• Clinical Research •

Focal choroidal excavation complicated with choroidal neovascularization in young and middle aged patients

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Abstract

• AIM: To investigate the clinical and optical coherence tomography (OCT) features of focal choroidal excavation (FCE) complicated with choroidal neovascularization (CNV) in young and middle aged patients.

• METHODS: We performed a retrospective review of 26 patients with FCE accompanied by CNV. All patients underwent a complete ophthalmic examination. We analyzed the clinical characteristics of patients, focusing on the spectral-domain OCT features. All patients received intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF) agents. And we assessed the changes of central retinal thickness and best-corrected visual acuity (BCVA) after anti-VEGF therapy.

• RESULTS: The mean age of 26 patients was 35.5±7.3y (range, 21-48y). Of the 26 FCE lesions, 11 were located subfoveal, 6 were parafoveal, and 9 were extrafoveal. The mean FCE depth was 129.8±50.3 μm, and the mean width was 901.3±306.0 μm. The FCE depth was correlated positively with the width, but not correlated with age or refractive error. CNV was located within the excavation (19 eyes) or adjacent to the excavation (7 eyes). After anti-VEGF therapy, the central retinal thickness was significantly reduced and the BCVA was significantly improved. In the absorption process of subretinal fluid, we found that the fluid in the excavations needed to be absorbed at the last. A small amount of residual fluid could still be seen in a few deep excavations even after a long-term follow-up.

• CONCLUSION: FCE may be an important reason to cause CNV. Especially in young patients with idiopathic CNV, we should pay attention to the use of OCT to check the presence of FCE. Anti-VEGF therapy is generally effective for CNV associated with FCE.

• KEYWORDS: focal choroidal excavation; choroidal neovascularization; optical coherence tomography
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INTRODUCTION

Focal choroidal excavation (FCE) is an idiopathic clinical entity, which can be clearly displayed by spectral-domain optical coherence tomography (OCT). In 2006, Jampol *et al*[1] firstly reported a case with unusual choroidal excavation at the macula using time-domain OCT. But due to the limitation of imaging resolution and scanning depth, it's difficult to make precise analysis of this clinical entity using time-domain OCT. Until 2011, Margolis *et al*[2] analyzed a series of 12 patients using spectral-domain OCT and firstly proposed the term "focal choroidal excavation". They defined FCE as an area of macular choroidal excavation without evidence of posterior staphyloma or scleral ectasia. In 2014, our group reported a series of Chinese patients with FCE[3]. These reports suggested FCE may be a congenital abnormality, and mainly diagnosed in young and middle-aged patients[2-4]. Most FCE lesions were found in normal eyes, but a few cases were diagnosed with concurrent central serous chorioretinopathy or choroidal neovascularization (CNV)[5-8].

There were only a few literature reports about FCE complicated with CNV. Lee *et al*[9] studied 16 patients who had FCE complicated with CNV. This case series had a wide range of age distribution (28 to 86y). And Xu *et al*[10] reported a series of 12 patients. The same limitation of these two studies was the small number of included patients. Then Kuroda *et al*[11] analyzed the characteristics of FCE in elderly patients (aged over 55y) with neovascular age-related macular

degeneration (AMD). However, it's still unclear about the detailed characteristics of FCE complicated with CNV in younger patients.

Therefore, our study aims to investigate the clinical and OCT features of FCE complicated with CNV in young and middle aged patients, and observe the efficacy of anti-vascular endothelial growth factor (anti-VEGF) therapy.

SUBJECTS AND METHODS

Ethical Approval We performed a retrospective review of the patients with FCE accompanied by CNV, who visited Eye and ENT Hospital of Fudan University from January 2015 to December 2016. The research followed the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Eye and ENT Hospital of Fudan University. All patients underwent a complete ophthalmic examination, including slitlamp biomicroscopy, indirect ophthalmoscopy and measurements of best-corrected visual acuity (BCVA), refractive error and intraocular pressure. Ancillary tests included fundus photography, spectral-domain OCT and fundus fluorescein angiography (FFA).

FCE was defined as a macular lesion of choroidal excavation detected on spectral-domain OCT without evidence of posterior staphyloma or scleral ectasia. The diagnosis of CNV was based on the fundus manifestation, OCT and angiography findings. The age range of included patients was from 20 to 50y. Exclusion criteria included choroidal inflammation, AMD, and any history of ocular trauma or intraocular surgery.

