Adult-Onset Foveomacular Vitelliform Dystrophy: Diagnosis and Correlation Fundus Autofluorescence, Optical Coherence Tomography Features and Visual Acuity

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ABSTRACT

Purpose: To describe the fundus autofluorescence (FAF) and optical coherence tomography (OCT) findings at adult-onset foveomacular vitelliform dystrophy (AOFVD) and to evaluate their correlation with best corrected visual acuity (BCVA).

Material and Methods: The records of 39 eyes were evaluated retrospectively. The BCVA, the findings of fundus examination, OCT and FAF images were noted.

Results: Twenty seven (69.2%) of all patients were referred with the diagnosis of age related macular degeneration (AMD). At initial examination 34 (87.1%) eyes presented vitelliform stage and 5 (12.9%) eyes presented the other stages. At last visit 2 (5.1%) eyes progressed to the atrophic stage from the vitelliform stage. At FAF images; we detected well-circumscribed, very high autofluorescence signal in the vitelliform stage, increased autofluorescence with horizontally level in the pseudohypopyon stage, irregular hyperautofluorescence in the vitelliruptive stage and loss of autofluorescence in the atrophic stage. At vitelliform stage 30.7% had patchy, 28.2% focal, 15.3% ring-like, 10.2% round-shape pattern. The correlation between BCVA and FAF patterns could not be shown. At OCT findings; there was a negative correlation between the maximal thickness of the lesion and BCVA, but the correlation between BCVA and maximal width of lesion and central macular thickness could not be shown. There was a negative correlation between presence of IS/OS interface disruption and BCVA. A correlation between subfoveal fluid, RPE alterations and BCVA could not be shown.

Conclusions: AOFVD is the most important disorder in the differential diagnosis of AMD. FAF and OCT imaging techniques are useful for confirming the diagnosis of AOFVD. OCT findings are more useful than FAF patterns of the lesions for predicting visual acuity prognosis.

Key Words: Adult-onset foveomacular vitelliform dystrophy, fundus autofluorescence, optical coherence tomography.

ÖZ

Amaç: Geç başlangıçlı foveomaküler vitelliform distrofinin, fundus otoflöresans (FOF) ve optik koherens tomografi (OKT) bulgularını tanımlamak ve bunların en iyi düzeltilmiş görme keskinliği (EİDGK) ile korelasyonunu değerlendirmek.

Gereç ve Yöntem: 39 gözün bulguları retrospektif olarak değerlendirildi. EİDGK, fundus muayene, OKT ve FOF bulguları kaydedildi.

Bulgular: Olguların 27'si (%69,2) yaşa bağlı makula dejenerasyonu (YBMD) tanısı ile kliniğimize refere edilmişti. Başlangıç muayenede 34 göz (%87,1) vitelliform, 5 göz (%12,9) diğer evrelerde idi. Son muayenede 2 göz (%5,1) vitelliform evreden atrofik evreye ilerledi. FOF görüntülemede, vitelliform evrede; iyi sınırlı, yüksek otoflöresan sinyal, psödohipopiyon evresinde; horizontal olarak seviye veren artmış hiperflöresans, vitellirüptif evrede; düzensiz hiperflöresans, atrofik evrede ise otoflöresansda kayıp izlendi. Vitelliform evredeki gözlerin; %30,7'i yamalı, %28,2'i fokal, %15,3'ü halka şeklinde, %10,2'si ise yuvarlak pattern özellikleri gösteriyordu. EİDGK ve FOF patternleri arasında ilişki gösterilemedi. OKT görüntülemede, EİDGK ile lezyonun maksimal yüksekliği arasında negatif korelasyon saptandı. Fakat EİDGK ile lezyonun genişliği ya da santral makula kalınlığı arasında ilişki gösterilemedi. IS/OS tabakasının hasarı ile EİDGK arasında negatif korelasyon vardı. Subfoveal sıvı, RPE düzensizliği ve EİDGK arasında ilişki gösterilemedi.

Tartışma: AVD, yaşa bağlı makula dejenerasyonu ayırıcı tanısında düşünülmesi gereken en önemli hastalıktır. FOF ve OCT görüntüleme AVD tanısının doğrulanmasında en temel görüntüleme teknikleridir. Görme keskinliği prognozunu tahmin etmede OCT bulguları FOF patternlerine göre daha faydalıdır.

