Long-Term Progression of Fundus Changes; Summary and Flow Charts

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Abstract

The progression pattern of myopic maculopathy based on META-PM classification is shown. Frequent natural progression patterns include a progression from peripapillary diffuse atrophy to macular diffuse atrophy, development of patchy atrophy in the area of macular diffuse atrophy, enlargement of lesions of patchy atrophy, enlargement of macular atrophy, progression to patchy atrophy from lacquer cracks, and development of MNV-related macular atrophy around myopic macular neovascularization (MNV).

Keywords

Long-term progression · META-PM classification · Diffuse atrophy · Patchy atrophy · MNV-related macular atrophy

In 2015, the Meta-Analysis of Pathologic Myopia (META-PM) study group proposed an International photographic classification system for myopic maculopathy [1]. This META-PM classification has been consistently used in many studies investigating the long-term natural course of myopic maculopathy [2–7]. In two population-based longitudinal studies, the 10-year progression rate of myopic maculopathy was 35.5% in the elderly Chinese (aged 40+) (the Beijing Eye study) [3] and the 5-year progression rate was 35.3% in rural Chinese adult population (aged 30+) (the Handan Eye Study) [4]. In a large highly myopic Chinese cohort (Zhongshan Ophthalmic Center-Brien Holden Vision Institute High Myopia Cohort Study), myopic maculopathy progressed in approximately 15% of 657 highly myopic eyes over 2 years [6].

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In this chapter, we aim to illuminate the progression pattern of myopic maculopathy mainly based on META-PM classification. The data are from a retrospective case series study including 810 eyes of 432 highly myopic patients who had been followed for ≥10 years in the High Myopia Clinic at Tokyo Medical and Dental University [2]. In the mean follow-up of 18 years, the progression of myopic maculopathy was observed in 58.6% for all and in 74.3% in eyes with pathologic myopia at baseline.

24.1 Progression Patterns and Clinical Characteristics of Each Lesion of Myopic Maculopathy at Baseline (Table 24.1)

24.1.1 From High Myopia to Pathologic Myopia

Pathologic myopia (PM) is defined as myopic maculopathy equal to or more severe than diffuse choroidal atrophy (category 2), or by a presence of "plus lesions" such as myopic macular neovascularization (MNV) or lacquer cracks, or by a presence of a posterior staphyloma [1, 8]. During a mean follow-up of 19.5 years, 27% of 289 highly myopic (HM) eyes without PM at baseline progressed to PM [2]. Within those 78 eyes with progression, 59 eyes (75.6%) progressed to diffuse choroidal atrophy, 16 eyes (20.5%) progressed to patchy atrophy, and the remaining 3 eyes (3.8%) progressed to MNV-related macular atrophy.

In 10-year follow-up in the Beijing Eye study [3], the progression from HM to PM was observed in 15 of 79 eyes (19%) with tessellated fundus at baseline. Twelve of the 15 eyes showed the progression to diffuse atrophy, 1 eye showed the progression to lacquer cracks, 1 eye with the progression to patchy atrophy and 1 eye with the progression to macular atrophy. Fang et al. [2] reported that the patients with progression were significantly older (40.6 ± 17.0 years vs.

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Table 24.1 The progression patterns and clinical characteristics at baseline and at last visit according to each lesion of myopic maculopathy

