

Optical Coherence Tomography Study of Typical and Atypical Cases of Retinitis Pigmentosa

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Abstract: Purpose: To use optical coherence tomography (OCT) to characterize the intra-retinal changes associated with typical and atypical cases of retinitis pigmentosa. **Design:** Observational case series. **Settings:** Research Institute of ophthalmology Cairo- Egypt. **Methods:** 24 eyes of 16 patients complaining of night vision and diagnosed as RP by fundus, field of vision, FFA, and electrophysiological examinations. Their retinæ were imaged by OCT using Humphrey2000 OCT system (Humphrey Co., SanLenardo,California). The following parameters were assessed; Retinal & nerve fiber layer (NFL) thickness.-Retinal pigment epithelium layer (RPEL) especially subfoveal area. -Presence of maculopathy (atrophic, cystoid, cellophane).Optic disc changes. **Results:** 16 cases, 24 eyes, 10 males, 6 females. Mean age 24, 5 y (range 10-38'). BCVA was 3/60-, 6/36. Fundus photography of 10 eyes of 5 patients had typical appearance of RP with gliotic waxy pallor of the optic nerve head, attenuation of the retinal arterioles, exaggerated choroidal pattern and mid peripheral bone specules. FFA showed delayed filling of the vessels, RPE transmission defect extending to the retinal mid-periphery, areas of blocked fluorescence corresponding to the bone specules in the mid periphery. OCT findings included: Retinal thickness was reduced in cases with typical as well as atypical fundus presentation. The macula showed total macular volume reduction, decrease central foveal thickness (ranging from 87 to 150 microns) with enlargement of central foveal depression. Cases which had cystoid macular edema (CMO) had increase thickness One Case which had epiretinal membrane showed increase retinal thickness above average normal in the central quadrant, while the inner and outer retinal quadrant showed decrease thickness. There was no correlation between RPEL thickness and either degree of retinal pigmentation seen in fundus photos or the change in NFL thickness. RPE under the fovea was not affected in all typical cases. Findings in atypical cases: Eight eyes of 5 patients had cystoid macular edema. Three of these patients had bilateral CME which was evident as intra-retinal cystic spaces with pooling of the dye in FA. OCT disclosed increased retinal thickness, with areas of low intra-retinal reflectivity prevailing in the outer retinal layers, and loss of foveal depression. One case with 2 eyes had mottled fundus appearance with absence of bone specules (RP simplex). OCT showed generalized reduction of the retinal thickness, generalized RPE atrophy with partial sparing of subfoveal RPE. Another atypical case of retinitis pigmentosa albescence showed white dots scattered thought the mid periphery of the fundus. OCT showed thinning of the RPE within the macular area with enlarged central foveal depression and generalized reduction in foveal thickness. The sister of a typical RP case presented with a bilateral fundus picture of Bull's eye maculopathy with waxy pallor of the optic disc. OCT showed total macular volume reduction, with marked decrease in NFL thickness and generalized RPE atrophy. **Conclusion:** OCT characterized the intra-retinal morphological changes in typical as well as atypical cases of RP.

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1. Introduction

Retinitis pigmentosa (RP) is a term used for a group of disorders that are characterized by inherited, progressive dysfunction, cell loss, and eventual atrophy of retinal tissue. RP is a slowly progressive disease, and typically affects the rods before the cones. Initial involvement of photoreceptors leads to subsequent damage to the inner retinal cells. Eventually there is widespread atrophy of several if not most layers of the retina. (1, 2) RP can be an isolated finding, or it can be associated with other systemic conditions. Several

genes have been found to be associated with RP, and it can be inherited as X-linked, autosomal dominant, or autosomal recessive condition. Cases with no inheritance pattern are known as RP simplex.(3) Diagnosis of RP is usually based on characteristic findings which typically include young adulthood onset of nyctalopia and peripheral vision loss, RPE disruption in the form of atrophy and "bone specules", disc pallor, retinal vessel attenuation, and characteristic electro retinogram (ERG) appearance showing diffuse photoreceptor disease. Scotopic b-wave reduction by about 50%, early cone system

affection with decrease amplitude of 30 Hz flicker ERG & delayed implicit time (1-3). RP can predispose patients to cystoid macular edema (CME), epiretinal membranes (ERM), posterior sub-capsular cataract, and syneresis of the anterior vitreous. Associated findings include; disc drusen, open angle glaucoma, keratoconus & myopia. Atypical forms include retinitis punctata albescence, sectorial & pericentric with exudative vasculopathy. (1-4)

