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VISUAL ACUITY LOSS IN RECESSIVE RETINITIS PIGMENTOSA AND ITS CORRELATION WITH MACULAR LESIONS

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Abstract

Purpose—To determine the visual acuity loss in patients with autosomal recessive retinitis pigmentosa and its relation to the presence of macular lesions.

Methods—A total of 145 patients were included in the visual acuity analysis, and 139 patients were included in the analysis of their macular status. Patients with a history of parental consanguinity or an affected sister and parents unaffected with retinitis pigmentosa were considered as having an autosomal recessive mode of inheritance.

Results—Regardless of age, 68 patients (47%) had visual acuity of 20/40 or better, 109 (75%) had better than 20/200 in at least 1 eye, and 36 (25%) had an acuity of 20/200 or worse in both eyes. An evaluation of the macular status demonstrated that 55 patients (39.6%) had no macular lesion and 77 (55.4%) had an atrophic lesion (either bull's-eye or geographic). Seventy-five percent of patients with no macular lesion had a visual acuity of 20/40 or better and 34 patients (44%) with an atrophic lesion had a visual acuity better than 20/70.

Conclusion—These data can be useful to counsel patients on the potential visual acuity impairment likely to be observed at different ages and identify the association of visual acuity loss with macular changes.

Keywords

autosomal recessive retinitis pigmentosa; visual acuity loss; macular lesions

Retinitis pigmentosa (RP) defines a group of inherited progressive retinal degenerations that are typically characterized by night blindness, progressive peripheral visual field loss, and eventually impairment of central vision generally later in life. Additionally, patients exhibit bone spicule-like pigment clumping and either reduced or nondetectable *a*-wave and *b*-wave amplitudes on electroretinogram testing. It has been estimated that the worldwide prevalence of RP is approximately 1 in 4000, with the autosomal recessive inheritance pattern accounting for approximately 50% to 60% of the cases, whereas 30% to 40% can be inherited as autosomal dominant and 5% to 15% as an X-linked recessive trait.¹

Previous authors^{2–4} have reported on visual loss in patients with RP. However, there have been a limited number of articles that define the functional loss in visual acuity and the macular lesions found in patients with autosomal recessive RP. The current study analyzes

the visual acuity in these patients within decades and defines the visual acuity loss in patients with or without a clinically observable macular lesion.

Patients and Methods

The medical records of all patients, who had previously been diagnosed with autosomal recessive RP seen by one of the authors (G.A.F.), were reviewed retrospectively by the authors to confirm the accuracy of the diagnosis and ocular findings. Patients were diagnosed based on either one or more of the following criteria: the presence of characteristic fundus changes, visual field loss, markedly reduced or nondetectable electroretinogram results, and a history of visual loss consistent with the disease. Criteria for recessive inheritance included either a positive history of parental consanguinity or an affected sister and parents unaffected by RP. One patient was included because a *CRB1* gene mutation had been isolated.

Two hundred and sixty-one patients were initially identified as possible study subjects. Those who did not meet the inclusion criteria as stated above, those with other ocular conditions, and/or those who had undergone intraocular surgery were excluded because of the potential impact on visual acuity. Patients with lens opacities, pseudophakia, and aphakia were included in the study. The final cohort consisted of 145 eyes of 145 patients (50 men and 95 women). The age range of the patients was 8 years to 86 years with a mean (SD) of 43 (± 18) years. The mean (SD) years of follow-up for the entire cohort was 8.5 (± 6) years, ranging from 1 year to 28 years with a mean (SD) of 3.5 (± 4) follow-up visits. Data from all 145 patients (145 eyes) were used in the analysis of visual acuity, whereas 139 patients (139 eyes) were included in the analysis of the macular status; data regarding the macular status were unavailable for 6 patients.

Patient records were initially reviewed by three of the authors (A.A., A.T., and M.G.) to document the following: patient demographics, best-corrected visual acuity, the total number of visits, duration of follow-up period (in years), the presence and extent of any ocular media opacification, and the appearance of the macula. The best-corrected visual acuity and macular findings were obtained from clinical notes made by one of the authors (G.A.F.) at the time of the initial and most recent clinical visits.

