Evaluation of Macular Optical Coherence Tomography in Patients with Retinitis Pigmentosa

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ABSTRACT

Purpose: To evaluate the frequency of macular optical coherence tomography findings in patients with retinitis pigmentosa in Turkish community.

Methods: In this case series study, the medical records of the adult retinitis pigmentosa cases those are followed in a tertiary referral center in Ankara, were retrospectively investigated. Demographic data and clinical findings were obtained from the medical records. Macula optical coherence tomography images recorded in the system were examined in detail for vitreomacular interface diseases, intraretinal hyper-reflective spots, foveal atrophy, and intraretinal cyst findings.

Results: The study included 145 eyes of 77 retinitis pigmentosa cases. The mean age of the subjects was 37.42 ± 15.3 years (18 – 65). 44 (57%) of the cases were male and 33 (43%) of the cases were female. The mean best corrected visual acuity was 0.51 ± 0.27 logMAR (0.00 – 1.50). The most common macula optical coherence tomography finding was vitreomacular interface disorders in 72 eyes (49.7%) (bilaterality rate 35.8%). Other common macula optical coherence tomography findings were intraretinal hyper-reflective spots in 69 eyes (47.6%) (bilaterality rate 85.9%), foveal atrophy in 66 eyes (45.5%) (bilaterality rate 65.6%), and intraretinal cyst in 45 eyes (31.0%) (bilaterality rate 27.5%), respectively.

Conclusion: A wide range of macular optical coherence tomography findings can be occurred in patients with retinitis pigmentosa that is a progressive degenerative disease. While the most common finding in retinitis pigmentosa cases in Turkish community is vitreoretinal interface diseases, the finding has the highest bilaterality rate is intraretinal hyper-reflective spots.

Keywords: Foveal atrophy, Hyper-reflective spots, Optical coherence tomography, Retinitis pigmentosa, Vitreoretinal interface.

INTRODUCTION

Retinitis pigmentosa (RP) is defined as an inherited disease characterized by progressive loss of photoreceptors.[1] In the disease in which rod, cone and retinal pigment epithelium are affected as a result of several mutation, the first histopathological finding is shortened outer segments of photoreceptor.[2] In RP, major symptoms are impaired night vision, progressive narrowing of visual field and reduced visual acuity. The classical clinical triad include pigmentary degeneration of mid-peripheral bone spicule, arteriolar narrowing and hyalinization and waxy pallor at optic disc.[1, 2]

Optical coherence tomography (OCT) can provide qualitative and quantitative data about retina and optic nerve, identifying pathologies in these tissues. By widespread use of OCT in ophthalmology practice, findings related to several retinal disorder can be elucidated more clearly while it has been observed that some disorders have effects beyond already known. OCT scans provide important data regarding comorbid pathologies, follow-up and prognosis in RP.[3]

RP is associated with varying patterns of genetic inheritance and shows clinical presentation varying in different populations. In Turkey, there is limited number of studies investigating OCT findings seen in RP cases. In a study, the relationship between central macular thickness and visual acuity was investigated.[4] In another study with larger sample size, diversity and frequency of macular OCT findings in RP cases by retrospective review of

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patients with RP who were followed in a tertiary center at Ankara province. When compared to previous studies, it was aimed to contribute national literature by more detailed and systematic investigation of OCT findings in our study.

MATERIAL AND METHOD

In this retrospective case series, we reviewed medical records of RP cases followed at Retina Unit of Ankara Ulucanlar Eye Training and Research Hospital, University of Health Sciences between January, 2016 and January, 2020. We included patients with classical clinical triad of classical RP who had complete medical records and no eye disorder (glaucoma, uveitis, neuro-ophthalmological disease etc.) other than mild-to-moderate cataract and < 3 diopter (D) spherical equivalent eye disorder. The patients with systemic diseases (such as sickle cell anemia, diabetes mellitus etc.) that may have potential to influence on retina, those with history of ocular trauma or surgery other than cataract surgery (vitrectomy, filtering surgery etc.), those on chronic medication (anti-tuberculosis agents, anti-malarial agents etc.) and history of alcohol or substance abuse were excluded. The study was conducted in accordance to tenets of Helsinki Declaration.