Optical coherence tomography (OCT) is a non invasive imaging technique that uses low coherence interferometer to form cross-sectional images of the retina with axial resolution of 10 micrometers (μm) and lateral resolution of 20 (μm). With high-resolution cross-sectional images of retinal structure, measurement of retinal thickness and reproducibility on sequential examinations, OCT provide clinically relevant, quantitative information regarding the retina and adjacent structures (5)

Applicable to a broad range of retinal diseases OCT (Stratus OCT Model 3000, Carl Zeiss Meditec, Inc., Dublin, California) is increasingly utilized in the initial assessment and follow up examination of retinitis pigmentosa used in conjunction with comprehensive ophthalmic examination, photography and fluorescein angiography.(8,9)

The purpose of this study is to analyze the OCT findings in different cases of retinitis pigmentosa especially typical forms and those with uncommon associations.

2. Patients and Methods

Sixteen patients (7 males and 9 females) presented to the Research Institute of Ophthalmology, Cairo from the period of January 2006 to February 2007 were included in this study. They were complaining of night vision problems, and had characteristic retinal pigmentary changes, visual field and electroretinographic abnormalities suggestive of retinitis pigmentosa. A baseline best-corrected Snellen visual acuity was obtained for each patient and slit-lamp biomicroscopy was performed.

The pupils were dilated with one drop each of phenylephrine 2.5% and tropicamide 0.1% ophthalmic solutions. The magnitude of any lens opacity, if present, was recorded. A dilated fundus examination was performed. Fundus photography (FP) and fluorescein angiography (FA) were performed. Baseline OCT (Stratus 3.0, Humphrey Instruments, San Leandro, California, USA) was performed utilizing to 6-mm single scans at axis 30 degrees, 60 degrees, 90 degrees, 180 degrees, 300 degrees, and 330 degrees by means of an inner fixation target Or by manual localization of center of anatomical foveal in non fixing eye. For each eye

OCT examination included a minimum of six vertical or horizontal scans of 5 mm. As it was our goal to find retinal lesions, we performed up to 12 OCT scans when no lesions were observed after six scans. The OCT scans were positioned so that the cross sectional cut would go through the bony specules based on color fundus photography and fundus blocked fluorescence in the fluorescence angiogram. The following parameters were assessed;

- Retinal & nerve fiber layer (NFL) thickness.
- Retinal pigment epithelium layer (RPEL) especially subfoveal area.
- Presence of maculopathy (atrophic, cystoid, cellophane).

3. Results

This study included twenty four eyes of 16 patients. Mean age was 24.4 ranging from 10 to 38 years old. Their best corrected visual acuity ranged from 4/60 to 6/36. The data of the patients is represented in Table (1)

Analysis of fundus photography and fluorescein angiography

Fundus photography of 8 eyes of 4 patients had typical appearance of retinitis pigmentosa with gliotic waxy pallor of the optic nerve head, attenuation of the retinal arterioles, exaggerated choroidal pattern and mid peripheral bone specules. Fluorescein angiography showed delayed filling of the vessels, RPE transmission defect extending to the retinal mid-periphery, areas of blocked fluorescence corresponding to the bone specules in the mid periphery. (Fig. 1)

Analysis of OCT findings: (Table 2)

Retinal nerve fiber layer thickness:

Retinal thickness was reduced in central quadrant, inner and outer quadrant in cases with typical as well as atypical fundus presentation. The macula showed total macular volume reduction, decrease central foveal thickness (ranging from 87 to 150 microns) with enlargement of central foveal depression. (Fig.1a)

These changes (Retinal thickness reduction) were noticed mainly in cases with pronounced waxy yellow optic disc color, generalized attenuation of blood vessels, heavier pigmentation and more RPE atrophy.

