A Korean Family with an Early-Onset Autosomal Dominant Macular Dystrophy Resembling North Carolina Macular Dystrophy

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***Purpose*:** To characterize and report the phenotype of a Korean family with an early-onset autosomal dominant macular dystrophy resembling North Carolina macular dystrophy (NCMD).
***Methods*:** Five members of a Korean family were examined clinically and underwent fundus photography, fluorescein angiography, indocyanine green angiography, optical coherence tomography, full field electroretinogram (ERG), multifocal ERG, electro-oculography (EOG), a color vision test, and a visual field test.
***Results*:** Visual acuity ranged from 20/200 to 20/20. Fundus findings demonstrated varying degrees of involvement ranging from drusen only to chorioretinal involvement. Central scotoma corresponded to retinal lesions in two patients. Full field ERG was normal but multifocal ERG showed decreased amplitude and delayed implicit time in the macular area. EOG was normal except in one patient. Color vision tests were also normal.
***Conclusions*:** The phenotype of this Korean family is consistent with NCMD. Linkage analysis is required to confirm the diagnosis. *Korean Journal of Ophthalmology 20(4):220-224, 2006*

Key Words: Autosomal dominant macular dystrophy, North Carolina macular dystrophy

Families with autosomal dominant macular dystrophy vary in age of onset, visual acuity, progression, prognosis, and electrophysiological test results. Although several different genes have been identified that cause macular dystrophy, they are not yet well understood.[1]

North Carolina macular dystrophy (NCMD), first reported in 1971 in North Carolina by Lefler et al., is an autosomal, dominantly inherited macular disorder with complete penetrance.[2] It is characterized by early-onset, a stable course, normal full-field electroretinogram (ERG) and electro-oculography (EOG), relatively normal color vision, and fundus findings.[2-5] The fundus findings have been divided into three stages: stage 1 - scattered drusen and pigment dispersion; stage 2 - confluent drusen with or without pigment clumping; and stage 3 - choroidal atrophy.[3] Affected families have also been found in Texas, central America, France, England, and Germany, but never in Asia.[6-10]

We describe five individuals of a Korean family whose phenotype is consistent with the diagnosis of NCMD.

Materials and Methods

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Five individuals (P1, P2, P6, P7, and P8 in Fig. 1) in two generations of a Korean family were assessed. Three additional patients (P3, P4, and P5) had a history of early deterioration of visual acuity but refused to be evaluated. The five consenting subjects gave their medical history and received a full ophthalmic examination. All five underwent fundus photography, fluorescein angiography (FA), indocyanine green angiography (ICGA), and optical coherence tomography (OCT; Carl Zeiss Meditec Inc., Dublin, CA, USA). Color vision tests were performed using Hardy-Rand-Rittler (HRR) plates (American Optical Company, New York, NY, USA). Electrophysiological studies included full field ERG, multifocal ERG and EOG. Multifocal ERGs were recorded using the RETIscan system (Roland consult, Brandenbrug, Germany). The stimulus was presented on a 20-inch CRT monitor with a 75-Hz frame rate and consisted of an array of 103 hexagonal elements across a field subtending about 30°. Signals were amplified (gain, 106), band-pass filtered (5-100 Hz), and recorded with a sampling interval of 0.83 msec (163 per video frame). All subjects also underwent visual field tests with a Goldman perimetry or Humphrey visual field analyzer (Humphrey-Zeiss Instruments, Dublin, CA). Full ophthalmic evaluations were repeated 6 months and 1 year after the initial examination.

Table 1. The clinical characteristics of 5 members of the Korean family resembling North Carolina macular dystrophy

	Age	Sex	Visual acuity		Fundus findings	Full-field ERG	EOG Arden ratio		Color vision*	Visual field	Other finding
			Right	Left			Right	Left			
P1	48	F	20/60	20/60	bilateral macular atrophy with subretinal fibrosis	N†	1.31	1.36	N	bilateral central scotoma	XT‡
P2	44	M	20/20	20/20	bilateral fine macular drusen-like deposits	N	1.8	1.7	N	N	
P6	18	F	20/100	20/200	loss of RPE with subretinal fibrosis	N	2.36	2.29	N	bilateral central scotoma	
P7	16	F	20/20	20/200	confluent drusen with subretinal fibrosis	N	2.12	1.8	N	N	XT
P8	12	M	20/30	20/25	loss of RPE with subretinal fibrosis	N	2.1	2.05	N	N	

*color vision test using Hardy-Rand-Rittler (HRR) plates, †N, normal, ‡XT, exotropia.

