

Second eye of patients with unilateral neovascular age-related macular degeneration: Caucasians vs Chinese

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Abstract

Purpose To investigate the correlation between morphological features of choroidal neovascularisation (CNV) secondary to age-related macular degeneration (AMD) in the first eye and the severity of age-related maculopathy (ARM) in the fellow eyes in two racial groups: Caucasians and Chinese.

Participants A total of 135, fluorescein angiograms of patients with unilateral neovascular AMD and ARM in the fellow eyes were included in the study: 38 Caucasians from King's College Hospital, UK; 45 Caucasians from West Kent Eye Centre, UK; 52 Chinese from Hong Kong Eye Hospital, Hong Kong.

Main outcome measures CNV subtype in the affected eye and ARM severity in the second eyes.

Results Although the proportion of CNV subtypes in the three groups were similar, the Chinese cohort showed significantly less ARM severity compared to the Caucasian cohorts ($P < 0.05$).

Conclusion Although drusen and retinal pigmentary changes may be prognostic indicators of CNV, this study suggest that other factors contribute significantly to the pathogenesis of CNV in AMD.

Eye advance online publication, 26 August 2005; doi:10.1038/sj.eye.6702056

Keywords: Drusen; racial differences; macular degeneration

Introduction

Neovascular age-related macular degeneration (NVAMD) is the leading cause of severe visual

loss in patients above the age of 50 years in the Western world.^{1–3} A number of epidemiological studies in several races and ethnic groups suggest that NVAMD is no longer a threat only to the Western population, but is emerging as a global cause of blindness in the elderly.^{4–10}

Based on clinical observations, the epidemiological features and predisposing factors for the development of choroidal neovascularisation (CNV) have been found to vary in different racial groups.¹¹ Natural history studies on fellow eyes of patients with unilateral NVAMD have identified important determinants for the development of CNV.^{12–16} The characteristics of drusen are an important indicator of the type of neovascular lesion in Caucasians.¹⁷ Abugreen *et al*¹⁸ reported that the severity of age-related maculopathy (ARM) in the fellow eye correlates with the CNV subtype in the affected eye of patients with unilateral NVAMD. They observed that patients with occult or minimally classic CNV in the affected eye had more severe form of ARM in the fellow eye compared to the fellow eyes of predominantly classic CNV.

In this study, we examined the relation between the morphological features of CNV in the first eye with the severity of ARM in the fellow eyes in two racial groups: Caucasians and Chinese.

Patients and methods

Consecutive colour fundus photographs and fluorescein angiogram images were examined from the digital retinal photography databases from three centres: King's College Hospital, UK,

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Received: 4 February 2005
Accepted in revised form: 28 June 2005

None of the authors have any proprietary or financial interest in this project

West Kent Eye Centre, UK, and Prince of Wales Hospital, Hong Kong.

The inclusion criteria were as follows: age > 50 years; evidence of macular CNV in one eye using the Macular Photocoagulation Study (MPS) group definition¹⁹ and ARM in the fellow eye (Grade 0b–3 based on Rotterdam Study).²⁰ Only Caucasian patients were included from the two UK centres and only Chinese patients were included from the centre in Hong Kong.

Exclusion criteria included: CNV secondary to other causes such as myopia, post-inflammatory and angioid streaks; retinal features suggestive of polypoidal choroidal vasculopathy; ungradeable CNV due to poor photographic quality.

The CNV subtype was determined from colour fundus photographs and early, mid and late frames of fluorescein angiograms, while the grade of ARM in the fellow eye was determined from colour fundus photographs. The images were cropped using the same template with Adobe Photoshop software version 7.0 (© Adobe systems incorporated 1990–2002) to delete any peripheral image features that might identify the site of origin. The images for each patient from each site were stored in separate folders and these were combined and recoded in random order by one of the authors not involved in the grading.

Grading

Grading of the digital colour photographs and fluorescein angiograms was performed by two independent graders from King's College Hospital. Any discrepancies were resolved by the senior author.

The CNV subtype in the affected eye was classified as shown below:

1. Predominantly classic CNV (PC) where the area of classic CNV > 50% of the area of the entire lesion.
2. Minimally classic CNV (MC) where the area of the classic CNVM is < 50% and > 0% of the entire lesion.
3. Occult CNV with no classic component (OC) included both fibrovascular pigment epithelial detachment and late leakage of undetermined source.

ARM in the second eye was graded according to the classification used in the Rotterdam study. For the purpose of analysis, following grading of ARM in the fellow eye into grades 0a to 3, all patients with ARM grade 0a were excluded in order to avoid inclusion of patients with idiopathic CNV. Each fellow eye was then assigned an ARM severity grade 1–6 so that each increasing grade of ARM corresponded to a one-point rise in ARM severity as shown in Table 1.

Statistical analysis

Data were analysed using the statistical package for the social sciences SPSS 11.0.0. (SPSS Inc., Chicago, IL, USA). Agreement between graders was assessed using Cohen's kappa statistics. Univariate analysis was done to explore the relationship between severity of ARM and CNV subtypes. Multiple ordinal analyses using STATA 7–8 were performed to determine the ARM severity in the three subtypes of CNV in the three groups (two Caucasians and one Chinese).

Results

A total of 135 patients were included in the study. In all, 38 Caucasians were recruited from King's College Hospital (KCH), UK, 45 Caucasians from West Kent eye Centre (WKEC), UK, and 52 Chinese from Prince of Wales Hospital (PWH), Hong Kong.

