·Clinical Research·

Fundus autofluorescence imaging of patients with idiopathic macular hole

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Abstract

• **AIM: To investigate the role of fundus autofluorescence (FAF) both in the diagnosis and the preoperative and postoperative evaluation of patients with idiopathic macular hole (MH).**

• **METHODS: Forty eyes of 40 patients diagnosed as idiopathic MH between May 2010 and May 2011 were included in this retrospective study. All patients underwent full ophthalmologic examinations and imagings including fluorescein angiography, fundus autofluorescence (FAF) and optical coherence tomography. Thirty of these patients underwent MH surgery. FAF findings were associated with duration of symptoms, visual acuity at presentation, stage of MH, and postoperative anatomical correction.**

• **RESULTS: The mean duration of patients´ symptoms was 3.8±2.0 (1-9) months. The MH was stage 2 in 4 (10%), stage 3 in 24 (60%) and stage 4 in 12 (30%) eyes. The median preoperative best corrected visual acuity was 20/200 (between 20/800 and 20/100). Twenty-eight of cases (70%) showed a stellate appearance with dark radiating striae. Having a visual acuity ⩾20/200 was significantly more common in eyes with stellate appearance (*P*<0.001). The mean duration of symptoms was significantly shorter in eyes with stellate appearance (2.75±0.8 *vs* 6.33±1.61 months) (*P*<0.001). The frequency of stage 4 MH was significantly higher in eyes with non-stellate appearance (*P*<0.001). Anatomical correction of MH was achieved in 91.3% (21/23) of eyes with stellate appearance and 71.4% (5/7) of eyes without this appearance (*P*=0.225).**

• **CONCLUSION: Stellate appearance in FAF is associated with earlier stages of macular hole, better visual acuity at presentation, shorter duration of symptoms, thus more favorable prognosis.**

• **KEYWORDS:** autofluorescence; imaging; macular hole; prognosis; surgery

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INTRODUCTION

Idiopathic macular hole (MH) occurs mostly in elderly population and thought to result from abnormal traction of the posterior vitreous cortex at the foveal center. It is an important cause for central visual loss [1]. Although the diagnosis of macular hole can be made by biomicroscopic evaluation only, it can be hard to differentiate a full thickness hole from pseudoholes. Optical coherence tomography (OCT) is a valuable technique providing the diagnosis and staging of MH. Fundus autofluorescence (FAF) is another diagnostic tool which has been used widely in the diagnosis of several retinal pathologies including MHs. The use of this simple and non-invasive technique gives valuable information about the diagnosis and follow-up MHs [2-6]. An increased autofluorescence similar to fluorescence obtained by fluorescein angiography has been demonstrated in macular holes [4,6]. Fundus autofluorescence is useful not only in the diagnosis and differentiation, but also in predicting and following the therapeutic success of MH[5,8].

This retrospective study aimed to investigate the role of FAF both in the diagnosis and the preoperative and postoperative evaluation of patients with MH. The implications of FAF findings in showing morphological and functional changes at and around the MH have been discussed and compared with conventional methods such as fluorescein angiography and OCT.

SUBJECTS AND METHODS

Subjects This study included 40 eyes of 40 patients diagnosed as idiopathic MH in Retina Division of Ulucanlar Eye Research and Training Hospital between May 2010 and May 2011. Macular holes associated with other causes such as trauma, diabetes and ocular inflammatory conditions were excluded. All patients underwent full ophthalmologic examinations including visual acuity measurement by Snellen chart, intraocular pressure measurement with non-contact tonometry, biomicroscopic and dilated fundus examination. This study has been approved by local ethics committee.