In all cases, data regarding demographic and clinical characteristics were extracted from medical records. By screening digitalized spectral domain (SD)-OCT (Spectralis Hiedelberg, Germany; 40.000 scans/second; mean Q value: 30.8±5.4 [21-40]), vitreomacular interface disorders, intraretinal hyper-reflective dots, foveal atrophy and intraretinal cyst findings were evaluated qualitatively. Vitreomacular interface disorders were identified using 2013 The International Vitreomacular Traction Study Group guideline and classified regarding presence of vitreomacular adhesion, vitreomacular traction, epiretinal membrane, full-thickness macular hole, lamellar hole and pseudo-hole.[6] Intraretinal hyper-reflective dots were classified as diffuse or local according to presence and localization of findings and inner or outer retinal layer localization of local findings were identified. Foveal atrophy was classified as diffuse or local damage according to retinal layer(s) involved and only irregularity of outer retinal layer was defined as localized and involved retinal layer was identified. Diffuse damage was defined as involvement of more than one outer retinal layer or inner retinal layers. Intraretinal cysts were classified into two major categories: cystoid macular edema and cystoid degeneration. OCT findings were assessed by independent clinicians and findings achieving consensus by at least clinician were included to statistical analyses.

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 20.0. Presence or absence of each finding was input into software and their incidence was evaluated using frequency analysis. Bilaterality rate of OCT findings was assessed in cases in which both eyes were included to the study.

FINDINGS

In this study, 145 eyes of 77 patients with RP fulfilling inclusion criteria were analyzed. Although RP was bilateral in all cases, one eye was included to the analysis due to media opacity or previous non-cataract surgery not allowing sufficient OCT assessment in 9 patients. Of the patients 44 (57.1%) were men while 33 (42.9%) women. Mean age was 37.42±15.3 years (18-65 years) in the study population whereas 41.09±16.7 years (18-65 years) in male patients and 33.18±14.1 years (18-65 years) in female patients.

Mean manifest refraction spherical equivalent was -2.19±1.3 D (-3 to 3) while best-corrected visual acuity was 0.51 ± 0.27 logMAR (0.00–1.50). Mean intraocular pressure was 16.56 ± 4.3 mmHg (8–21). Of eyes included, 101 (69.7%) were phakic while 44 (30.3%) were pseudophakic. There was somewhat cataract in 61 eyes (60.4% of phakic eyes) while lens was transparent in 40 eyes (39.6%).

In patients with RP, the most common OCT finding was vitreomacular interface disorders seen in 72 eyes (49.7%) with bilaterality rate of 35.8%. The most common vitreomacular interface disorder was epiretinal membrane seen in 37 eyes (25.5%) (Figure 1); followed by full-thickness macular hole in 11 eyes (14.4%), vitreomacular adhesion in 10 eyes (13.8%) and vitreomacular traction in 6 eyes (4.1%).

The second most common OCT finding was intraretinal hyper-reflective dots (Figure 2) seen in 69 eyes (47.6%) with bilaterality rate of 85.9%. In 40 eyes (27.6%), intraretinal hyper-reflective dots were seen in both inner and outer retinal layers while they were seen only in inner retinal layers in 17 eyes (11.7%) and only in outer retinal layers in 12 eyes (8.3%).

The third most common OCT finding was foveal atrophy (Figure 3) seen in 66 eyes (45.5%) with bilaterality rate of 65.6%. Foveal atrophy was localized to one of outer retinal layers in 46 eyes (31.7%) while it involved more than one outer retinal layers or inner retinal layers in 20 eyes (13.8%). In eyes with localized foveal atrophy, photoreceptor outer segment-retinal pigment epithelium complex was most common involved retinal layer with 11 eyes (7.6%); followed by outer nuclear layer with 10 eyes (6.9%) and ellipsoid zone with 9 eyes (6.2%).