All OCT images were obtained by a spectral-domain OCT instrument (Spectralis; Heidelberg Engineering, Heidelberg, Germany). During the follow-up period, the eyes were scanned by the eye-tracking-based follow-up function in Spectralis OCT. The depth and width of each FCE was measured with a built-in caliper tool. The distance between the center of FCE and the fovea was measured. According to the distance measurement, the location of FCE was classified into subfoveal (<200 μm), parafoveal (200-500 μm) and extrafoveal (>500 μm). The positional relationship between CNV and FCE was evaluated. The central retinal thickness was also manually measured with a built-in caliper tool. The central retinal thickness at the fovea was measured from the vitreoretinal interface to the inner border of retinal pigment epithelium (RPE).

All patients received intravitreal injection of anti-VEGF agents (ranibizumab 0.5 mg). Anti-VEGF treatment was performed on an as-needed basis, after either an initial 2 or 3 consecutive injections or a single injection. Intravitreal anti-VEGF injection was repeated, if an increase of central retinal thickness was detected on follow-up OCT.

Statistical Analysis The spherical equivalent of refractive error was analyzed. Myopia was classified according to degree of myopic diopter (D) as follows: low myopia (-0.5 to -3.0 D), moderate myopia (-3.0 to -6.0 D), high myopia (greater or equal to -6.0 D). The measured decimal visual acuity was converted to the logarithm of the minimum angle of resolution (logMAR) for statistical analysis. The statistical analysis was performed with Stata 11.0 statistical software (Stata Corporation, College Station, TX, USA). The correlation between two parameters was analyzed by Spearman correlation coefficient. The changes of central retinal thickness and BCVA after anti-VEGF therapy were analyzed by Wilcoxon matched-pairs signed-rank test. A two-tailed P value of <0.05 was considered statistically significant.

RESULTS

A total of 26 patients (26 eyes) with FCE accompanied by CNV were included in this retrospective study. All patients were Chinese, including 14 female patients and 12 male patients. The mean age was 35.5±7.3y (range, 21-48y). These 26 eyes included 5 emmetropic eyes, and 21 myopic eyes (mean -3.35±1.57 D; range, -1.0 to -6.5 D). Of the 21 myopic eyes, 7 were mildly myopic, 12 were moderately myopic, and only 2 were highly myopic.

On fundus photos, we could see the submacular hemorrhage and exudates caused by CNV (Figure 1). FFA could show hyperfluorescent CNV and blocked fluorescence corresponding to submacular hemorrhage (Figure 1). But the FCE lesion could not be identified on fundus photos or FFA. In our series, all eyes had a single FCE lesion detected by spectral-domain OCT. Of the 26 FCE lesions, 11 were located subfoveally, 6 were parafoveal, and 9 were extrafoveal. The mean FCE depth was 129.8±50.3 μm (range, 60-247 μm), and the mean width was 901.3±306.0 μm (range, 437-1372 μm). The FCE depth was correlated positively with the width (r=0.60, P<0.01). The FCE depth was not correlated with age (P=0.45) or refractive error (P=0.38). CNV was located mainly within the excavation (19 eyes) or adjacent to the excavation (7 eyes; Figure 1).

All patients received intravitreal injection of anti-VEGF agents. Twenty-six patients respectively received 1 injection (4 patients), 2 injections (9 patients), 3 injections (9 patients), and 4 injections (4 patients). The mean follow-up duration was 14.0mo (range, 5-22mo). All of patients responded well to intravitreal anti-VEGF therapy, the CNV lesions regressed and the macular edema resolved. After the patients received anti-VEGF therapy, the central retinal thickness was significantly reduced from baseline (304.0±93.4 μm) to last visit (180.8±33.7 μm; P<0.001). The mean BCVA at baseline (0.43±0.24 logMAR) was significantly improved to 0.21±0.20 logMAR at the last visit (P<0.001). In the absorption process of subretinal fluid, we found that the fluid in the excavations needed to be absorbed at the last (the representative case was shown in Figure 2). A small amount of

