Original Article

Analysis of Optic Coherence Tomography for Congenital Macular Retinoschisis

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Abstract

Purpose: To investigate the pathological characteristics of congenital macular retinoschisis by optic coherence tomography (OCT).

Methods: The data of 7 cases(14 eyes) with congenital macular retinoschisis were collected. Electroretinogram (ERG), fundus fluorecein angiography (FFA) and OCT examination were performed, respectively.

Results: The OCT images showed schisis cavity in all eyes. Schisis was confined to the fovea and parafovea in 2 eyes (1 patient). Schisis was involved in entire macular area in 12 eyes (6 patients). Inner nuclear layer (INL) schisis was seen in all eyes. Schisis was located at both INL and outer nuclear layer (ONL)/outer plexiform layer (OPL) in 2 of the 14 eyes. Besides the schisis cavity, small cysts within ganglion cell layer were found in 3 eyes. The small cysts were confined to parafoveal area. The OCT images of both eyes in one patient were similar but not exactly the same or symmetrical.

Conclusion: Morphology, extension and schisis location in congenital macular retinoschisis have respective diversities. (***Eye Science 2011;26:80-84***)

Keywords: Congenital macular retinoschisis; Optical coherence tomography; Macular

Introduction

Congenital macular retinoschisis (also known as X-linked retinoschisis)is a macular degenerative condition that tends to affect young boys and can pose significant impact on central vision. Previously, the diagnosis of this condition was mainly based on slit lamp examination with preset lens, three-mirror contact lens, fundus fluorescein angiography (FFA) and electroretinogram (ERG). Since optical coherence tomography (OCT) was introduced into clinical ophthalmology, its technological aspect has been constantly updated. Now that time-domain OCT has evolved into frequency-domain OCT, it is possible to reveal precise anatomical locations of schisis in different layers of the retina, thus providing further understanding and knowledge on this condition. We performed OCT examinations in 7 patients(14 eyes) with congenital macular retinoschisis who were confirmed by FFA and ERG in our clinic during the past three years, and analyzed the characteristics of this condition. The results were reported hereunder.

Data and methods

Data

During January 2008 and December 2010, 7 patients(14 eyes) with congenital macular retionschisis sought medical treatment in our clinic. All these patients were males whose both eyes were affected, with no established family history. They aged between 4 to 25 years, including three patients aged between 4 to 8 years and four aged between 21 to 25 years, with a mean age of 15.4±9.0 years old. In all affected eyes, visual acuity started to decline at very young age. Corrected visual acuity was ≤ 0.05 in 3 eyes(21.4%), 0.1-0.3 in 6 eyes (42.9%) and 0.4-0.5 in 5 eyes (35.7%).

Equipments and methods

All these patients underwent conventional ocular examination and slit lamp, three-mirror contact lens, FFA, ERG, and OCT examinations. FFA examination was conducted using Zeiss FF450 ocular fundus camera to provide fundus fluorescence angiograph. ERG examination was performed using a vi-

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sual electrophysiology testing system by ROLAND, Germany to provide a full field electroretinogram.

OCT examination

A frequency-domain OCT (TOPCON 3D OCT-1000, Japan) was used to detect all the patients. Before the examination, patients were administered tropicamide eye drop for mydriasis. During the examination, the patients were asked to gaze at the fixation point in the camera and had each of their eyes tested. Scanning was conducted from upper to lower fields under macular fixation mode and three-dimensional scanning, using a scanning length of 6.0 mm × 6.0 mm and a resolution of 512×128. The results were presented as retinal thickness plots that documented the thickness of retina in central fovea of macula, and in nasal and temporal regions.

Results

Changes in fundus oculi

All patients presented macular abnormalities, which manifested as a typical vesicle-like schisis in the macula. Among 6 eyes, four (42.9%) had schisis in both central-peripheral retina and peripheral retina, with apertures in inner wall at various size and number; vessels along apertures in inner wall were covered by branch-like whitish sheath. Another 2 eyes in 2 patients (14.3%)had concurrent downward heterotopy of macula.

Characteristics of FAA

In early phase, all patients showed small patches of petal-like strong fluorescence that changed with background fluorescence in their FFAs; however the appearance and size remained unchanged. In late phase, fluorescence weakened with background fluorescence, presenting window-like defect and transmitted fluorescence; leakage of fluorescein was never found during the entire time. In 6 eyes with peripheral retinoschisis, a hyper-fluorescent band was seen forming in the retina around the inner-wall aperture in FFA, with irregular patches of strong fluorescent and dark fields covered by pigments; in late phase, fluorescence in inner-wall aperture gradually subsided, whereas strong fluorescence around the aperture was slightly reduced, but was still present.