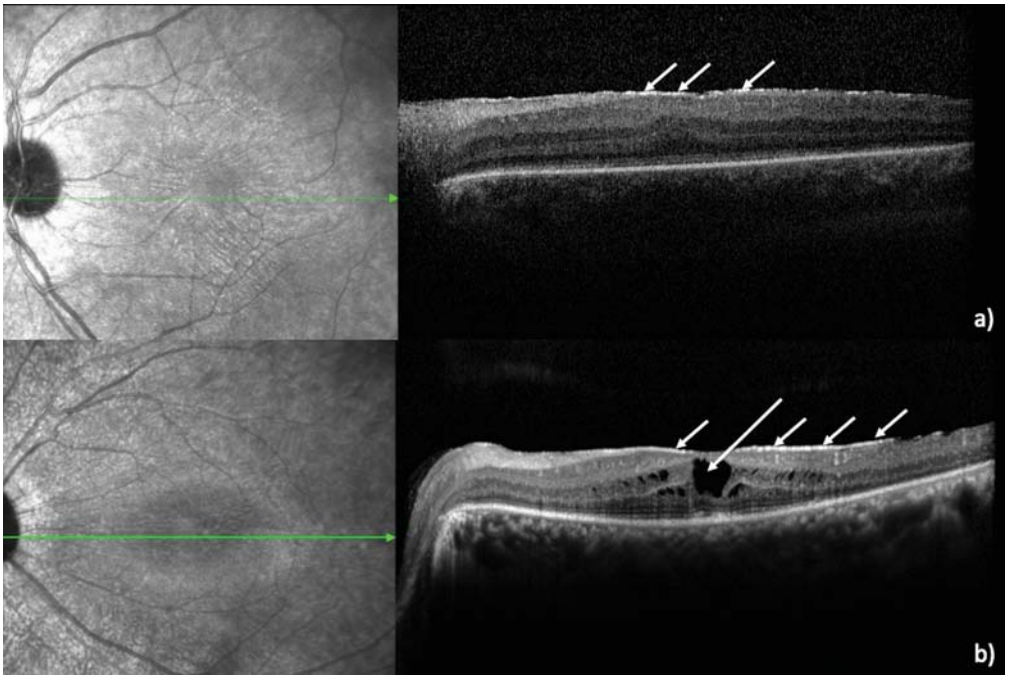

Figure 1: *Vitreomacular interface disorder; a) macular wrinkling is seen on red-free image at left while short arrows indicate hyper-reflective epiretinal membrane at right; b) macular wrinkling is seen on red-free image at left while short arrows indicate hyper-reflective epiretinal membrane and long arrow indicates epiretinal membrane-related intraretinal cyst at right.*