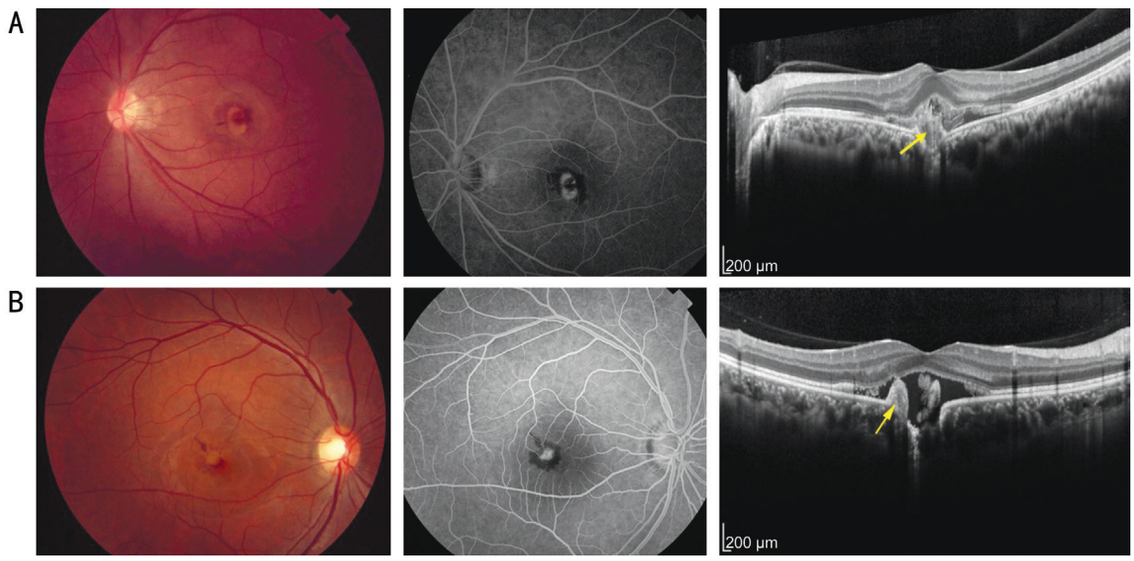

Figure 1 Fundus photos, FFA and OCT images of two patients at the time of presentation The fundus photos of these two patients both show submacular hemorrhage and exudates caused by CNV. FFA images of these two patients show hyperfluorescent CNV and blocked fluorescence corresponding to submacular hemorrhage. The OCT images reveal the positional relationship between CNV and FCE. A: The CNV lesion is located mainly within the excavation; B: The CNV lesion is adjacent to the excavation. The hyperreflective CNV lesions on the OCT images are indicated by arrows.

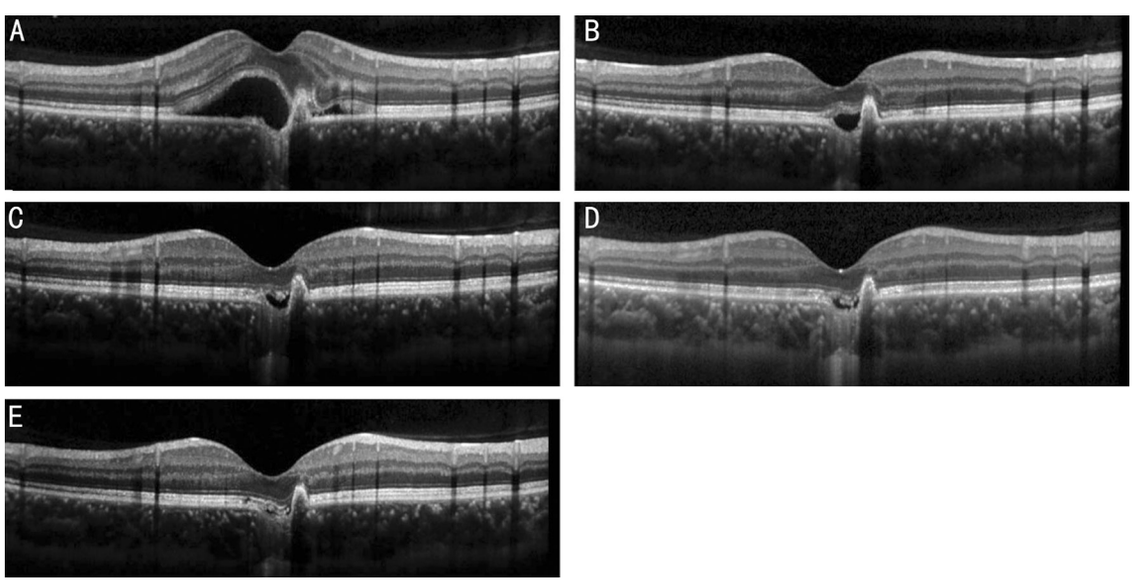

Figure 2 OCT scans from a 28-year-old male patient showing the gradual absorption of subretinal fluid after 3 anti-VEGF injections A: At the initial visit, the OCT image revealed a CNV lesion adjacent to the excavation, with obvious subretinal fluid; B: One month after the 1st intravitreal injection, the subretinal fluid was reduced. But the choroidal excavation was full of fluid. C: One month after the 2nd intravitreal injection; D: One month after the 3rd intravitreal injection, the residual fluid in the excavation was still seen; E: Three months after the 3rd intravitreal injection, the fluid in the excavation was completely absorbed at last.

residual fluid could still be seen in a few deep excavations (4 patients) even after a long-term follow-up (the representative case was shown in Figure 3).

DISCUSSION

In this study, we reported the clinical characteristics of FCE complicated with CNV in young and middle aged patients, focusing on the spectral-domain OCT features. The spectral-domain OCT provides high-resolution image of the retina and choroid[12-13], therefore it's able to clearly display the FCE lesion. FCE is considered to be a congenital abnormality, arising from the focal defect of chorioretinal differentiation[3,8]. But sometimes FCE could be acquired from choroidal inflammation or infection[14-16], so we have excluded these secondary factors in our study.