For a majority of the patients (139) in the study, the best-corrected monocular visual acuities were obtained using a Snellen projection chart, 3 of the patients with lens opacities were evaluated with a potential acuity meter (Marco Ophthalmic, Jacksonville, FL), and 6 of the patients had best-corrected monocular visual acuities measured with a Feinbloom low vision chart. As done in a previous study,⁴ the best-corrected acuity of the better eye at the most recent visit was used for the data analysis.

As in an earlier study,⁵ the macular status (of the better eye) was classified as having no lesion, a bull's-eye-appearing atrophic lesion, a geographic atrophic lesion, or a cystic lesion. Those with no clinically apparent macular lesion by funduscopy examination included patients who showed a blunted foveal reflex, an epiretinal macular membrane, or mild nonspecific macular pigment mottling. A bull's-eye lesion was defined as a red or reddish brown lesion in the fovea accompanied by surrounding retinal pigment epithelial hypopigmentation. A geographic atrophic lesion was described as a homogenous hypopigmented degenerative change in the macula that included the fovea. The definitions of a bull's-eye-appearing and geographic atrophic lesion were based on the clinical funduscopy observation. A cystic lesion was diagnosed on the clinical fundus examination and/or fluorescein angiography ($n = 3$), in addition to optical coherence tomography ($n = 4$)

when available. Figure 1 illustrates an example of a bull's-eye-appearing lesion and a geographic atrophic macular lesion.

This study was approved by the Institutional Review Board of the University of Illinois at Chicago. As per the Health Insurance Portability and Accountability Act regulations, all patients included in the study signed an informed consent form.

Results

An analysis of the data on the 145 patients showed that regardless of age, 68 patients (47%) had a visual acuity of 20/40 or better, 95 (66%) had a visual acuity of 20/70 or better, and 109 (75%) had a visual acuity better than 20/200 in at least 1 eye. The remaining 36 (25%) were classified as legally blind using the criteria of central visual acuity of 20/200 or worse in the better eye. Of these 36, 15 (10%) had a visual acuity of count fingers or worse. None of the patients in our cohort were found to have no light perception in both eyes (Tables 1 and 2; Figure 2). As mentioned previously, patients with lens opacities were included in the study, and their information was used in the visual analysis of their eye with better vision. Of the 145 patients in the cohort, 8 patients had either a moderate cataract ($n = 4$), defined as 3+ nuclear, or an extensive cataract ($n = 4$), defined as either a 4+ nuclear or 3+ posterior subcapsular opacification, as graded on a 1 to 4 basis qualitatively. Of these eight patients, three had their visual acuity tested by a potential acuity meter, and these results were used in their data analysis. Table 3 represents the visual acuities of these patients along with the macular status in the same eye. These data (Table 3) suggest that there was no consistent association between cataract severity and visual acuity.

An evaluation of the macular status at the most recent clinical visit in our cohort (145 patients, 139 eyes) demonstrated that 55 patients (39.6%) had no macular lesion, 26 (18.7%) had a bull's-eye-appearing atrophic lesion, 51 (36.7%) had a geographic atrophic lesion, and 7 (5%) had a cystic lesion at the most recent presentation. The age ranges for patients with no lesion was 8 years to 76 years (mean and median of 38 years), 12 years to 71 years for a bull's-eye lesion (mean of 43 years and median of 44 years), 17 years to 86 years in those with a geographic atrophic lesion (mean of 49 years and median of 45 years), and 27 years to 48 years with a cystic lesion (mean and median of 38 years).

We found that 41 of the 55 patients (75%) with no macular lesion had a visual acuity of 20/40 or better and all 55 had a visual acuity that was better than 20/200. All 7 of the patients with cystic macular lesions had a visual acuity of 20/40 or better, with 5 of the 7 having a better than 20/30 acuity. Of the 77 patients who had an atrophic macular lesion (either bull's-eye or geographic), 41 (53%) had a visual acuity better than 20/200, and 36 (47%) had a visual acuity 20/200 or worse. Of note, 18 (23%) of these 77 patients had a visual acuity of 20/40 or better. All 15 patients who had a visual acuity of counting fingers or worse had a geographic atrophic macular lesion (Table 4).