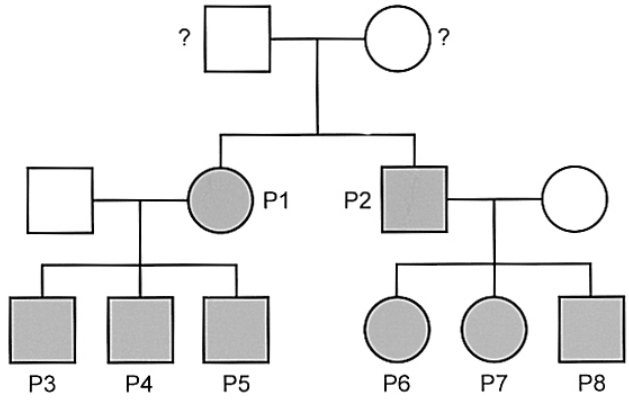

Fig. 1. The pedigree of a Korean family with macular dystrophy demonstrating the characteristics of an autosomal dominant inheritance trait.

Results

The pedigree demonstrates the characteristics of an autosomal dominant inheritance trait (Fig. 1). The clinical characteristics of the 5 members of the Korean family are shown in Table 1. Visual acuity in the five affected members ranged from 20/200 to 20/20. None of the subjects complained of progressive decrease in visual acuity and after 1 year of follow-up their visual acuity and fundus findings remained unchanged.

NCMD stage 1 - like macular changes were seen in one patient with normal visual acuity (P2) (Fig. 2). This patient had bilateral drusen in the macular area only. The right eye had confluent drusen. FA and ICGA revealed no suspicious choroidal neovascularization. OCT showed a minimally thickened retinal pigment epithelium (RPE) and choroid layer. In three patients (P6, P7, and P8), NCMD stage 2-like macular changes of varying degrees were found (Fig. 3),

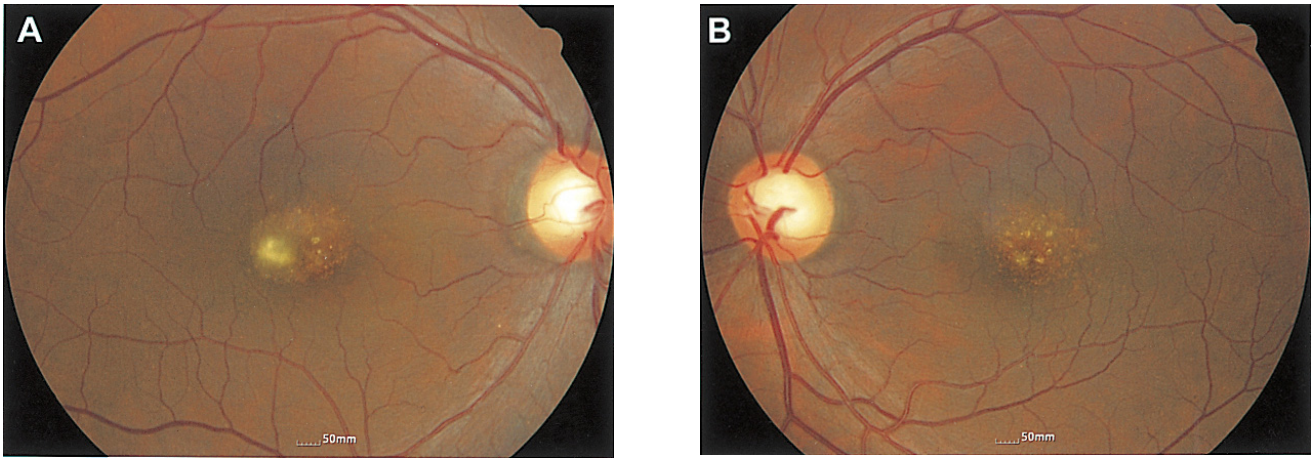

Fig. 2. Fundus photographs of patient 2. There are multiple fine drusen-like lesions in the macular area consistent with stage 1 North Carolina macular dystrophy.