Eight eyes of 5 patients had cystoid macular edema.(Fig.3) .Three of these patients had bilateral CME which was evident as intra-retinal cystic spaces with pooling of the dye in FA.

OCT images of these eyes showed generalized reduction of retinal thickness. There was also increase thickness in central, all inner quadrants and superior and inferior outer quadrant, with areas

of low intra-retinal reflectivity prevailing in the outer retinal layers, and loss of foveal depression. (Fig.3a)

One case which had epiretinal membrane (Fig.4) showed increase retinal thickness above average normal in the central quadrant, while the inner and outer retinal quadrants showed decrease thickness. (Fig.4a)

In another case, evidence of epiretinal membrane was detected with partial thickness macular hole. (Fig. 5 &5a).

OCT images in Retinal pigment epithelial (RPE) changes including subfoveal RPE:

There was no correlation between RPEL thickness and either degree of retinal pigmentation seen in fundus photos or the change in NFL thickness.

In cases where bone specules were found, there was intra-neural hyper-reflectivity with cone shadow effect due to pigment deposits. The majority of the pigment deposits were in mid retinal layer. In other cases, the deposits were in the outer layer and perivascular areas in the inner retinal layer. (Fig.6 &6a)

Mid peripheral generalized retinal pigment epithelial (RPE) atrophy was represented by hyper-reflectivity and backscattering.

RPE under the fovea was not affected in all typical cases.

Findings in atypical cases:

One eye had mottled fundus appearance with absence of bone specules; FIG.2 this patient was diagnosed as retinitis pigmentosa based on complaint of night blindness, visual field and electroretinographic abnormalities. FFA showed alteration between transmitted hyper fluorescence and blocked fluorescence and irregular FAZ.

OCT of this case showed generalized reduction of the retinal thickness, generalized RPE atrophy with partial sparing of subfoveal RPE. (Fig.2a)

Another atypical case of retinitis pigmentosa albescence showed white dots scattered through out the mid periphery of the fundus. FA showed mottled hyper fluorescence in the mid periphery, irregular enlarged FAZ.

OCT showed thinning of the RPE within the macular area with enlarged central foveal depression and generalized reduction in foveal thickness.

The sister of a typical case of retinitis pigmentosa presented with a bilateral fundus picture of Bull's eye maculopathy with waxy pallor of the optic disc. FA revealed annular RPE transmission defect encircling the macular area and extending to the fundus mid periphery. FIG.7. OCT showed total macular volume reduction, with marked decrease in NFL thickness and generalized RPE atrophy.

One case with high myopia (minus 10 diopters) showed macular hole which appeared as faint hyperfluorescent spot at the fovea showing window defect. OCT confirmed the presence, the stage and the measurement of the hole.

4. Discussion

Chauhan S et al 1999 found that invitro the mean thickness of the human inner OCT bands (131 micron) was 7.3 times that of RNFL. The inner aspect of the outer OCT band corresponds to the apical RPE, but the mean thickness of this band in human tissue(55 micron) was 2.6 times the thickness of RPE-Chorio-capillares complex, OCT measurement of total retinal thickness was accurate.(7)

In our study retinal thickness was reduced in central quadrant, inner and outer quadrant in cases with typical as well as atypical fundus presentation . The macula showed total macular volume reduction, decrease central foveal thickness (ranging from 87 to 150 microns) with enlargement of central foveal depression. These changes was noticed mainly in cases with pronounced waxy yellow optic disc color, generalized attenuation of blood vessels, Heavier pigmentation and more RPE atrophy

Sachiko et al 2000 studied 3 patients with retinitis pigmentosa (RP). OCT showed that retinal thickness was reduced in the retinal areas affected by RP (+/- 90 micron) & nearly normal in the unaffected macular area. Reflectivity was partially decreased in the affected retinal areas and pigment masses were hyper -reflective. Reflectivity of the macular area was nearly normal except when there is edema in the fovea it decreases. (8) KO TH. et al 2005,found that there is marked atrophy of photo receptor cells in the peripheral macular region, but other intraretinal layers appear normal except outer nuclear layer which becomes abnormally thin in the periphery of the macula. Progressive thinning of photo receptor inner segment & outer segment also occurs out side the foveal region. (9)