Anahtar Kelimeler: Geç başlangıçlı foveomaküler vitelliform distrofi, fundus otoflöresans, optik koherens tomografi.

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INTRODUCTION

Adult-onset foveomacular vitelliform dystrophy (AOFVD) was first described by Gass in 1974.[1] It is also known as adult-onset foveomacular pigment epithelial dystrophy,[2] adult vitelliform macular degeneration[3] and pseudovitelliform macular degeneration.[4] The onset of the disease is usually between 30 and 50 years of age with symptoms of blurred vision or mild metamorphopsia and generally, the visual loss is slowly progressive.

The disease is characterized by yellowish, round or oval, slightly elevated lesions with third to one half disc diameter size, often accompanied by a central pigmented spot. The involvement is bilateral although unilateral cases have been described. AOFVD has an incomplete penetrance with variable expression, although some have suggested an autosomal dominant inheritance pattern.

Lipofuscin accumulation is the main pathogenetic mechanism at AOFVD. Excessive lipofuscin accumulation in the retinal pigment epithelium (RPE) is a common pathway associated with several diseases including age-related macular degeneration, inherited retinal dystrophies such as Best disease, pattern dystrophy, AOFVD, and Stargardt disease.[5,6] At AOFVD histopathological studies show accumulation of lipofuscin pigments within the macular RPE and atrophic outer retinal layers.[7] Lipofuscin is a brown-yellow, autofluorescent molecule which is produced by partially digestion of photoreceptor outer segments due to photooxidative damage[6,8] and its photoreactive components produce free radicals that cause RPE apoptosis. Fundus autofluorescence (FAF) is a non-invasive imaging modality that generally refers to the fluorescent emission obtained from lipofuscin in the RPE and provides a topographical map of lipofuscin. Since lysosomal damage in RPE and consequently accumulation of lipofuscin are considered in the pathogenesis of AOFVD, FAF has become the most important imaging technique in the early diagnosis and monitorization of AOFVD.[9] Also optical coherence tomography (OCT) can provide cross sectional images of the retina and the vitelliform material can be located.[10] At previous studies the relationship between OCT, FAF findings and best corrected visual acuity (BCVA) were evaluated, and contradictory results were determined.[11-13]

In this study, our purpose was to describe the FAF and OCT findings of AOFVD and to evaluate their correlation with BCVA.

MATERIALS AND METHODS

A total of 39 eyes from 24 patients with AOFVD who were diagnosed at Ankara University Faculty of Medicine, Department of Ophthalmology between April 2000 and May 2012 were included in this study. The records of patients were retrospectively reviewed. Best corrected visual acuity, fundus examination results, the findings of OCT and FAF images were noted.

The patients with AOFVD were classified into 4 stages according to the clinical manifestation for definition of their FAF patterns; 1) The vitelliform stage with a yellowish or orange macular elevation looks like an egg-yolk 2) The pseudohypopyon stage with a horizontal sedimentation of the vitelliform material 3) the vitelliruptive stage with nonhomogeneous dispersion of vitelliform material 4) the atrophic stage with the atrophy at the center of macula.

Using the macular cube 512x128 scan mode with spectral domain OCT (Cirrus high-definition OCT; Carl Zeiss, Meditec, Dublin, CA, USA); central macular thickness, maximal width of the lesion, maximal thickness of the lesion, inner/outer segment (IS/OS) interface disruption, RPE layer alterations and presence of subfoveal fluid were evaluated. The IS/OS interface was classified as 1) normal 2) partial disruption and 3) total disruption. Disruption less than 50% at 1000 μm central area was described as partial disruption and more than 50% was described as total disruption.

The FAF images were recorded at a 488 nm wavelength via ≥ 500nm barrier filter and infrared images were also recorded at 787 nm wavelength via ≥ 800nm barrier filter using Heidelberg retinal angiography (II) device and confocal scanning laser ophthalmoscope. The stages of the disease were evaluated on FAF images. The FAF patterns of vitelliform stage were classified as focal, patchy, ring-like and round pattern. Focal pattern was characterized by the presence of at least one hyperautofluorescent spot smaller than 200 μm diameter. Patchy pattern was characterized by hyperautofluorescent areas larger than 200 μm diameter. At ring-like pattern there was a hypoautofluorescent spot surrounded with hyperautofluorescent area, the round-shape pattern was described as hyperautofluorescent areas like round shaped.

