Hydroxychloroquine-induced Maculopathy: enface Imaging as a Sign of Damage

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Purpose
To describe the findings in a case of hydroxychloroquine-induced maculopathy using optical coherence tomography (OCT) Spectralis (Heidelberg Engineering) with en-face transversal section.

Case
A 77-year-old woman on hydroxychloroquine for treatment of erythematous systemic lupus was referred from to screen for hydroxychloroquine-induced toxicity. The daily dosage was 50 mg for 8 years (approximated accumulate dose: 146g). Clinical examination was normal with a best-corrected visual acuity of 20/20 on both eyes (OU). Humphrey visual field 10-2 white showed significant persistent paracentral defect on right eye (OR) and a subtle superior paracentral defect on pattern deviation map on left eye (OS) without correlation on grey scale map. A multifocal electroretinogram (mERG) confirmed the diagnosis of premacularopathy. The Spectral Domain OCT (Heidelberg Engineering) showed aberration of ellipsoid layer and pigmentary epithelium defects using Retina Fast protocol but those findings were nonspecific and difficult to correlate with the HFA results in right eye and left eye appears to be unaffected. Using the enface protocol on right eye hiperreflectance lesions where described as well as in left eye which had been previously informed as normal OCT using sectional protocols.

Conclusions:
Hydroxychloroquine maculopathy OCT findings are subtle and difficult to assess using the common OCT B-mode retinal scans. Using enface protocol OCT alterations could be correlated to visual field scotoma and even present lesions prior to visual field changes which could be missed using other protocols. These findings have not been reported earlier in other cases of hydroxychloroquine maculopathy could be implemented as a detector on the screening of these patients among the other commonly used tests. Nevertheless, it is need to perform larger studies to determine the diagnostic feasibility of this test.

Keywords: Optical coherence tomography, Hydroxychloroquine-induced maculopathy, enface protocol
nonspecific and difficult to correlate with the HFA results on OD, although OS appears to be unaffected (Figures 3 and 4). Using the enface protocol on OD hypo/hyperreflective lesions where described as well as in OS which had been previously informed as normal OCT using sectional protocols (Figures 3 and 4).

Discussion

Hydroxychloroquine is a wide range used drug for rheumatologic or dermatological disorders. It may induce retinal toxicity due to the deposit of the drug at the RPE causing alterations at that level that induce cellular death and secondary to the metabolically disturbance, photoreceptor loss.

Since 2011, the recommendations for surveillance of these patients include spectral domain OCT (SD-OCT), ophthalmological exploration and 10-2 perimeter. If available, it is recommended to perform an auto fluorescence and mERG among others tests [3]. There is not a gold standard method, so the use of a combination of tests is recommended [4].

SD-OCT examination interpretation can be done in either a qualitative or quantitative method. The qualitative methods take into consideration the alterations on RPE or the disruption of the inner segment (IS) layer due to cellular loss [5-7]. On the other hand, the quantitative analysis uses the thinning of inner layers to measure the thickness from inner limiting membrane (ILM) to RPE [8]. Johson, et al. found a significant relationship between the thinning of inner nasal and temporal quadrants related to the accumulated dose and, according to its reproducibility, it could be used as an early detector. However, it presents a low sensitivity, being very specific (97%), so in case of presenting a pathological exploration, the thinning of the ILM – RPE measurement would be pathognomic for toxicity [9], but being useless as an screening method due to the low sensitivity. The qualitative analysis showed even lower sensibility than the quantitative, and also less reproducibility because of the difficulty for surveillance, so it won’t be recommended as a screening method [10].

As Browning, et al. suggests, mERG may be affected on an early stage being very sensible, nevertheless, associating a high rate of false positives so its role as an screening method is also questioned [11].

In our case, the right eye is affected with a subtle scotoma that maintained persistent on nasal inferior quadrant, using autofluorescence (HFA-AF) a hypoautofluorescent lesion could be observed at temporal superior quadrant. The topographical correspondence of the lesion correlates with the lesions.
well as the autoflourescence, however, using en-face protocol, hyporreflective lesions were shown at the inferior and paracentral area of ellipsoid layer.

Recently, Itoth Y, et al. [12] obtained using ellipsoid mapping with en-face OCT a volumetric scale of this layer showing a decrease in volume of those patients with hydroxichloroquine intake among other maculopathies such as geographical atrophy and after

**Figure 3:** OCT Spectralis (Heidelberg Engineering) Right eye: A. HFA mode showing a hypoautofluorescent parafoveal lesion. B. B-mode OCT scan with non-specific alteration of IS/OS layer. C. Hyporreflective lesion affecting parafoveal area at ellipsoid layers. D. Hyperreflective lesion affecting parafoveal area at inner layers.

**Figure 4:** Left eye: A. HFA mode, non hypo/hyperautofluoresce lesions. B. B-mode OCT scan. C. Hyporreflective lesion affecting parafoveal area at the ellipsoid layer.
ocriplasmin injection. Also there are described morphologic changes that could be associated, in pattern-based analysis, with bull-eye maculopathy in advanced cases and with the disruption of ellipsoid layer in cases of moderate affection. Using en-face protocol, other cases of paramaculopathies have been studied, such as retinal artery obstruction. On those patients, were found hyperreflective lesions at ischemic areas which coincide with the areas of hypoperfusion using angioOCT. In addition, en-face protocol produce images with enough reproducibility to perform an accurate follow-up [13]. In the case of diabetic patients, the reconstruction showed the decrease of photoreceptors at IS layer, being unremarkable at the B mode imaging [14]. Similar findings are described affecting outer retina using different methothes such as adaptive optics, microperimetry, HFA, with good topographical correlation with the images produced by en-face OCT scans [15-17].

This evidence suggests that there is a good feasibility between the OCT en-face imaging and the demonstration of cellular lost. The findings of the en-face OCT scan in this case would correlate the lesions attributed to cellular lost with the evidence of a subtle sensibility decrease by the 10-2 perimeter pattern deviation map. The early detection of this lesions using enface instead of B-scan sectional protocol may be due to a more precise scanning avoiding the loss of defects in non-obtained cuts and, on the other hand, due to the layer reconstruction, making more evident the defects that affect a specific region or cellular population [12,18].

These findings have not been reported earlier in other cases of hydroxychloroquine maculopathy could be implemented as an early detector on the screening of these patients. Nevertheless, it is need to perform larger studies to determine the diagnostic feasibility of this test.

References