Sandberg MA et al 2005, studied 162 RP patients, the retinal thickness (mean +/- SD) was 170 +/- 3 micron at fixation. (6)

In our study, there was no correlation between RPEL thickness and either degree of retinal pigmentation seen in fundus photos or the change in NFL thickness. In cases where bone specules were found, there was intra-neural hyper-reflectivity with cone shadow effect due to pigment deposits .Mid peripheral generalized retinal pigment epithelial (RPE) atrophy was represented by hyper-reflectivity and backscattering. RPE under the fovea was not affected in all typical cases.

Chauhan S et al 1999, performed OCT scans of RP patients. They found that although inner& outer band could be identified, the inner band was less intense. Scans passing through bony specules hyperpigmentations had discrete regions of very high signal and deep to inner most border of inner band. (7).

In our study, one eye had mottled fundus appearance with absence of bone specules.

Another atypical case of retinitis pigmentosa (albescence) showed white dots scattered throughout the mid periphery of the fundus. FA showed mottled hyper fluorescence in the mid periphery, irregular enlarged FAZ. OCT showed thinning of the RPE within the macular area with enlarged central foveal depression and generalized reduction in foveal thickness. Qureques G. et al. 2006 analyzed 26 cases with flecked retinae with OCT. The aim was to determine the precise localization of these flecks within the retinal layers. Hyper- reflective deposits classified into two types were observed on Stratus OCT: type 1 lesions (94% of eyes) presented as dome-shaped deposits located in the inner part of the retinal pigment epithelium (RPE) layer and type 2 lesions (86% of eyes) presented as small linear deposits located at the level of the outer nuclear layer and clearly separated from the RPE layer. (10)

In our cases eight eyes of 5 patients had cystoid macular edema. Three of these patients had bilateral CME which was evident as intra-retinal cystic spaces (13) OCT findings in CME include increased retinal thickness in the macula with areas of low intra -retinal reflectivity. Cystoid spaces appear as small round hyper reflective lacunae with well defined boundaries. Outer retinal swelling appears as ill defined wide spread hypo-reflective area of thickening (14-16). Catier A. et al 2005 reported on OCT finding of the macular changes of 8 RP patients. Increased retinal thickness was 373 +/- 55 mic. Seven cases had external cystoid spaces, 5 cases had central foveal cystoid space and 1 case had outer retinal swelling. None had partial vitreous detachment. (11)

Sandberg MA et al 2005 found that 15 % of 191 RP patients included in their study had CME. Cysts ranged from small vacuoles 50 mic, in height at the level of INL to multiple vacuoles of more than 400 mic. in height that distorts the cysto-architecture. (6) In this study one case with RP & high myopia (minus 10 diopters) showed macular hole which appeared as faint hyperfluorescent spot at the fovea showing window defect. OCT confirmed the presence, the stage and the measurement of the macular hole. Adel M et al 2004 found 6 % of cases with macular hole in their OCT study of 100 cases of high myopia, but none was diagnosed as RP (17)

