Maculopathy associated with Prior Tamoxifen Use Diagnosed with Commercially Available Fourier-Domain Optical Coherence Tomography: A Case Series

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Abstract

Introduction: Tamoxifen retinopathy is usually diagnosed on fundoscopy and fluorescein angiography. Microcystoid maculopathy associated with tamoxifen was reported previously using a research-grade high resolution Fourier-domain optical coherence tomography (Fd-OCT) in a patient with vision loss unexplained on fundoscopy, fluorescein angiography and Stratus OCT. This report describes two new cases of microcystoid maculopathy diagnosed using commercially available Fd-OCT in patients who have been previously treated with tamoxifen.

Case presentation: Two patients had visual complaints which started while on tamoxifen but persisted or worsened after stopping tamoxifen at least two years earlier. Both patients had normal or near normal visual acuity and fundoscopy. Fluorescein angiography was normal in all but one eye which showed foveal hyperfluorescence. No angiographic cystoid macular edema was noted. Commercially available Fd-OCT (RTVue and Cirrus) showed microcystoid changes in the central macula with patches of loss of photoreceptor inner segment-outer segment junction (IS-OS) near the fovea in all four eyes. The eye with foveal hyperfluorescence on fluorescein angiography had foveal detachment on Fd-OCT in addition which resolved spontaneously on follow-up Fd-OCT nine months later. The microcystoid changes and IS-OS loss persisted on follow-up Fd-OCT.

Conclusion: Maculopathy associated with prior tamoxifen use may be detected using commercial Fd-OCT though not evident on fundoscopy or fluorescein angiography. Maculopathy may persist over 2 years after stopping tamoxifen.

Keywords: Tamoxifen; Toxicity; Maculopathy; Optical coherence tomography

Introduction

Tamoxifen is a drug used to treat estrogen receptor positive breast cancer that can induce retinopathy [1,2]. The diagnosis of tamoxifen retinopathy is traditionally established by macular edema seen on fluorescein angiography and retinal crystalline deposits seen on funduscopy [1,2]. Macular edema associated with tamoxifen retinopathy has been reported to be reversible after cessation of the drug but the retinal crystalline opacities usually persist [2]. Recently, a case of bilateral microcystoid maculopathy with patches of photoreceptor loss associated with concurrent tamoxifen use was detected using a research-grade high resolution Fourier-domain optical coherence tomography (Fd-OCT) in a patient with vision loss unexplained by funduscopy, fluorescein angiogram (FA), multifocal electroretinography and Stratus OCT [3]. This report describes two new cases of maculopathy associated with prior tamoxifen use in which similar morphologic changes were seen using commercially available Fd-OCTs, Cirrus (Carl Zeiss Meditec, Dublin, CA) and RTVue (Optovue, Fremont, CA), in eyes that appeared unremarkable on funduscopy.

Case Presentations

Case 1

A 58 year old woman presented with a five year history of blurry vision OU which started two years after starting tamoxifen. She was seen by an ophthalmologist at that time with no definitive diagnosis. Her past medical history was significant for hypertension and heart disease. She was diagnosed with breast cancer and treated with lumpectomy with lymph node dissection, radiotherapy and chemotherapy with docetaxel, followed by tamoxifen which was discontinued two year earlier (dose unknown). Her current medications included nitroglycerine, metoprolol, losartan, spironolactone, clonidine, amlodipine, ticlopidine, ezetimibe, simvastatin, propylthiouracil, anastrozole, esomeprazole, bupropion, gabapentin.

Best corrected visual acuity (BCVA) was 20/25 OU. Anterior segment examination was unremarkable. Dilated funduscopy revealed minimal pigment alteration in the fovea bilaterally and a possible single refractile deposit temporal to the macula in the left eye (Figure 1). FA was unremarkable OU except for subtle mottled hyperfluorescence in the temporal macula in the left eye (Figure 1F). RTVue Fd-OCT revealed patches of loss of inner segment-outer segment (IS-OS) junction of photoreceptor layer in central macula OU with probable microcystoid changes in the central macula (Figure 1G to J). The patient refused further diagnostic testing and follow-up examination.

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Figure 1: Fundus photographs, fluorescein angiogram and fourierdomain optical coherence tomography (RTVue) images of Case 1. Fundus photograph of the right eye (A) is normal, while that of the left eye (B) shows a possible single refractile body/crystal (arrow) temporal to the macula. Red free fundus photograph of the right eye (C) is unremarkable, while the left eye (D) shows the single possible refractile body (arrow). Middle (Arteriovenous) phase fluorescein angiograms of right (E) and left (F) eyes are unremarkable. RTVue images of the right (G and I) and the left (H and J) eyes show patches of loss of inner segment-outer segment junction of photoreceptor layer (black arrows). Possible microcystoid changes (white arrows) are also seen in both (I and J) the eyes.