We assessed the status of macular lesions in patients who were followed for 5 years ($n = 45$, follow-up range of 5–28 years) to determine if there was a change in the presentation of the initial macular status throughout the follow-up period. We found that 26 patients (57%) of a total 45 who were followed for 5 years had no change in their macular status. Of the 21 patients who were not clinically observed to have a macular lesion at their initial visit, 15 (71%) did not develop a macular lesion within the follow-up period of 5 years to 26 years (mean of 10.3 years and a median of 8 years).

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Discussion

Previous literature has commented on visual acuity impairment in patients with RP²⁻⁴; however, limited publications have described the visual acuity loss in those patients with recessive RP. A previous study⁴ from our department reported that 39% of recessive RP (n = 117) patients exhibited a visual acuity of 20/40 or better in at least 1 eye. Similarly, Grover et al² reported that 42% of patients with recessive RP (n = 149) aged 45 years had a visual acuity of 20/40 or better in at least 1 eye and 20% had 20/200 or worse in both eyes. We found that 37% of our patients had a visual acuity of 20/30 or better, 47% with 20/40 or better, and 66% with 20/70 or better in at least 1 eye.

Although the legal blindness criterion includes central visual acuity and peripheral visual fields, our study analyzed legal blindness from a visual acuity standpoint alone. Legal blindness defined from visual acuity occurs when best-corrected visual acuity is no better than 20/200 in at least 1 eye. In our population of 145 patients, 36 (25%) were considered legally blind based on the visual acuity criterion, and 15 of these patients had hand motion, count fingers, or light perception vision. A further analysis demonstrated that 18 (50%) of the patients classified as legally blind were aged 51 years, and only 1 of these patients was under the age of 21. Regarding total blindness, we found no patients in our cohort who had no light perception in both eyes.

Our data showed that 70% of patients with an acuity of 20/40 or better were 50 years of age, whereas 43% of the patients aged >51 years had a visual acuity of 20/40 or better and 22% of this age group (51+) had a visual acuity of 20/200 or worse. Of interest, 56% of the patients under the age of 21 had a visual acuity of 20/40 or better, and only 1 patient in this age group had a visual acuity of 20/200 or worse. This finding in the <21 years age group was similar to the findings observed by Marmor³ who found that 60% (and up to 90%) of his patients under the age of 20 had a visual acuity of 20/40 or better. Similarly, Grover et al⁴ found that 55% of their patients in a similar age group had a visual acuity of 20/40 or better.

Our findings showed that 75% of the patients who had no macular lesion had a visual acuity of 20/40 or better, whereas none of these patients (in our population) demonstrated worse than 20/100 visual acuity. Of note, 71% of patients who did not show a macular lesion at the initial visit, when followed for a period of 5 years (n = 21), did not develop a macular lesion. Eighty-eight percent of the patients with a bull's-eye-appearing lesion had a visual acuity of 20/70 or better. Conversely, 35 of the 51 patients (68%) who exhibited a geographic atrophic lesion had a visual acuity of 20/200 or worse. Fifteen of these patients with a geographic atrophic lesion accounted for the 15 patients in our total cohort who had count fingers, hand motion, or light perception visual acuity.

Flynn et al⁵ showed that patients who had an atrophic macular lesion (either a bull's-eye-appearing or geographic lesion) at their initial visit were at greater odds of losing 3 or more lines of visual acuity than those with no macular lesion at their initial presentation.

Additionally, they reported that those patients presenting initially with no macular lesion had a predicted change in their visual acuity measurement of no more than 1 line over a 5-year follow-up period. In the current study, 41 (75%) of those patients who had no macular lesion had a visual acuity of 20/40 or better.

Although we only included a total of 7 patients (5%) classified with a cystic macular lesion in our cohort, we recognize that we likely underestimated the presence of macular edema in our group of patients because an optical coherence tomography was not obtained on every patient who was included in the study. Hajali and Fishman⁶ reported on 63 RP patients that even in the absence of cystic macular changes on fundus examination, 32% of the patients showed cystoid macular edema on optical coherence tomography testing in at least 1 eye and 18% in both eyes.

Although a retrospective study is limited by a lack of comprehensive standardizations of procedures and measurements, this cross-sectional study analyzed visual acuity impairment with and without the association of a clinically significant macular lesion in a large cohort of patients with recessive RP. The data reported in this study have relevant implications for the selection of patients in future treatment trials, where visual acuity may be used as an inclusion criterion. Perhaps even more significantly, these findings will be of value in counseling patients about the ranges of visual acuity impairment likely to be observed in different age groups.