Kuroda *et al*[11] previously reported the mean depth of FCE in elderly patients was 53.3 μm (range, 22-106 μm). But our study found that the depth of FCE was 129.8 μm (range, 60-247 μm), which was greater than the data reported by Kuroda

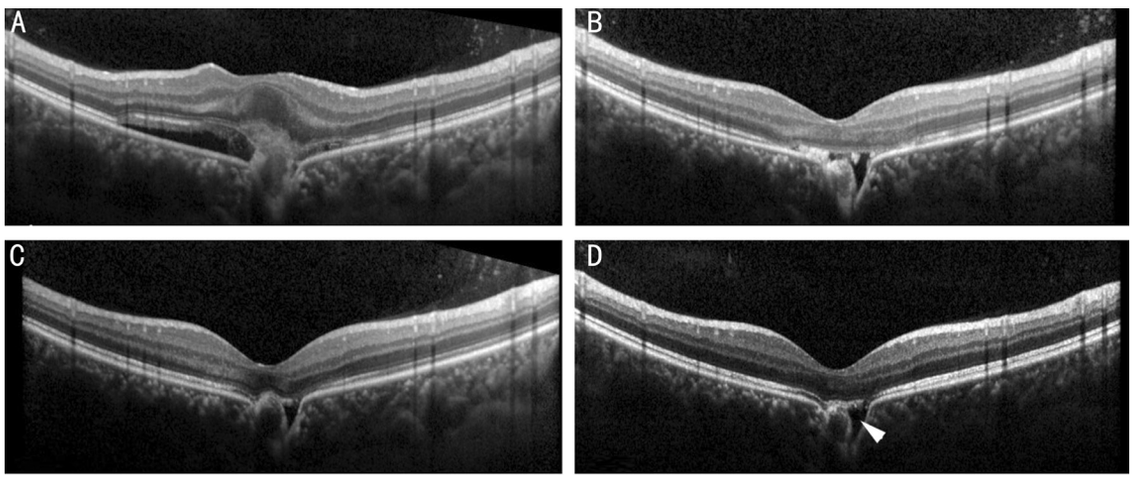

Figure 3 OCT scans from a 29-year-old female patient who received 2 intravitreal injections of anti-VEGF agents A: At the initial visit, the OCT image revealed a CNV lesion in a deep choroidal excavation, with obvious subretinal fluid; B: One month after the 1st intravitreal injection, the CNV atrophied and the subretinal fluid was reduced; C: Three months after the 2nd intravitreal injection, the subretinal fluid continued to be absorbed, but the residual fluid in the excavation was still seen; D: Twelve months after the 2nd intravitreal injection, a small amount of residual fluid (arrowhead) could still be seen in the deep excavation.

et al[11]. The inconsistence of FCE depth could be explained by age difference between the two studies. The RPE atrophy and choroidal thinning occurred in elderly patients[17-19], which may influence the morphology of the FCE and shallow the depth of the FCE. Therefore, our study of younger patients can avoid the aging influence on the characteristics of FCE.

In our study, we analyzed the proportion of different degrees of myopia in the patients who had both FCE and CNV. We found most eyes were emmetropic or mildly to moderately myopic, and only a few were highly myopic. The results indicated that the formation of FCE was different from posterior scleral staphyloma in high myopia.

All of CNV lesions grew within the excavation or near the margin of excavation. This close positional relationship suggested that the structure of FCE play an important role in the development of CNV. Choroidal excavation can result in focal choroidal thinning, and then may induce ischemic changes and development of CNV[6]. Another explanation is that the Bruch membrane may be impaired in the area of choroidal excavation[9]. The degeneration and break of the Bruch membrane can lead to the CNV formation[20-21]. Thus, the young patients previously diagnosed as idiopathic CNV may be reconsidered, and OCT can be used to check whether FCE exists.

Due to the limitation of this retrospective study, the anti-VEGF treatment did not follow a consistent standard protocol. Even though, we could see that all of patients responded well to intravitreal anti-VEGF therapy and had good prognosis. And we found the absorption process of subretinal fluid followed certain rules. Because of the special structure of choroidal excavation, the fluid in the excavations needed to be absorbed at the last. Although the CNV lesion atrophied after treatment, a small amount of residual fluid still existed in a few deep excavations after a long-term follow-up.

In conclusion, FCE may be an important reason to cause CNV. Especially in young patients with idiopathic CNV, we should pay attention to the use of OCT to check the presence of FCE. Anti-VEGF therapy is generally effective for CNV associated with FCE.

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