All analyses were conducted with the SPSS 15.0 software package (SPSS Inc., Chicago, ILL., USA). The p value less than 0.05 was considered to be statistically significant. Spearman's and Mann-Whitney U tests were used to compare the BCVA and OCT, FAF findings.

RESULTS

The mean age of patients was 67.3 (48-81) years. Fifteen (62.5%) of them were female and 9 (37.5%) were male. Twenty seven (69.2%) of all patients were referred to our clinic with the diagnosis of age related macular degeneration. The mean follow up period was 21.1 (6-52) months. The mean BCVA at baseline was 0.4 (0-1.5) logMAR and did not change at last visit.

We detected well-circumscribed, very high autofluorescence signal in the vitelliform stage, increased autofluorescence with horizontally level in the pseudohypopyon stage, irregular hyperautofluorescence in the vitelliruptive stage and loss of autofluorescence in the atrophic stage (Figure 1). At initial examination 34 (87.1%) eyes presented with vitelliform stage. Of the remaining 5 (12.9%) eyes, 1 (2.6%) presented with pseudohypopyon stage, 2 (%5.1) vitelliruptive stage and 2 (5.1%) atrophic stage. At last visit 2 (5.1%) eyes progressed to the atrophic stage from the vitelliform stage (Figure 2). The BCVA at vitelliform stage were 0.4/0.3 logMAR in these eyes and remained stable during the atrophic stage.

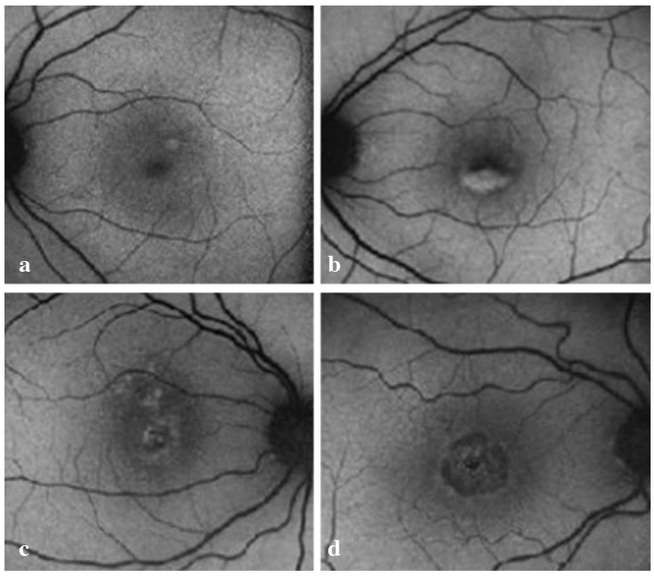

Figure 1a-d: *FAF images of AOFVD stages. a) vitelliform stage b) pseudohypopyon stage c) vitelliruptive stage d) atrophic stage.*

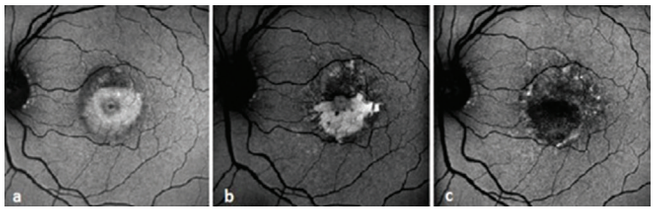

Figure 2a-c: *A 61 year-old man with bilateral AOFVD, progression in his left eye. a) vitelliform stage (ring-like pattern) b) vitelliruptive stage c) atrophic stage.*

At vitelliform stage 30.7% had patchy pattern, 28.2% focal pattern, 15.3% ring-like pattern, 10.2% round-shape pattern (Figure 3). Any correlation between BCVA and FAF patterns could not be shown.