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Fig. 1. Fundus photographs illustrating a bull's-eye-appearing lesion (**A**) and a geographic atrophic lesion (**B**) as seen in patients with RP.

Fig. 2.
Graph showing number of patients at various levels of visual acuity.

Table 1

Visual Acuity Distribution of the Study Population

Age (years)	20/15 to 20/40	20/50 to 20/70	20/80 to 20/100	20/200 to 20/400	10/140 to 3/200	CF/HM/LP	NLP
1-10	1	-	2	-	-	-	-
11-20	8	3	1	1	-	-	-
21-30	7	10	3	1	1	1	-
31-40	16	2	1	5	-	2	-
41-50	16	9	1	3	3	2	-
51-60	9	1	1	1	2	4	-
61-70	6	0	3	3	-	4	-
71-80	5	2	1	1	-	2	-
81+	-	-	-	1	-	-	-
n = 145 patients/145 eyes (%)	68 (47%)	27 (19%)	13 (9%)	16 (11%)	6 (4.1%)	15 (10.3%)	0 (0%)

CF, counting fingers; HM, hand motion; LP, light perception; NLP, no light perception.

Table 2

Visual Acuity Breakdown of the Patient Population

Visual Acuity	Number of Patients (n = 145) (%)	Age Range (years)	Median	Mean	SD
20/15	1 (0.70)	17	—	—	—
20/20	12 (8.30)	12–15	34.5	32.8	13.2
20/25	14 (9.70)	17–76	40.5	44.1	17.1
20/30	27 (18.60)	8–76	48	47.4	14.7
20/40	14 (9.70)	14–77	41	40.5	19.9
20/50	10 (6.90)	23–50	42.5	39.7	9.3
20/60	9 (6.20)	20–78	26	38.2	22.4
20/70	8 (5.50)	12–51	28.5	30.3	13.6
20/80	6 (4.10)	14–75	40.5	42.2	23
20/100	7 (4.80)	10–69	23	36.4	26.2
20/160	1 (0.70)	51	—	—	—
20/200	5 (3.40)	25–44	40	38.4	7.7
20/300	1 (0.70)	45	—	—	—
20/400	9 (6.20)	17–86	62	53.8	22.6
10/140 to 3/200	6 (4.10)	29–57	46.5	46	10
CF	1 (0.70)	44	—	—	—
HM	9 (6.20)	22–80	57	53	19.8
LP	5 (3.40)	51–70	63	60.6	7.9
NLP	0 (0.00)	—	—	—	—

CF, counting fingers; HM, hand motion; LP, light perception; NLP, no light perception.

Table 3

Visual Acuity and Macular Status in Those Patients with Significant Cataracts

Cataract Classification	Visual Acuity	Age (years)	Macular Status
Moderate [*]	LP	63	Geographic atrophy
Moderate	20/60	74	Geographic atrophy
Moderate	20/40	77	No lesion
Moderate	LP	70	Geographic atrophy
Severe [†]	HM	68	Geographic atrophy
Severe	LP	65	Geographic atrophy
Severe	20/50	45	Bull's-eye-appearing lesion
Severe	20/30	42	No lesion

^{*} Moderate cataract graded as a 3+ nuclear opacification.

[†] Severe cataract graded as 4+ nuclear and/or 3+ posterior subcapsular opacification.

LP, light perception; HM, hand motion.

Table 4

Visual Acuity Related to Macular Status

Macular Status	20/15 to 20/40	20/50 to 20/70	20/80 to 20/100	20/200 to 20/400	10/140 to 3/200	CF/HM/LP	NLP	n = 139 eyes (%)
No lesion	41	11	3	—	—	—	—	55 (39.6)
Bull's-eye-appearing atrophic lesion	15	8	2	1	—	—	—	26 (18.7)
Geographic atrophic lesion	3	8	5	15	5	15	—	51 (36.7)
Cystic lesion	7	—	—	—	—	—	—	7 (5)

CF, counting fingers; HM, hand motion; LP, light perception; NLP, no light perception.