Methods Before imaging, the pupil was dilated with a combination of 1% tropicamide and 2.5% phenylephrine. The autofluorescence images were obtained using the Heidelberg Retina Angiograph-2 (HRA-2, Heidelberg Engineering, Heidelberg, Germany) which is a confocal Scanning Laser Ophthalmoscope (cSLO). An excitation wavelength of 488nm generated by an argon blue laser was used and emission over 500nm was detected with a barrier filter. Fundus autofluorescence images of a rectangular 30 degree field of view were recorded. Approximately 32 single high-quality images for each eye were selected for automatic alignment. Following the alignment of single images to correct for eye movements during acquisition, a mean image measuring 512×512 pixels was calculated. Fundus autofluorescence images are considered as hypoautofluorescent and hyperautofluorescent according to the intensity of the autofluorescence. A relatively decreased intensity compared with the diffuse background signal is called hypoautofluorescent, whereas increased intensity is called hyperautofluorescent. An Optical Coherence Tomography (OCT) (SD-OCT, HRA Spectralis, Heidelberg Engineering GmbH, Heidelberg, Germany) and fluorescein angiography (FA) (KOWA VX-10 Alpha, Japan) were performed in each preoperative patient.

Macular hole surgery was performed in 30 cases. Ten of our cases did not accept the surgical procedure. Macular hole surgery was combined with phacoemulsification and intraocular lens implantation in 17 patients. As the remaining 13 patients were already pseudophakics, these patients had undergone pars plana vitrectomy only. A 23 gauge sutureless transconjunctival pars plana vitrectomy (TPPV) and internal limiting membrane (ILM) peeling was carried out in all cases. Following a core vitrectomy, posterior hyaloid was separated and removed using the 23-gauge vitreous cutter. The vitreous traction on the macular hole was removed and the ILM was stained with brilliant blue before peeling. The area of ILM peeling was about 2-3 optic disc diameters. The surgery was ended with fluid-air and air-gas (C3F8, 15%) exchange. Patients are asked to stay in prone position for a one week period.

Statistical Analysis The images of FAF and OCT were repeated 1 week and 1 month after the surgery. Student's t- and Chi-square tests were used in statistical analysis and statistical significance was set as $P<0.005$.

RESULTS

The mean age of patients at presentation was 64.4±6.1 (55-78) years. Six patients (15%) were male and 34 (85%) were female. The mean duration of patients' symptoms was 3.8 ± 2.0 (1-9) months. The symptoms were present since <3 months in 25 (62.5%) and between 3-9 months in 15 (37.5%) patients. The MH was stage 2 in 4 (10%), stage 3 in 24 (60%) and stage 4 in 12 (30%) eyes.The median preoperative best corrected visual acuity was 20/200 (between 20/800 and 20/100).

A posterior vitreous detachment with B-scan ultrasonography was detected in 12 (30%) patients. Fluorescein angiography revealed a hyperfluorescence due to window defect at the hole area and FAF showed marked foveal hyperautofluorescence correlating with the size of the MH in all patients. Around the hyperautofluorescent area corresponding to full thickness MH, a hypoautofluorescent ring was present. Outside this ring shaped area, again a circumferential area of relatively reduced FAF was observed (Figure 1A, 2A, 3A). In this relatively reduced FAF area, 28 of cases (70%) showed a stellate appearance with dark radiating striae (Figure 1A, 3A). This appearance was not present in 12 (30%) cases (Figure 2A). The visual acuity at presentation was ≥20/200 in 23/28 (82.1%) of eyes with stellate appearance and 1/12 (8.3%) of eyes without this appearance. Having a visual acuity ≥20/200 was significantly more common in eyes with stellate appearance ($P<0.001$). The mean duration of symptoms was 2.75 ±0.8 months in eyes with stellate appearance and 6.33 ±1.61 months in eyes without this appearance ($P<0.001$).

Most of the eyes with stellate appearance had Stage 2 or 3 MH (26/28, 92.8%) and most of the eyes with non-stellate appearance had Stage 4 MH (10/12, 83.3%). The frequency of Stage 4 MH was significantly higher in eyes with non-stellate appearance ($P<0.001$).

