopathological point of view, it may be classified into 3 types: hyaline-vascular, plasma and mixed cell types (the latter being the most common type). The hyaline-vascular type is characterized by a germinal center giving the lymph node the appearance of a “lollipop on a stick” with a zone of lymphocytes in a concentric or “onionskin arrangement” surrounding a lymph vessel.2 The plasma cell type is characterized by hyperplastic germinal centers and the presence, in the interfollicular areas, of sheets of plasma cells and hypervascularity. The mixed type presents hyaline degeneration in the same lymphatic follicles with sheets of plasma cells arranged in the same patterns as both types described above.3,4 The hyaline-vascular type was originally described by Castleman and is most commonly found as a solitary mass in the mediastinum (70%), abdomen, neck and axilla.1 It is extremely rare in the orbit; actually, only a few cases of CD with orbital involvement have been reported so far.5-12

Case Report

A 55-year old woman was referred to us with a three-year history of proptosis of the left eye which had increased over the last month. There was no history of an overall condition. Examination showed corrected visual acuity of 20/20 OD and 7/20 OS. There was complete ipsilateral ptosis and proptosis and downward displacement of the eye globe. Hertel exophthalmometer measurements were 18mm OD and 22mm OS. Ocular motility evaluation showed pain and some restricticon. Under slit lamp

Figure 1: Conjunctival injection and chemosis in the left eye.

Figure 2: MRI showed a T1 hyperintense lesion and a T2 isointense lesion with irregular margins displacing the eye globe.

Figure 3: A highly vascularized friable mass was found.
examination, there was conjunctival injection and chemosis (Figure 1). MRI showed a T1 hyperintense lesion and a T2 isointense lesion with irregular margins displacing the eye globe (Figure 2).

An excisional biopsy was performed through an anterior orbitotomy via upper eyelid crease. A highly vascularized friable mass was found (Figure 3). Histopathology studies revealed a lymphoproliferative lesion consistent with CD of a mixed type (Figure 4 and 5).

Clinical and hematological evaluation showed absence of systemic complications. The patient was diagnosed with unicentric CD, confined to the orbit. The patient underwent radiotherapy as an ancillary treatment. She was later referred to the hematological service and was free of disease recurrence at 16-months’ follow up.

Discussion

Since the disease was first described in 1950, only a few cases of ocular and orbital involvement have been reported.5–12

The latest hypothesis explaining the cause of CD is related to the overproduction of interleukin-6 (IL-6), estimated by HHV-8 or an unidentified endogenous infection (Clonal proliferation) or exogenous factor (cytokines). IL-6 promotes the proliferation of plasma cells, increases resistance to apoptotic signals, induces differentiation of precursors of regional B-cells, and has a paracrine role in the production of vascular endothelial growth factor—production by plasma cells. An extensive analysis of immunophenotyping using flow cytometry and/or immunohistochemistry and molecular analysis are important to distinguish CD from pseudo tumors, lymphomas, HIV related lesions, Kaposi’s sarcoma and other reactive disorders.12

The unicentric variant is more favorable and is treated with surgical resection. The multicentric form is associated with fever, chills, night sweats with widespread lymphadenopathy, organomegaly and polynuropathy; in addition to anemia, trombocytopenia, hypoalbuminemia, hyPOCHOLESTEROLEMIA, hypergammaglobulinemia, an elevated erythrocyte sedimentation rate (ESR), increased lactate dehydrogenase and high levels of interleukin-6 (IL-6), and bone marrow plasmacytosis. The prognosis for localized intraorbital CD is good.12,13

There are reports that surgical resection of the lesion could be curative in the unicentric CD of any histopathological type. However, there is no standard treatment for multicentric CD and it usually requires more aggressive systemic treatments. Both the choice of therapy and their results are varied, including surgical resection combined with chemotherapy, radiotherapy, immunomodulators (corticoids, interpheron, retinoic acid, and thalidomide), antiviral therapy, and monoclonal antibodies (monoclonal antibody anti-IL-6 and anti-CD20).14,15,16

Conclusion

Castleman’s disease is an infrequent pathology and orbital involvement is extremely rare. The prognosis for unicentric CD is fairly good and surgical resection is curative in most cases. In any case, it’s important to perform a complete screening to rule out systemic complications.16

References