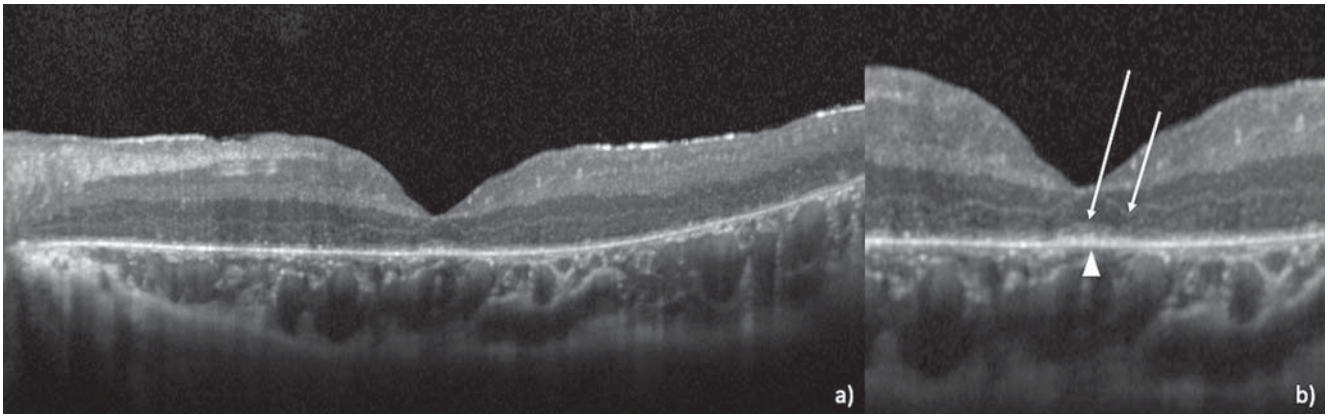

Figure 2: *Intraretinal hyper-reflective dots; a) horizontal section passing through central fovea; b) in magnified image involving central fovea, short arrows indicate hyper-reflective dots at inner retinal layer while long arrows indicate hyper-reflective dots at outer retinal layer.*

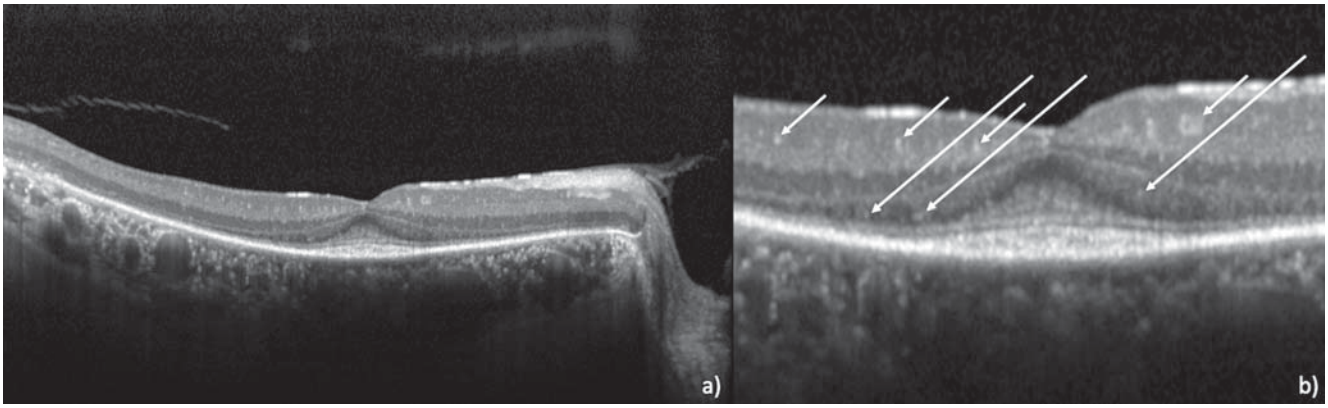

Figure 3: *Foveal atrophy; a) horizontal section passing through central fovea; b) in magnified image involving central fovea, short arrows indicate outer plexiform layer while long arrow indicate irregular outer limiting membrane and arrow head indicates irregular ellipsoid zone and photoreceptor-retinal pigment epithelium complex.*

Intraretinal cyst was detected as OCT finding in 45 eyes (31%) with bilaterality rate of 27.5%. In detailed analysis, it was found that there was cystoid macular edema (Figure 4) in 24 eyes (16.5%) and cystoid degeneration in 21 eyes (14.5%). Table 1 presents a summary of common OCT findings in patients with RP.