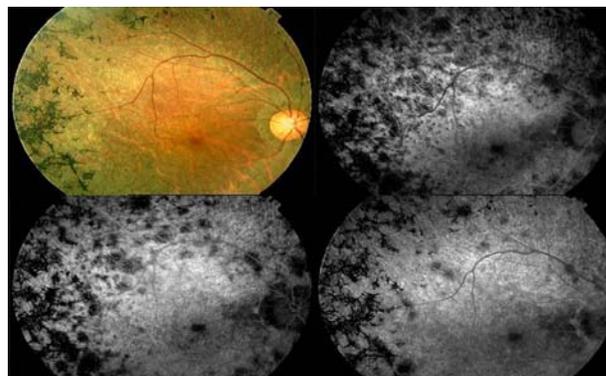


Fig. 1 Fundus colored photo and FFA of typical case of RP

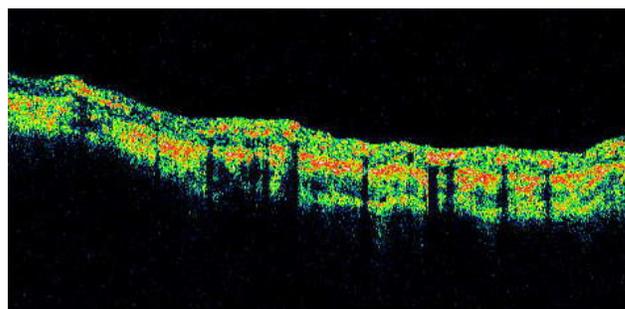


Fig.1a OCT photo of typical case of RP showing Hyper-reflective intra-retinal pigments deposited in mid retinal tissue with cone shadow effect and RPE atrophy

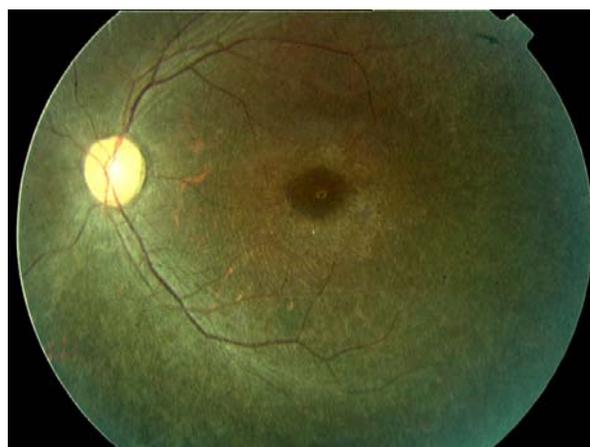


Fig.2 Generalized RPE atrophy

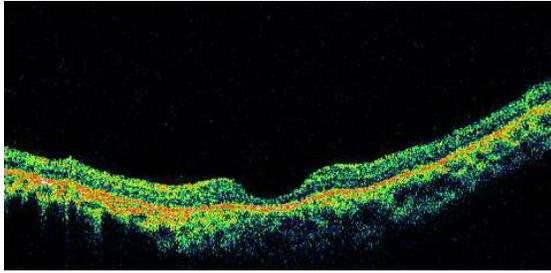


Fig.2a OCT photo of generalized RPE atrophy

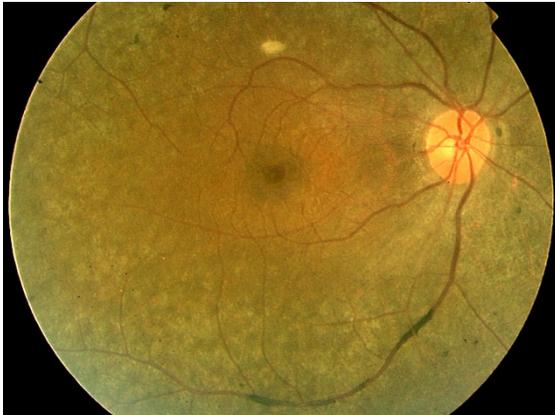


Fig.3 Fundus photo of atypical case with cystoid macular edema.

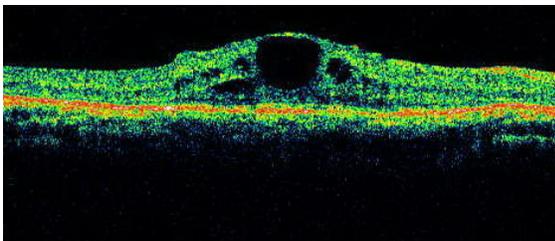


Fig.3a OCT photo of atypical case with Intra-retinal fluid accumulation in cystic spaces with large foveal cyst & intact subfoveal RPE