OCT findings at inital and last visit were shown in table. There was a statistically significant negative correlation between the maximal thickness of the lesion and BCVA (p= 0.019), but the correlation between BCVA and maximal width of lesion and central macular thickness could not be shown. There was a statistically significant negative correlation between presence of IS/OS interface disruption and BCVA (p=0.016). A correlation between subfoveal fluid and RPE alterations and BCVA could not be shown.

DISCUSSION

Adult-onset foveomacular vitelliform dystrophy is a heterogeneous macular disorder with different clinical, histopathological and imaging findings.[7,14] Although it is a rare macular disorder, its differential diagnosis is important for the other macular disorders. Patients with AOFVD are generally misdiagnosed as age related macular degeneration and can be treated by anti-angiogenic agents unnecessarily. In this study 27 (69.2%) patients had been referred to our clinic with the diagnosis of age related macular degeneration. OCT and especially FAF imaging is useful for the differential diagnosis in these cases.[15] The location of lipofuscin accumulation, tissue structures and anatomical features can be shown by using different imaging modalities.

The visual acuity of these patients is usually preserved for years. As the disease progresses and retinal atrophy occurs, visual acuity may deteriorate. Renner et al. evaluated 61 patients with AOFVD and showed limited progression of functional loss and reduced visual acuity in the majority of patients.[16] It was thought that the central RPE atrophy may be the main reason for the lower visual acuity. Querques et al.,[17] evaluated the correlation between the disease stage and BCVA in 35 eyes with AOFVD and they found that there was a statistically significant correlation between reduced BCVA and stage progression.

Table: *OCT findings at inital and last visit.*

OCT Parameters	Initial Visit	Last Visit
Mean Central Macular Thickness (μm)	276.2	272.1
Mean Maximal Width of the Lesion (μm)	764.4	797.2
Mean Maximal Thickness of the Lesion (μm)	192.8	190.3
IS/OS Interface %		
Normal:	20.6	10.4
Partial Disruption:	25.6	35.8
Total Disruption:	53.8	53.8
Subfoveal Fluid %		
No:	25.6	23.1
Yes:	74.4	76.9
RPE Alterations%		
No:	35.9	33.3
Yes:	64.1	66.7

OCT; Optical Coherence Tomography, IS/OS; Inner Segment/Outer Segment junction, RPE; Retina Pigment Epithelium.

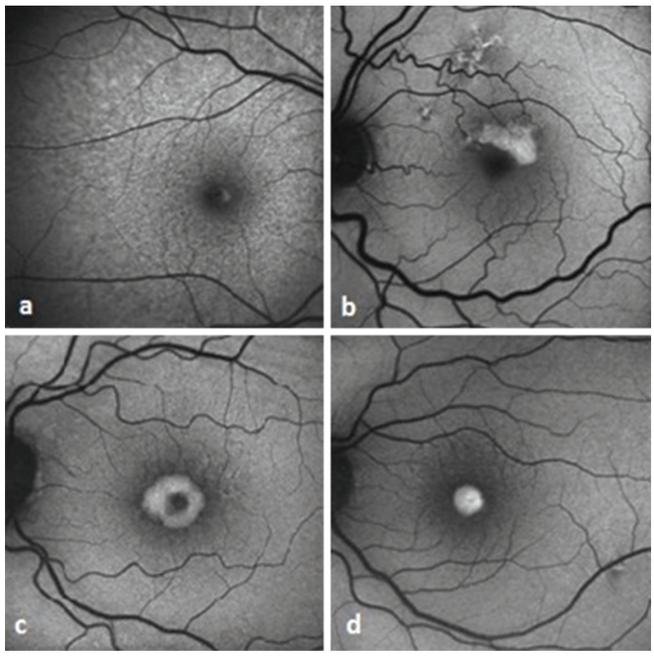

Figure 3a-d: *FAF patterns of vitelliform stage. a) focal pattern b) patchy pattern c) ring-like pattern d) round-shape pattern.*

In our study the mean BCVA at initial and last visit were similar. There was no correlation between the disease stage and BCVA substantially due to the small number of cases.