The MH was successfully repaired in 26 of 30 eyes (86.7%) which had been operated (Figure 2C, 2D, 3C, 3D). Of these 26 eyes, 21 (80.8%) had stellate appearance and 5 (19.2%) had not. Thus the anatomical correction of MH was achieved in 91.3% (21/23) of eyes with stellate appearance (Figures 3C, 3D) and 71.4% (5/7) of eyes without this appearance (2A, 2D). This difference was not statistically significant ($P=0.225$). The preoperative visual acuity was ≤20/400 in all eyes with unclosed MH. The comparison of cases with stellate and non-stellate appearance has been shown in Table 1.

Postoperative FAF imaging showed a significant decrease in autofluorescence in all eyes with surgically repaired MH (Figure 2C, 3C).

DISCUSSION

Idiopathic MH is an important cause for central visual loss for people between 60-70 years old. Blurred vision and metamorphopsia are the most common symptoms of the disease and the visual acuity is usually around 20/200. Visual loss is associated with several factors such as the absence of neural retina on the MH, cystic degenerations around the hole area, localized retinal detachment surrounding the MH and loss of photoreceptors [9-11]. Tangential traction caused by the

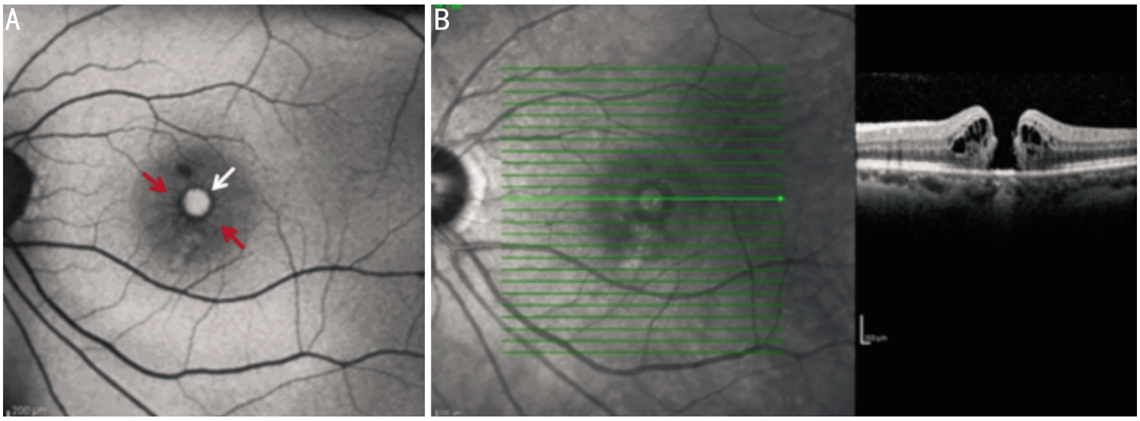

Figure 1 FAF and OCT imagines in patient with stage 4 macular hole A: Sixty years old female patient with stage 4 MH. Her visual acuity is 20/200. The lesion showed hyperautofluorescence corresponding to the hole area, surrounding hypoautofluorescent ring (white arrow) and a circumferential area of relatively reduced FAF around this ring (red arrows). A stellate appearance with dark radiating striae is present within this circumferential area; B: SD-OCT of the same patient showed full thickness MH and intraretinal cystic changes around the hole area.