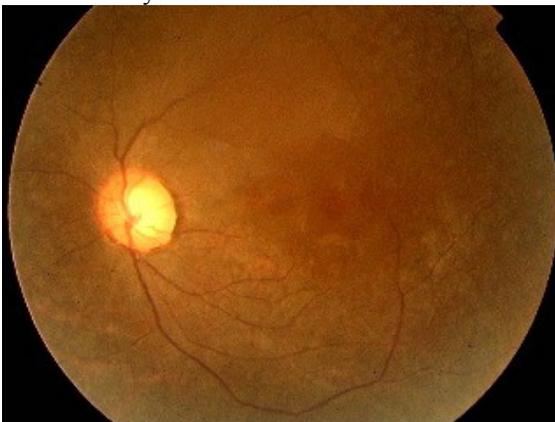


Fig.4 Fundus photo of atypical case with epiretinal membrane

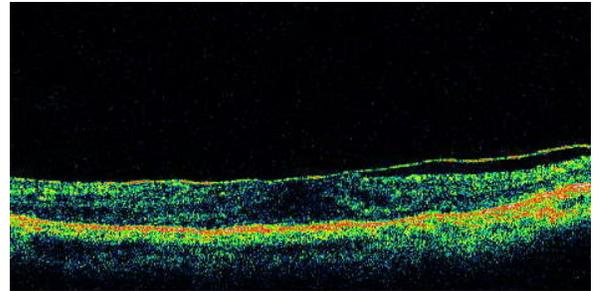


Fig.4a: OCT photo of atypical case with tightly adherent hyper-reflective epiretinal membrane, retinal edema and intact sub-foveal RPE.

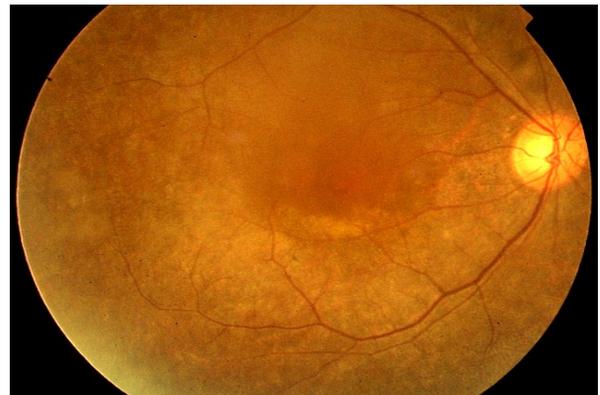


Fig. 5 Fundus photo of atypical case with lamellar macular hole

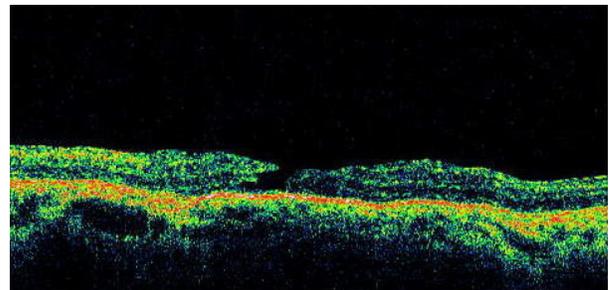


Fig.5a : OCT photo of atypical case with evidence of hyper-reflective tightly adherent RPE with lamellar macular hole.

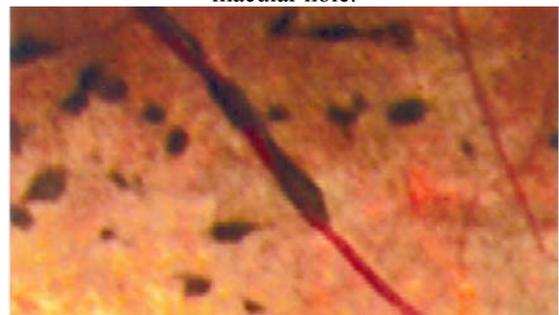


Fig. 6 Fundus picture of a typical case of RP with peri-vascular pigment deposits and bony speckles.