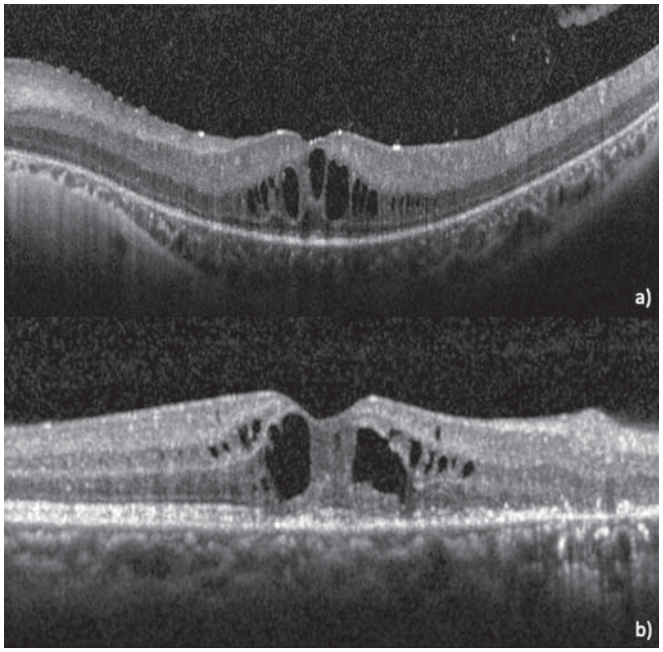

Figure 4: *Intraretinal cyst; a) cystoid macular edema; b) cystoid degeneration formation where cyst are fused to form a larger cavitation.*

DISCUSSION

In the literature, there is a tendency to present vitreoretinal interface disorders mainly epiretinal membrane or macular hole, as distinct findings. Liew et al. reported epiretinal membrane rate as 22.8%.[7] In a RP series from Italy, epiretinal membrane rate was found as 16%.[8] In a similar study, Triolo et al. reported frequencies of macular hole and identifiable epiretinal membrane as 4.5% and 27.3%, respectively. Authors reported that some vitreomacular interface disorders that could not be defined as epiretinal membrane precisely were present in 94.3% of cases. In last two decades where OCT has been introduced, major advances have been noted in imaging vitreomacular interface and definition of vitreomacular interface-related diseases. In 2013, The International Vitreomacular Traction Study Group revised definition of vitreomacular interface disorders based on novel OCT findings.[6] Unlike previous studies, in our study reviewed macular OCT findings in patients with RP using The International Vitreomacular Traction Study Group guideline, most common OCT finding was found to be vitreoretinal interface disorders seen in 49.7% of cases. In our study, three most common vitreoretinal interface disorders were reported as epiretinal membrane, full-thickness macular hole and vitreomacular adhesion. In a study from Turkey, Oner et al. reported that most common vitreomacular interface disorders were epiretinal membrane and macular hole in agreement

Table 1. *Frequency of macular optical coherence tomography findings in cases with retinitis pigmentosa.*

Findings	n (%)	Bilaterality (%)	Detailed analysis	n (%)
Vitreomacular interface	72 (49.7)	35.8	Epiretinal membrane	37 (25.5)
			Other vitreomacular interface disorders	35 (24.1)
			• Vitreomacular adhesion	10 (6.9)
			• Vitreomacular traction	6 (4.1)
			• Full-thickenss macular hole	11 (7.6)
			• Lamellar hole	3 (2.1)
			• Pseudo-hole	5 (3.5)
Intraretinal hyper-reflective dots	69 (47.6)	85.9	Diffuse	40 (27.6)
			Local	29 (20)
			• Inner retinal layers	17 (11.7)
			• Outer retinal layers	12 (8.3)
Foveal atrophy	66 (45.5)	65.6	Diffuse damage	20 (13.8)
			Local damage	46 (31.7)
			• Outer plexiform layer	8 (5.5)
			• Outer nuclear layer	10 (6.9)
			• Outer limiting membranee	8 (5.5)
			• Ellipsoidal zone	9 (6.2)
			• PR outer segment-RPE complex	11 (7.6)
Intraretinal cyst	45 (31.0)	27.5	Cystoid macular edema	24 (16.6)
			Cystoid degeneration	21 (14.5)

PR: Photoreceptor. **RPE:** Retinal pigment epithelium

with our study.[4] Given these results, the finding that most common OCT finding was vitreoretinal interface disorders with reported rates was in agreement with literature.