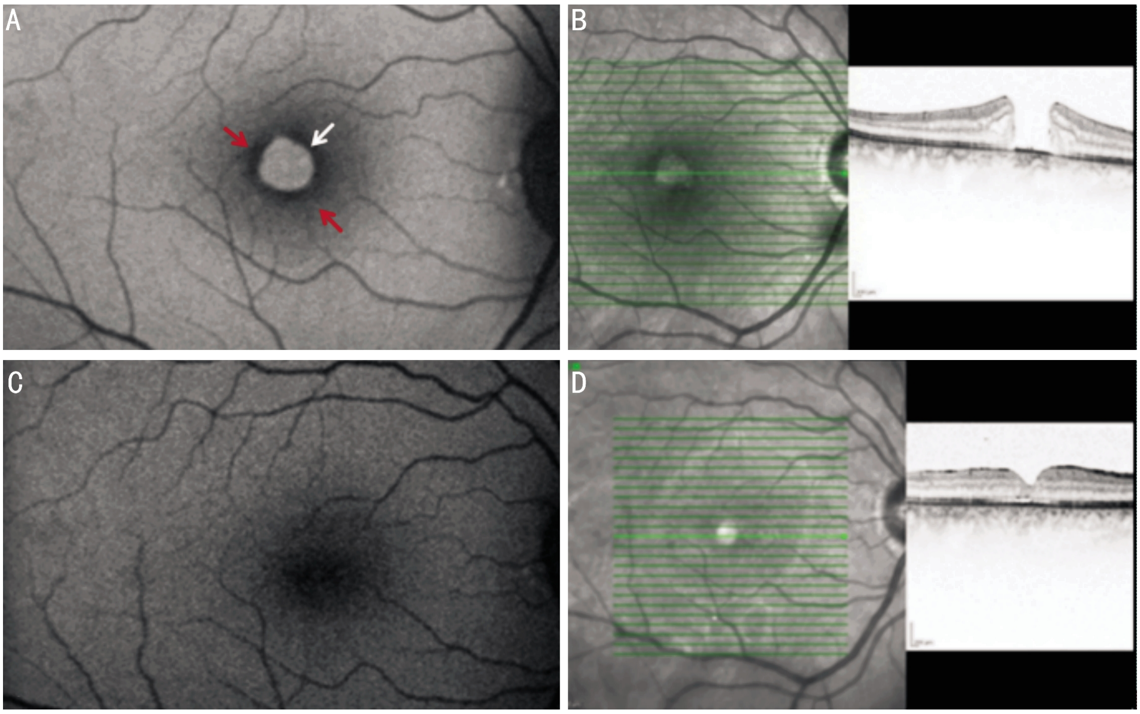

Figure 2 Pre-operative and postoperative FAF and OCT imagines in patient with stage 4 macular hole A: Sixty-two years old female patient with 20/400 visual acuity and stage 4 MH showing hyperautofluorescence corresponding to the hole area, surrounding hypoautofluorescent ring (white arrow) and a circumferential area of relatively reduced FAF (red arrows). The stellate appearance is not present within this circumferential area; B: SD-OCT of the same patient showing full thickness MH and intraretinal cystic changes around the hole area; C: Foveal hyperautofluorescence observed in Figure 2A decreased significantly 1 month after the surgery; D: SD-OCT showed successfully repaired MH of this patient.

Table 1 Comparison of cases with stellate and non-stellate appearance

	Stellate appearance n=28 (70%)	Non-stellate appearance n=12 (30%)	^1P
Stage 2 MH	3 (10.7%)	1 (8.3%)	^{1}0.000
Stage 3 MH	23 (82.1%)	1 (8.3%)	^{1}0.000
Stage 4 MH	2 (7.1%)	10 (83.3%)	^{1}0.000
Duration of symptoms	2.75±0.80	6.33±1.61	^{2}0.000
VA≥20/200	23 (82.1%)	1 (8.3%)	^{1}0.000
Repaired MH	21 (%91.3)	5 (%71.4)	^{1}0.225

^{1}Chi-square test; ^{2}Student's t-test; MH: Macular hole; VA: Visual acuity.

posterior vitreous which is firmly attached to the macula has been suggested to be the most important factor for the development of MH[10,12-14]. The fact that MH does not develop in eyes with posterior vitreous detachment supports this thesis[10,15,16].