In AOFVD, lipofuscin accumulation in RPE cells is the common pathogenetic pathway, excessive lipofuscin accumulation can compromise RPE cells and cause photoreceptor degeneration and dysfunction.[18] FAF is the main imaging technique that analyses lipofuscin accumulation. The relationship between FAF patterns and BCVA was evaluated in different studies.[11,12] Parodi et al. evaluated 29 eyes with AOFVD and defined the FAF patterns as normal, patchy and focal pattern.[11] Fifty nine% of the eyes had patchy pattern and they found that the BCVA of these eyes was worse than other patterns. Furino et al. also evaluated the FAF patterns in 18 eyes of AOFVD and defined patchy, ring-like, focal and linear patterns.[12] They could not find any correlation between the patterns and BCVA. In accordance with previous studies, we classified the patterns as patchy, focal, ring-like and round-shape at vitelliform stage and there was no correlation between BCVA and FAF patterns.

Optical coherence tomography provides optical cross sectional images of the retina and is useful to comment about tissue structures and anatomical features. Pierro et al. evaluated 72 eyes with AOFVD and for the first time they showed a well defined region of thickening in the reflective band representing the retinal pigment epithelium with the earliest generation of OCT.[19] IS/OS line integrity has been shown to have an important role in evaluating the retinal function. Several studies have demonstrated the relationship between the IS/OS abnormalities and BCVA in different retinal diseases such as age related macular degeneration, diabetic macular edema and retinal vein occlusion.[20-23] Since the vitelliform material is located between the IS/OS and the retinal pigment epithelium - choriocapillaris complex, IS/OS line integrity has an important role also in AOFVD.[24] Arnold et al. showed that the photoreceptors were traced towards the centre of the lesion and they became progressively abnormal with fall out of nuclei.[25] Also they showed the distorted photoreceptor outer segments and stunted inner segments in the retina around the lesions, the prominent feature was focal loss of photoreceptor nuclei with loss of inner and outer segments overlying the lesion. Querques et al. showed the location of lesion, tissue structures and anatomical features with high-resolution spectral domain OCT in 46 eyes.[13] They found that the eyes with IS/OS disruption had decreased BCVA. In this study we showed that there is a statistically significant negative correlation between the IS/OS disruption and BCVA. Also in accordance with previous study reported by Furino et al, we showed statistically significant negative correlation between maximal deposit thickness and BCVA.[12] As the deposit thickness rises, the connection between IS/OS and RPE-choriocapillaris complex deteriorates and this may be the cause of decreased BCVA (Figure 4).

In conclusion, AOFVD is the most important disorder that must be considered in the differential diagnosis of age related macular degeneration. FAF imaging is useful for confirming the exact diagnosis of AOFVD and different patterns of vitelliform material can be demonstrated. The OCT findings rather than FAF features of the lesions may be predictive for determining the visual acuity in patients with AOFVD.

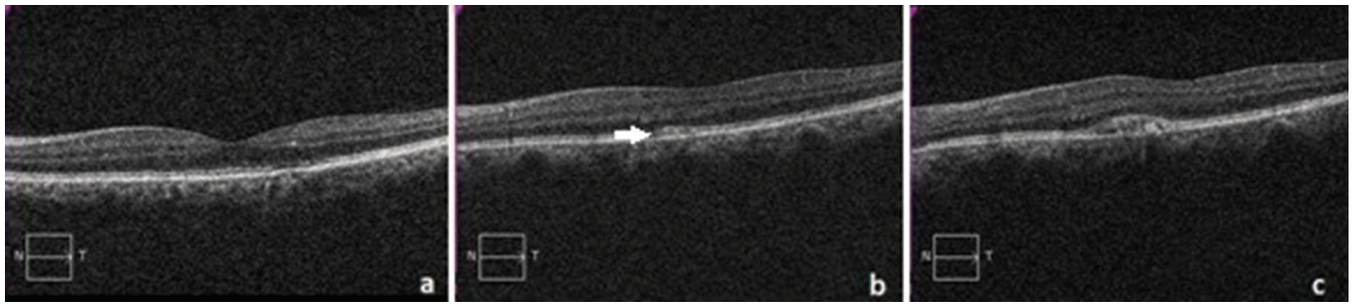

Figure 4: *OCT images of a 65 year-old woman with AOFVD. a) There was no vitelliform material at the initial visit b) Vitelliform material accumulation at 12 months follow-up (arrow) c) Increasing in the thickness of vitelliform material at 23 months follow-up.*

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