The mean ARM severity score is compared in the two groups (Caucasian and Chinese cohort) in Table 2. On univariate analysis, the Chinese cohort showed significantly less ARM severity compared to the Caucasian group (mean difference = 1.0; 95% CI 0.31–1.8; $P = 0.005$).

Although the proportion of CNV subtypes in the two ethnic groups was similar (Table 3); multiple ordinal regression analysis showed that the mean ARM severity

Table 1 ARM severity scale based on the Rotterdam Study

Rotterdam study	Definition of ARM	ARM severity scale
0b	Hard drusen (< 63 μ m) only	1
1a	Soft distinct drusen (\geq 63 μ m) only	2
1b	Pigment abnormalities only (no soft drusen)	3
2a	Soft indistinct drusen (\geq 125 μ m) or reticular drusen only	4
2b	Soft distinct drusen (\geq 63 μ m) with pigment abnormalities	5
3	Soft indistinct drusen (\geq 125 μ m) or reticular drusen with pigment abnormalities	6

Table 2 Mean ARM severity in fellow eyes of the 2 races

Race	N (%)	Mean ARM severity (95% CI)
Caucasians	83 (61)	2.5 (1.9–3.2)
Chinese	52 (39)	1.4 (1–2)
Total	135 (100)	2.0 (1.8–2.4)

in the Chinese cohort was significantly less than the Caucasian population ($P = 0.001$).

When we correlated the CNV subtype in the affected eye with the ARM severity in the fellow eye, predominantly the classic group showed significantly less ARM severity in the fellow eye compared to the minimally classic and occult CNV groups in the Caucasian group as previously reported. However, the Chinese cohort did not show a similar pattern. The CNV subtype did not correlate to the ARM severity in the Chinese group (Table 4).

Discussion

The incidence of CNV in the fellow eyes of Caucasians is high with prospective studies estimating the incidence of 6–8.8%/year.^{15,21} MPS study reported that CNV developed in 35% of fellow eyes within 5 years. Data from the Asian population suggest a lower incidence of CNV in the second eye.^{6,8,22}

The MPS study has shown that characteristics of drusen and retinal pigmentary abnormalities are independent prognostic indicators for development of CNV.^{15,16} These findings have been quantified in large population-based studies^{1–3} and they provide a strong rationale for using these features to design a universally accepted grading system for stratifying ARM. The Rotterdam study incorporates the International ARM Epidemiological study group nomenclature to classify ARM into mutually exclusive stages.^{20,23} Early ARM is

defined as the presence of drusen and/or retinal pigment epithelial abnormalities in the absence of late ARM.

Based on this grading system, it has been observed that ARM characteristics in the fellow eye correlate with the type of CNV in the affected eye. The fellow eyes of predominantly classic CNV have significantly less severe ARM compared to the fellow eyes with occult CNV.¹⁸

In this study, we also used the Rotterdam classification to assess ARM severity in the fellow eyes of Caucasian and Chinese patients with unilateral NVAMD. Our data suggests that a clear relation exists between increasing severity of ARM in the fellow eye and the proportion of occult CNV in the affected eye in the Caucasians, but the Chinese cohort developed CNV at a much lower severity of ARM.

The prevalence of drusen and retinal pigmentary abnormalities in the oriental races has been observed to be less than that in Caucasians.^{7,23,24} In the Caucasian population, drusen characteristics such as soft drusen and large and confluent drusen are particularly high risks for developing CNV, corresponding to grade 2a–3.^{25–27} However, soft drusen are not as prevalent in the Orientals.^{22,24,28} In addition, the prevalence of retinal pigmentary changes is lower in the Orientals.²² These findings contribute to the fact that the Chinese cohort has less ARM severity compared to Caucasians.

However, this study also shows that the proportion of CNV subtypes in the different races is similar. Therefore, it suggests that though drusen and retinal pigmentary changes may be prognostic indicators of CNV, other factors contribute significantly to the pathogenesis of CNV in AMD. This is further substantiated by the fact that serous pigment epithelial detachments (PED) were found to be a higher risk factor for development of CNV in the Chinese and Japanese compared to soft drusen.^{22,24,28} Serous PEDs are not included in the Rotterdam grading. It may be that if ARM severity is analysed by including all morphological abnormalities in the retina, there may not be significant differences in ARM severity between races.

The present study is limited by its retrospective series and cross-sectional approach. Further longitudinal studies of fellow eyes with unilateral NVAMD in different races are required to assess risk factors in fellow eyes in various races.

Table 3 CNV subtypes in the two ethnic groups

Race	Predominantly classic CNV (%)	Minimally classic CNV (%)	Pure occult CNV (%)
Chinese	15 (29)	10 (19)	27 (52)
Caucasians	25 (30)	16 (19)	42 (51)
<i>P</i> -value	NS	NS	NS

NS: nonsignificant.

Table 4 Mean ARM severity in fellow eye categorised by CNV subtype in affected eye

Race	CNV subtypes	Mean ARM severity
Chinese	Predominantly classic CNV	1.5
	Minimally classic CNV	1.4
	Pure occult CNV	1.3
Caucasians	Predominantly classic CNV	2.0
	Minimally classic CNV	2.5
	Pure occult CNV	3.0

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