Macular hole can be directly diagnosed by biomicroscopic and indirect ophthalmoscopic examination. The Watzke-Allen slit beam test, FA and OCT which has an important role in the evaluation of vitreoretinal interface are all helpful in diagnosing MH [5]. As a non-invasive and relatively easy method, FAF has attracted considerable attraction in

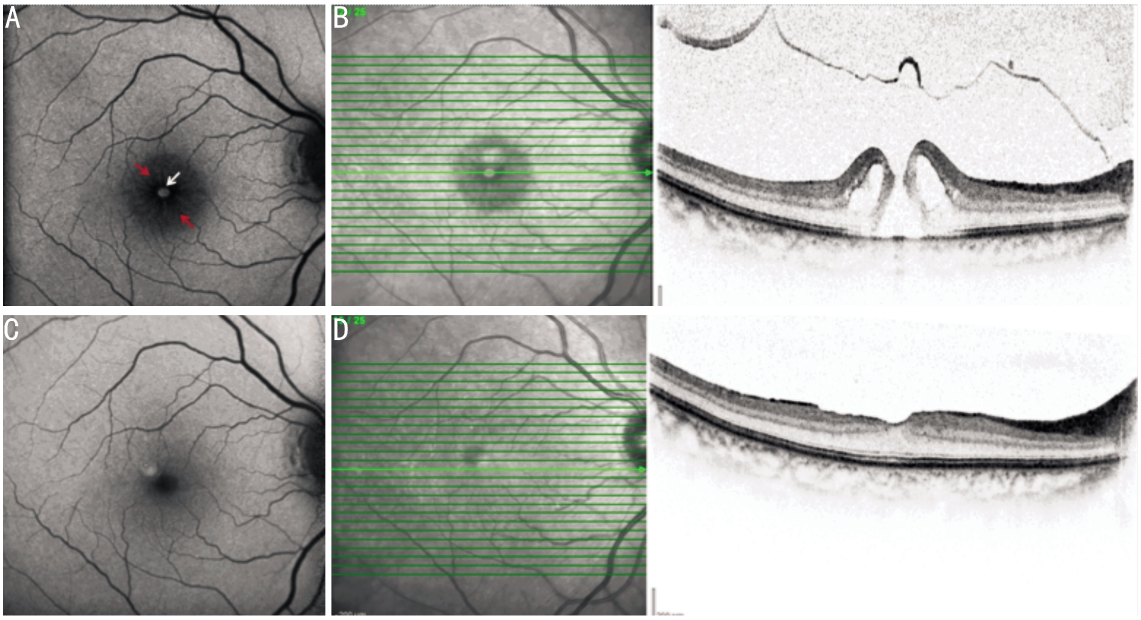

Figure 3 Preoperative and postoperative FAF and OCT imagines in patient with stage 3 macular hole A: Sixty-three years old male patient with stage 3 MH. His visual acuity is 40/200. A hyperautofluorescence corresponding to the hole area and a circumferential hypoautofluorescence area (white arrow) can be seen. A stellate appearance with dark radiating striae is present within this circumferential area (red arrows); B: SD-OCT of the same patient showed full thickness MH and intraretinal cystic changes localized at the outer plexiform layer around the hole area; C: Foveal hyperautofluorescence observed in Figure 3A decreased significantly 2 months after the surgery; D: SD-OCT showed successfully repaired MH of this patient.