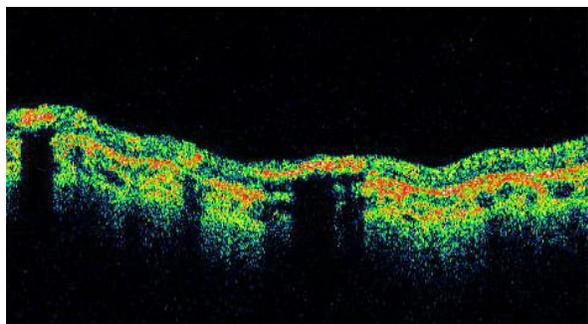


Fig.6a OCT photo of a typical case with hyper-reflective intra-retinal pigment deposited around the wall of retinal vessels in mid retinal tissue with cone shadow effect and RPE atrophy.

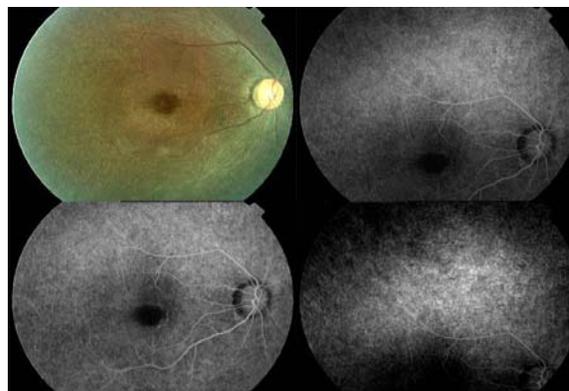


Fig.7 Fundus colored photo and FFA of atypical case of RP with Bull's eye like maculopathy

Table 1 Examples of data of patients included in the study

Name	Sex	DOB	Eye	Colored Fundus photo	FFA	Foveal thickness	Central macular thickness
M. Rabiea	♂	7/1/63	OU	Bone spec. retinal atrophy Bone spec. 4 Q periphery	Blocked F	133 + 3 142 + 9	184 188
Amal M.	♂	10/6/79	OU	Bull's eye macula	Hypofl. Surrounded by hyperfl		154 164
Mohamed Sayed	♀	20/7/86	OU	Bone spec. retinal atrophy	Enlarged FAZ retinal mottling	86 + 4 91 + 7	115 OD 110 OS
Nader S.	♀	14/2/79	OU	Peripheral bone specules attenuated vessels Left same less spec/macular old exudates	Block F by specules	102 + 5 87 + 2	130 129
Amal Ramadan	♂	29/4/96	OU	Bone specules	Retinal mottling window defect	100 _+3 102 _ +4	122 145
Esam Gomaa	♀	13/7/68	OU	Peripheral bone specules attenuated vessels	Retinal mottling window defect Cystoid	140 180	144 203

Table 2 OCT finding in Retinitis Pigmentosa

- Main finding in all cases was generalized reduction in retinal thickness in most macular quadrants compared to normative data for patient's age group.
- All cases with reduced retinal thickness showed generalized RPE atrophy, characterized by loss of the RPE hyper-reflective reflex with increased back scattering of hyper-reflective signal from the choroidal layer and sclera. This was true even in atypical cases in which no pigmented deposits was found (bony specules)

- In spite of the generalized RPE atrophy, the sub-foveal RPE was found to be intact in the majority of cases despite other macular pathology.
- In typical cases pigmented deposits were found (bony specules.) the deposits were found to be at different retinal layers .The majority were mid retinal hyper reflective deposits, in others, deposits were found to be on outer retinal layers and para-vascular area in inner layers (retinal nerve layer). Fig 6&6a.
- Macular pathology includes:
 - Cystoids edema with large intra foveal cyst.
 - Epiretinal membrane ERM with diffused macular edema
 - Lamellar or full thickness macular hole due to rupture cyst or ERM traction.
 - Bull's eye maculopathy

5. Conclusion:

OCT is very useful tool to define the pathological changes of cases of typical as well as atypical cases of retinitis pigmentosa. Not only that, but it can help prediction of the visual prognosis of these patients. Retinal thickness reduction was noticed mainly in cases with pronounced waxy yellow optic disc color, generalized attenuation of blood vessels, heavier pigmentation and more RPE atrophy There was no correlation between RPEL thickness and either degree of retinal pigmentation seen in fundus photos or the change in NFL thickness.

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