Case 2

A 63 year old woman presented with metamorphopsia OS which started almost five years earlier while on tamoxifen for breast cancer. Tamoxifen was discontinued 18 months earlier after a five year course but metamorphopsia worsened somewhat.

BCVA was 20/20 OU, but Amsler grid testing revealed some metamorphopsia just temporal to fixation OS. Anterior segment examination was unremarkable. Dilated funduscopy revealed some mild pigment alteration in the fovea OU (Figure 2A and 2B). No refractile retinal deposit was seen. FA was unremarkable OD but OS had foveal hyperfluorescence (Figure 2C and 2D). Cirrus and RTVue Fd-OCT revealed focal patches of photoreceptor IS-OS loss with microcystoid changes near the fovea OU and a subtle foveal detachment OS (Figure 2E to M). The foveal detachment resolved on Cirrus Fd-OCT nine months later with some improvement of metamorophosia OS, but microcystoid changes and photoreceptor IS-OS loss persisted OU (Figure 2I).

Discussion

This report describes two cases of maculopathy associated with prior tamoxifen use detected using commercially available Fd-OCT where the characteristic refractile retinal deposits suggestive of tamoxifen retinopathy were not definitively seen [1]. The morphologic changes noted in this report with commercially available Fd-OCT



Figure 2: Fundus photographs, fluorescein angiogram and fourierdomain optical coherence tomography (Cirrus and RTVue) images of Case 2. Fundus photographs of the right (A) and the left (B) eye are unremarkable except for mild pigment alteration in the fovea with some loss of foveal reflex in both the eyes. Middle (Arteriovenous) phase fluorescein angiogram of the right (C) eye is unremarkable, while that of the left (D) eye shows foveal hyperfluorescence. Cirrus (E to I) and RTVue (J to M) Fd-OCT images of case 2 were obtained. The right (E) and the left (F) eyes show patches of loss of inner segment-outer segment junction of photoreceptor layer (black arrows) and possible microcystoid changes (white arrows). One of the sections through right macula (G) appears normal. A foveal detachment suggestive of an impending macular hole or outer lamellar hole (arrow-head) is seen in the left eye (H). The same scan nine months later (I) shows resolution of foveal detachment with persistence of microcystoid changes (white arrows) and photoreceptor IS-OS loss (black arrows). A single horizontal line scan through right central macula (J) appears normal while the higher resolution horizontal line scan through the left central macula (K) show patches of loss of inner segment-outer segment junction of photoreceptor layer (black arrows) with possible microcystoid changes (white arrows). Lower resolution radial scan through the right macula (L) shows patches of loss of photoreceptor layer (black arrow) while scans through the left eye (M) shows microcystoid changes with foveal detachment suggestive of an outer lamellar hole or an impending macular hole (arrow-head)

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instruments are similar to those reported previously using a research prototype high resolution Fd-OCT on another subject with vision loss OU on tamoxifen which was unexplained by funduscopy, FA and Stratus OCT [3]. These morphologic changes are also similar to that reported using Stratus OCT in two subjects with clinical diagnosis of tamoxifen maculopathy and vision loss [4]. These cases demonstrate that subtle visually significant maculopathy associated with tamoxifen use may be detected using Fd-OCT in eyes even in the absence of crystalline retinopathy and angiographic cystoid macular edema. In addition, the cases also illustrate that vision loss and photoreceptor IS-OS loss associated with tamoxifen use may persist for at least a couple of years after discontinuation of the drug and may be irreversible. Since these morphologic changes were detected using commercially available Fd-OCT in the asymptomatic right eye in Case 2, these morphologic changes may precede vision loss. Thus, Fd-OCT may be a useful tool to screen for tamoxifen maculopathy in conjunction to funduscopy.

Case 2 also demonstrates a morphologic abnormality on Fd-OCT not previously reported to be associated with tamoxifen exposure, i.e. foveal detachment. The foveal detachment was associated with foveal hyperfluorescence on FA and resolved spontaneously on followup evaluation without obvious posterior vitreous detachment on Fd-OCT or funduscopy. It is unclear whether the foveal detachment was a manifestation of tamoxifen toxicity or an impending macular hole that spontaneously resolved. Of note, Cronin et al reported an increased incidence of tamoxifen exposure among women diagnosed with macular hole when compared to the age-matched control female population [5]. Among patients diagnosed with macular hole, there appeared to be an increased incidence of bilateral macular hole among patients with history of tamoxifen use [5]. These observations raise the question whether the morphologic changes in the macula associated with tamoxifen use seen on Fd-OCT may predispose these eyes to macular hole formation [5]. Further studies are needed to test this hypothesis.

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In summary, these two cases demonstrate that commercially available Fd-OCT may be an important tool to use in addition to funduscopy to screen patients for tamoxifen maculopathy. Subtle maculopathy may be diagnosed using commercially available Fd-OCT even in the absence of visual symptoms or funduscopic abnormalities. Early diagnosis of maculopathy and cessation of the drug may prevent irreversible vision loss associated with tamoxifen use.

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