diagnosing, staging and following macular holes [4-8]. This technique based on the evaluation of lipofuscin distribution within the retina pigment epithelium (RPE) gives insight into metabolic condition of RPE [3,17]. In a normal fundus, the distribution of FAF is diffuse, with reduced intensity at the fovea due to absorption by macular pigments (lutein and zeaxanthin) and also at the optic disc because of the absence of RPE and on the retinal vessels due to absorption of blue light by blood elements. Fundus autofluorescence images are considered as hypoautofluorescent and hyperautofluorescent as in fluorescein and indocyanine green angiographies [2,18]. In the MH, because the macular pigments absorbing the blue light are absent, the light reaches directly the lipofuscin within the RPE and fovea which is physiologically hypoautofluorescent looks pathologically hyperautofluorescent. Following a successful surgery, the disappearance of hyperautofluorescence is due to retinal and glial tissue which cover the macular hole area [5,19]. Fundus autofluorescence has been proved to be an imaging technique demonstrating the anatomically and functionally disturbed retinal areas. Wakabayashi *et al* [8] demonstrated increased foveal FAF in all of their 20 patients with stage 3 or 4 MH. The hypoautofluorescent ring shaped area surrounding the MH has been shown to be subretinal fluid cuff by OCT. Finally, the relatively reduced area of FAF seen around this ring shaped area has been suggested to associate with the thickened retina blocking the signal and also the luteal pigment shifted during the formation of MH resulting in attenuation of excitation light. These findings of MH showed with FAF and OCT are all compatible with the results of histopatological studies [8]. Histopatologically, a hole at the centre of the macula, a surrounding area of retinal detachment and cystic edema involving outer plexiform layer and inner nuclear layer have been reported by Frangieh *et al* [20] All of our cases showed similar FAF findings consisted of foveal hyperautofluorescence, hypoautofluorescent ring shaped area and another area of decreased autofluorescence surrounding this ring (Figures 1A, 2A, 3A). All these findings were confirmed with OCT (Figures 1B, 2B, 3B). The study of Wakabayashi *et al* [8] was also reported stellate appearance with dark radiating striae within the relatively reduced FAF area in 75% of cases and correlated with intraretinal cystic changes in the outer plexiform area (Figures 1A, 3A). These eyes had better preoperative vision compared to those without, probably due to shorter duration of symptoms, lower rate of stage 4 MH and a tendency of smaller hole size[8]. This stellate appearance was observed in 28 (70%) of our cases. In concordance with Wakabayashi *et al's* [8] study,these eyes had better visual acuity at the time of presentation (82.1% *vs* 8.3%, P<0.001) and shorter duration of symptoms (2.75 *vs* 6.33 months, P<0.001). Furthermore, stage 4 MH was significantly less common in eyes with stellate appearance (7.1%) compared to eyes with non-stellate appearance (83.3%) (P<0.001) corresponding to better surgical outcome in the former group. Although no statistically significant rate of closed MH after surgery was higher in eyes with stellate appearance (91.3% *vs* 71.4%). The relation between MH size and the presence of stellate appearance had not been evaluated in the present study.

Since first reported by Kelly and Wendel [21] in 1991, several studies have reported successful results concerning surgical correction of MH [19,21-23]. However, complete anatomical correction does not always result in good visual outcome. Chung *et al* [19] reported that the functional improvement following a successful MH surgery can be estimated by FAF. Authors showed a markedly decrease of FAF following successful MH surgery in all eyes. They suggested that using the decrease in FAF as an index, gives valuable information about photoreceptor and RPE function and their interaction in patients with repaired MH [19]. The decrease in FAF in successfully repaired MH has been observed in all of our cases and this finding was in concordance with previous studies[4,6-8,19] (Figure 2C, 3C). Thus FAF is an easy and useful way of imaging not only for the diagnosis, but also the follow-up of patients with MH. On the other hand, evaluation of inner segment/outer segment (IS/OS) junction representing the photoreceptor integrity is very important in determining the visual outcome of MH surgery. The extent of IS/OS junction breakdown correlates strongly with the visual outcome and a poorer prognosis has been reported in eyes with larger IS/OS defect. Thus OCT providing a detailed analysis of IS/OS defects, is essential in predicting the visual outcome of MH surgery[24].

As conclusions, compared to FA, FAF is an easier, quicker and non-invasive method for the diagnosis, differential diagnosis and follow-up of full thickness MHs. Whereas OCT is still the imaging method considered as the gold standard for the diagnosis, staging and evaluation of the prognostic factors. However, the stellate appearance observed in 70% of our cases and associated with more favorable prognosis is a finding that can be observed with FAF only. Thus OCT and FAF are methods providing complementary findings for the diagnosis of MH and the prediction of visual outcome following the MH surgery.

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