Features of macular OCT images

OCT clearly revealed broad bands of cystic changes in macula in all 14 eyes; nerve epithelium was separated into two or more layers; layers were connected to one another by bridging tissue, which divided the inter-space into multiple cystic low reflective areas. Presentations were rated into type 1 or type 2 based on scope of the schisis: in type 1, schisis was confined to central fovea or paracentral fovea; a total of 1 patient (2 eyes)(14.3%) was rated as type 1 (Figure 1); in type 2, the schisis affected the entire macula, or even beyond the macula; such change was seen in 6 patients (12 eyes, 85.7%). (Figure 2)

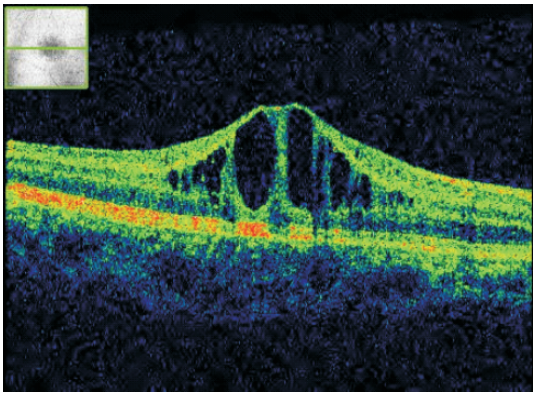

Figure.1 Macular OCT image of the right eye in a 22-year-old patient. Visual acuity was 0.5 in affected eye. The schisis was located in retinal inner nuclear layer in central fovea and paracentral fovea of the macula, with small cystic cavity in ganglion cell layer.

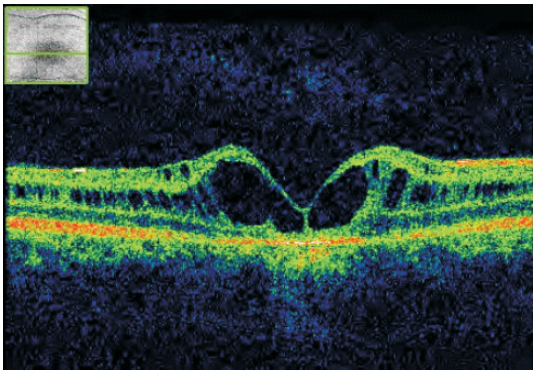

Figure.2 Macular OCT image of the right eye in a 25-year-old patient. Visual acuity was 0.25 in affected eye. The schisis was located in retinal inner nuclear layer, affecting the entire macula and invading beyond macula into retina in posterior pole. Small cystic cavity was seen in ganglion cell layer.

All affected eyes had schisis in inner nuclear layer

(Figures 1 and 2); however, in two of these eyes (14.3%), schisis was also found concomitantly in outer nuclear layer and outer plexiform layer, thus the retina was split into three layers (Figure 3); in addition to schisis cavity, three affected eyes (21.4%) with schisis cavity only in inner nuclear layer also showed a few small cystic cavities in ganglion cell layer (Figures 1 and 2). These small cystic cavities were only seen in paracentral fovea. Neither posterior vitreous detachment nor other vitreous retraction-related change was found.

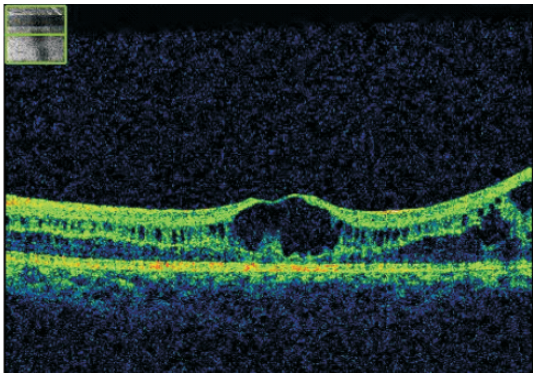

Figure.3 Macular OCT image in the left eye of a 6-year-old patient. Visual acuity was 0.2 in affected eye. Inner nuclear layer of the entire macula and retina in posterior pole were involved by the schisis, with concomitant schisis in outer nuclear layer/outer plexiform layer in temporal paracentral fovea.

Although OCT changes were similar between two affected eyes in a patient, they were not identical or symmetrical (Figures 2 and 4). In three younger patients, the schisis affected the entire macula; while in four adult patients, the schisis also affected the entire macula in affected eyes, except in 1 patient (2 eyes) where the schisis was confined to central fovea and paracentral fovew. No significant differences were detected in fundus oculi and the appearance and location of schisis in OCT between young patients and adult patients.

ERG features

All patients showed abnormalities in scotopic ERG (scotopic mixed rod-cone response); b/a ratios ranged from 1.61 to 0.3, which were significantly lower than the lower limit of normal range 2.3.

Discussion

Congenital retinoschisis, also known as hereditary retinoschisis, is a relatively rare condition. Patients are mostly males, generally with both eyes affected. It is an X-linked recessive hereditary condition. In this study, all patients were male with both eyes involved. Disease onset was during early age, but no established family history was seen in any patients.