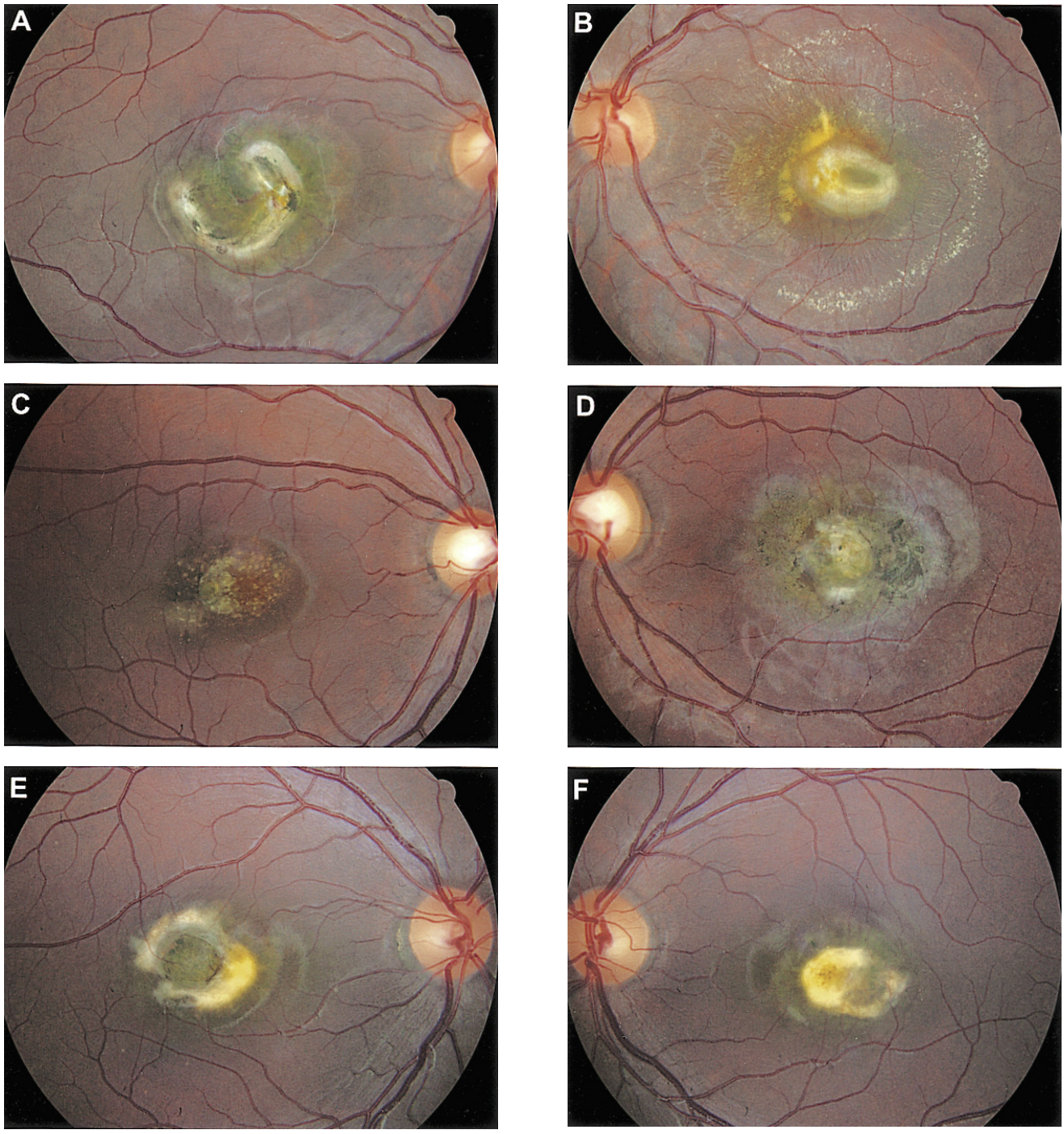

Fig. 3. Fundus photographs of patients 6 (A, B), 7 (C, D), and 8 (E, F). There are confluent drusen-like lesions, depigmented lesions, visible large choroidal vessels, and fibrotic lesions consistent with varying degree of stage 2 North Carolina macular dystrophy.

including confluent drusen, RPE atrophy, subretinal fibrosis, depigmentation, and pigment clumping. One patient (P1) had deep, bilateral, relatively large circumscribed excavated lesions (Fig. 4). FA and ICGA visualized choroidal vessels with loss of RPE. OCT revealed severe atrophy of the neurosensory retina and RPE (Fig. 4). Optic discs in all 5 patients showed no evidence of abnormality.

Visual field analysis showed bilateral central scotoma in 2 patients and the others were normal. Standard full-field ERG in all 5 subjects disclosed no abnormal findings. Multifocal ERG demonstrated decreased and delayed response of the central area in all patients except Patient 2 who had