Although there is no consensus regarding etiopathogenesis of intraretinal hyper-reflective dots that can be detected by OCT, two hypotheses have been proposed. In the first hypothesis, it is proposed that hyper-reflective dots are lipoproteins that are precursor of exudates and leaked out of vessels.[10] The most frequent occurrence of the hyper-reflective dots in diabetic retinopathy and retinal vein occlusion supports this hypothesis.[11] However, in a study by Turgut et al., it was reported that hyper-reflective dots were also seen in series excluding diabetic retinopathy and retinal vein occlusion which are frequently associated with exudate.[12] In the second hypothesis, it is proposed that hyper-reflective dots are activated microglia, supported by presence of hyper-reflective dots in patients without retinopathy.[13] Nagasaka et al. reported intraretinal reflective dots in 42.9% of RP cases in relation with inflammation and photoreceptor degeneration.[14] In our study, hyper-reflective dots were seen in 47.6% of cases and it was found that intraretinal hyper-reflective dots were concurrently present in both inner and outer retinal layers. However, hyper-reflective dots were identified as macular OCT finding with highest bilaterality rate; to best of our knowledge, similar finding hasn't been reported so far.

It is known that thinning of photoreceptor outer segment is followed by outer nuclear layer thinning in RP.[2] Unlike thinning in outer retinal layers, thickness of inner retinal layer is preserved until terminal stages of disease.[15] However, there are publications indicating that thinning in outer retinal layers occurs at intermediate-advanced stages of disease.[16] In our study on adult RP patients, foveal atrophy at any stage was detected in 45.5% of patients which is higher than 24.4% reported by Vingolo et al..[17] In our study, relatively higher rate may be due to methodological differences as well as the fact that our hospital is a reference center where advanced cases are referred. Another issue related to foveal atrophy is the criteria and assessment method to identify foveal atrophy on OCT; thus, a methodological difference is normal between two studies using qualitative analysis. In a detailed analysis of retinal layers, Parodi et al. reported intact outer limiting membrane rate as 52% and ellipsoid zone rate as 43%, which indicates there is a somewhat foveal damage or atrophy in cases excluded in reported rates. In our study, it was seen that there was localized involvement in majority of eyes and that most commonly involved layer was photoreceptor outer segment-retinal pigment epithelium, followed by outer nuclear layer and ellipsoid zone. However, when compared to overall findings, it was found that diffuse damage involving more than one retinal layer was more common than overall single layer involvement.

Cystoid macular edema is one of the common complications in RP, which can result in loss of vision. In RP, reasons for macular edema development haven't been fully elucidated. Thus, several agents acting on different pathways are used in the treatment of RP-related macular edema. In the literature, macular edema frequency has been reported as 10-50% in RP cases.[19] In our study, rate of RP-related intraretinal cyst was found as 31% as cystoid macular edema being more common than cystoid degeneration. In addition, bilaterality rate for intraretinal cyst was found to be lower than those reported for intraretinal hyper-reflective dots, foveal atrophy and vitreoretinal interface disorders.

In this study, major limitation is retrospective design. The inclusion of patients with a wide spectrum of age and lack of classification as early or terminal RP allow more detailed analysis of different findings. In addition, the relationship of OCT findings with age and visual acuity is beyond scope of our study.

CONCLUSION

In conclusion, RP is a progressive disorder in which several macular OCT findings can be observed. Our study with larger sample size is important as it reflects Turkish population. In our community, the most common OCT findings were vitreomacular interface disorders, intraretinal hyper-reflective dots and foveal atrophy in adult RP patients. However, hyper-reflective dots were macular OCT finding with highest bilaterality rate.

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