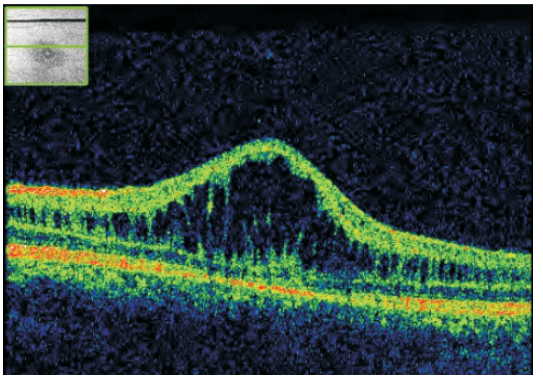

Figure.4 Macular OCT image in the left eye for the same patient as in figure 2. Visual acuity was 0.3 in affected eye. The inner nuclear layer of the entire macula was affected by the schisis. As compared to the right eye, appearance of OCT image was not completely symmetrical.

Previous pathological reports revealed that congenital macular retinoschisis was characterized by changes around central fovea, schisis separating retinal nerve fiber into layers, and glial tissue connecting inner and outer layers. However, since it was not possible to observe in retinal microstructures in vivo in the past, there was no observation conducted in large sample size[1,2]. The emergence of time do main OCT provides in-vivo examination evidence of different layers of human retina, and is able to prove the presence of retinoschisis in vivo. In addition, it is characterized by non-invasiveness and good safety. Therefore, it is enormously important to reveal the pathological and morphological features of this condition. Due to less favorable resolution of time-domain OCT, it fails to precisely identify the location of the schisis in the retina; but it can be used to determine the thickness of inner and outer layers. Some authors found similar thickness for inner and out layers in central fovea for most schisis; if retinoschisis was located at nerve fiber layer, then the thickness of the outer layer could be as much as 2/3 to 3/4 of the retina; only a thin inner layer would be seen in OCT image, and its thickness

should be significantly less than that of the outer layer, which was not consistent with the measurement results. It was thereby speculated that the schisis was probably located in deeper layer of the retina beyond retinal nerve fiber layer[3]. With further progress in OCT technology from time domain into frequency domain, it provides clearer image and higher resolution, and is able to better visualize the tissue structure and pathological changes in various layers of the retina in addition to allowing three-dimensional reconstruction of the lesions. It enables vivid visualization of the changes in different layers of macular retina, offering detailed imaging information for a more comprehensive understanding on the characteristics and pathogenic mechanisms of macular retinoschisis[4]. New studies have shown that, as a matter of fact, in most cases macular schisis occurred in the inner nuclear layer of retinal nerve epithelium, and in some cases in outer nuclear layer or outer plexiform layer, except for a few schisis in paracentral fovea, which involved retinal nerve fiber layer[5,6].

Using a novel generation of frequency-domain OCT (with a resolution of 5 μm), we observed 7 patients (14 eyes) with congenital macular retinoschisis and found that OCT images were not identical or symmetrical between two eyes in patients whose both eyes were affected, though images of fundus oculi were similar. Schisis cavity was seen in inner nuclear layer in all 14 eyes, some of which presented concomitant schisis cavity in outer nuclear layer/outer plexiform layer (14.3%) and small cystic cavity in ganglion cell layer (21.4%). These results were similar to previous results[5,6]. Currently it is still unknown whether small cystic cavity is an early form of schisis or other pathological changes. However, the difference from previous results[6] was that we had not found any schisis cavity in nerve fiber layer; this might be due to the small sample size in our study, or because we had not performed OCT examination for schisis in locations other than macula. Moreover, we found no evidence of vitreous retraction in any affected eyes, which was also different from previous results[6]. The main cause for the formation of congenital retinoschisis is XLRS1 gene defect in X chromosome, leading to functional defect of RSI protein. This is a protein found in various layers of the retina, but is mainly expressed in photoreceptor and bipolar cells and responsible for maintaining the connection between photoreceptor synapse and bipolar cells[7]. Functional abnormality of RSI protein leads to abnormal connection among cells, giving rise to the formation of schisis cavity. We assumed that vitreous retraction was a complication of this condition that could accelerate its progression, rather than one of the underlying causes of this condition.

Macular retinoschisis progresses faster in juvenile patients, but slower in elderly people. If no complication is seen in adulthood, the patients can maintain a stable visual acuity over quite a long period of time[8]. We found no significant differences among three juvenile patients who aged less than 8 years old and four patients who aged more than 21 years old. For example, the schisis affected the entire macula and retina in posterior pole in three juvenile patients and three adult patients, and was confined to central fovea and paracentral fovea in only one adult patient. Yet, due to the small sample size and limited follow-up duration in this study, it is still unknown whether the pathological changes manifest as extending schisis, or retinal atrophy and thinning, or gradually shrinking schisis with further progression of the schisis.

Prior to OCT introduction, this condition was generally confirmed by FFA and ERG examinations. With FFA examination, the condition is characterized by window-like defect or transmitted fluorescence in macula, without any leakage of fluorescein. Although there are no specific changes in this condition by angiography, it is distinguishable from other ocular conditions: diabetic retinopathy, retinal venous occlusion, retinal vasculitis, uveitis, and cystoids macular edema caused by retinal pigment degeneraton. Since OCT results are similar between cystoids macular edema and retinoschisis, and FFA examination reveals significant leakage of strong fluorescence in macula in cystoids macular edema, which is a significant difference as compared to retinoschisis; Therefore, OCT combined with FFA provides differential diagnosis for this condition in a more accurate and reliable way.

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