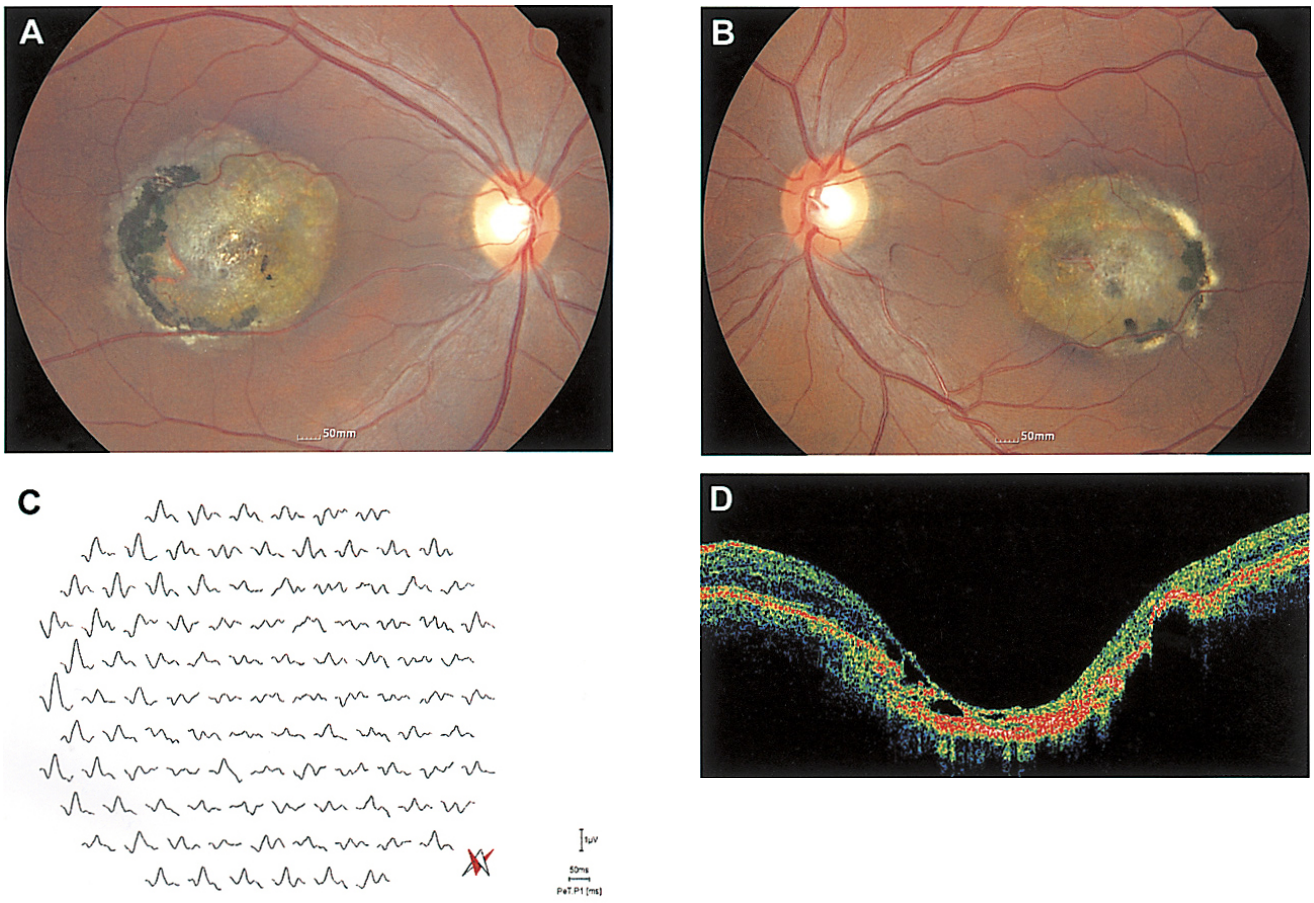

Fig. 4. Fundus photographs of patient 1 (A, B) showing large chorioretinal atrophic lesions with visible choroidal vessels. Multifocal ERG (C) shows abnormal responses in the macular area and normal responses outside the lesion. OCT (D) indicates extensive macular atrophy.

drusen only. Multifocal ERG responses of outside macular lesions were normal in both amplitude and implicit time. EOG results were mildly abnormal in only one affected patient (P1). Color vision assessment by HRR test was normal in all patients. None of the patients had nystagmus and 2 patients exhibited exotropia.

Discussion

The fundus appearances of affected subjects in this family were consistent with the diagnosis of NCMD. Fundus findings varied from drusen only to relatively large chorioretinal atrophy and could be divided into three stages as reported by Frank.[3] This diagnosis is further supported by the apparent autosomal dominant inheritance, normal full field ERG, normal to subnormal EOG, normal color vision, and stable course.

The normal full-field ERG implies that only the macular area is involved and peripheral retinal function is intact. This implication is further supported by multifocal ERG, which can evaluate local functional abnormalities. Multifocal ERG has detected macular dysfunction in some retinal dystrophy with normal full field ERG.[11,12] In this family, multifocal ERG detected macular dysfunction that corresponded to the fundus findings. There was a normal ERG response in retinal areas with drusen only (P2).

OCT revealed a thick subretinal highly reflective band in stage 2 and 3 patients and extensive retinal atrophy in stage 3 patients (Fig. 4). The nature of this thickened highly reflective band is uncertain, but subretinal fibrosis or accumulation of unknown material under the lost RPE layer are possibilities.

This Korean family shows clinical features very similar to NCMD, which has not yet been reported in Asia. Linkage analysis is essential to confirm the diagnosis of NCMD.

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