Lesion of myopic maculopathy at baseline	Progression and its patterns	No. of eyes (%)	Age at baseline (yrs.)	Age at last visit (yrs.)	Axial length at baseline (mm)	Axial length at last visit (mm)	Follow-up (yrs.)
No maculopathy (22 eyes)	Total	14/22 (63.6%)	21.8±18.9	41.1±20.3	26.3±1.2	28.3±11.7	20.2±15.9
	Development of tessellated fundus	**10/14 (71.4%)**	17.4±17.4	36.6± 19.1	26.2±1.2	28.2±1.8	20.0±16.6
	Development of diffuse choroidal atrophy	4/14 (28.6%)	32.8±20.4	52.5±21.3	26.4±1.2	28.7±1.5	20.8±4.5
Tessellated fundus (266 eyes)	Total	74/266 (27.9%)	39.4 ± 16.8	60.3 ± 17.2	28.3 ± 1.4	29.9 ± 1.7	20.9 ± 6.3
	Development of diffuse choroidal atrophy	**55/74 (74.3%)**	38.6 ± 17.6	59.4 ± 18.2	28.2 ± 1.5	29.7 ± 1.7	20.8 ± 6.6
	Development of patchy choroidal atrophy	16/74 (21.6%)	39.3 ± 14.3	61.0 ± 14.0	28.8 ± 1.2	30.8 ± 1.2	21.7 ± 5.4
	Development of myopic MNV (including MNV-related macular atrophy)	5/74 (6.8%)	53.8 ± 13.3	72.0 ± 11.6	28.6 ± 1.6	30.2 ± 1.6	18.2 ± 4.0
	Development of new lacquer cracks	8/74 (10.8%)	43.5 ± 9.0	61.5 ± 8.1	29.4 ± 0.9	30.7 ± 0.7	18.0 ± 2.8
Peripapillary diffuse choroidal atrophy without plus lesions (158 eyes)	Total	82/158 (51.9%)	43.5 ± 15.8	65.2 ± 14.0	29.0 ± 1.7	30.4 ± 1.8	21.7 ± 7.5
	Development of macular diffuse choroidal atrophy	**64/82 (78.0%)**	42.8 ± 16.2	64.6 ± 14.7	29.1 ± 1.7	30.6 ± 1.9	21.8 ± 7.7
	Development of patchy choroidal atrophy	27/82 (32.9%)	42.0 ± 16.7	63.7 ± 14.2	28.5 ± 1.5	30.3 ± 1.6	21.7 ± 8.1
	Development of myopic MNV (including MNV-related macular atrophy)	13/82 (15.9%)	47.3 ± 16.8	68.0 ± 46.6	28.6 ± 1.7	29.6 ± 1.5	20.7 ± 5.5
	Development of new lacquer cracks	8/82 (9.8%)	26.9 ± 18.4	50.3 ± 9.8	28.1 ± 1.4	30.9 ± 2.1	23.4 ± 9.2
	Development of patchy-related macular atrophy	3/82 (3.7%)	53.7 ± 4.5	80.0 ± 4.6	31.0 ± 2.3	31.5 ± 2.2	26.3 ± 4.0
Macular diffuse choroidal atrophy without plus lesions (59 eyes)	Total	29/59 (49.2%)	53.4 ± 13.1	72.1 ± 11.7	29.9 ± 1.7	30.9 ± 1.9	18.6 ± 5.8
	Development of patchy choroidal atrophy	**23/29 (79.3%)**	53.6 ± 12.6	72.1 ± 12.2	29.8 ± 1.6	30.9 ± 1.8	18.6 ± 5.4
	Development of myopic MNV (including MNV-related macular atrophy)	5/29 (17.2%)	58.4 ± 10.7	75.0 ± 7.9	29.9 ± 2.3	30.1 ± 1.4	16.6 ± 5.9
	Development of new lacquer cracks	1/29 (3.4%)	26	56	31.4	35	30
	Development of patchy-related macular atrophy	0	–	–	–	–	–
Patchy atrophy without plus lesions (63 eyes)	Total	60/63 (95.2%)	49.3 ± 13.7	68.9 ± 12.6	31.1 + 1.4	31.9 ± 1.6	19.6 ± 7.8
	Enlargement of the original patchy atrophy	**59/60 (98.3%)**	49.6 ± 13.5	69.1 ± 12.7	31.1 ± 1.4	31.9 ± 1.6	19.4 ± 7.7
	Development of new patchy choroidal atrophy	29/60 (48.3%)	49.8 ± 13.9	71.4 ± 12.3	31.1 ± 1.5	31.9 ± 1.6	21.7 ± 8.3
	Development of myopic MNV (including MNV-related macular atrophy)	13/60 (21.7%)	47.1 ± 8.2	69.8 ± 8.2	31.0 ± 1.3	31.3 ± 1.6	22.7 ± 7.6
	Development of patchy-related macular atrophy	5/60 (8.3%)	50.8 ± 17.5	73.8 ± 12.4	30.7 ± 1.7	31.5 ± 2.0	23.0 ± 7.0
Macular atrophy without plus lesions (35 eyes)	**Enlargement of macular atrophy**	**35/35 (100%)**	51.1 ± 12.7	68.1 ± 13.0	29.7 ± 1.8	30.2 ± 1.5	17.2 ± 7.7
Lacquer cracks (66 eyes)	Total	43/66 (65.2%)	42.8 ± 10.4	62.1 ± 11.5	30.1 ± 1.5	31.5 ± 2.0	19.1 ± 7.4
	Development of new lacquer cracks	7/43 (16.3%)	35.3 ± 14.2	51.7 ± 12.5	30.3 ± 0.7	31.0 ± 0.7	16.7 ± 6.6
	Development of new patchy atrophy	**38/43 (88.4%)**	43.7 ± 9.2	63.3 ± 10.7	30.0 ± 1.6	31.6 ± 2.1	19.4 ± 7.3
Myopic MNV (109 eyes with active or scar phase without macular atrophy)	**Development of MNV-related macular atrophy**	**101/109 (92.7%)**	54.2 ± 12.2	69.5 ± 11.6	28.6 ± 1.6	29.5 ± 1.7	15.8 ± 6.1

Yrs. years, *med* median, *MNV* macular neovascularization, *PDCA* Peripapillary diffuse choroidal atrophy, *MDCA* macular diffuse choroidal atrophy; Reproduced and modified with permission from [2]

29.4 ± 15.3 years) and had longer axial length at baseline (28.3 ± 1.5 vs. 27.3 ± 1.3 mm) than those without progression. The progression from HM to PM was significantly associated with older age, longer axial length at baseline, greater axial elongation during a follow-up and the development or enlargement of parapapillary atrophy after adjusting for gender, myopic maculopathy at baseline, and a duration of follow-up [2].

Diffuse atrophy usually begins at around the age 40. Li et al. confirmed that myopic maculopathy developed or progressed disproportionally more commonly among people aged 40 years and older [6]. This findings was compatible with that no subjects progressed to diffuse atrophy in 44 highly myopic Chinese adolescents aged 12-16 at baseline who had been followed up for 10 years in Singapore Cohort Study of Risk Factors for Myopia (SCORM) [5]. Fang et al. [2] reported that the strongest risk factor associated with the progression from HM to PM was the development or enlargement of parapapillary atrophy. A longer term observation is required to assess if those eyes with enlargement of parapapillary atrophy will eventually become PM in the future and if there are any other parameters for a higher risk of the development of myopic maculopathy.

It is important and challenging to determine whether or not simple childhood myopia will become eventual PM in adulthood. A retrospective case series study conducted in the High Myopia Clinic at Tokyo Medical and Dental University included 56 eyes of 29 children and adolescents aged 15 years or younger who were followed up for over 20 years [9]. At the last visit, 35 eyes (63%) showed PM in adulthood, of which 29 eyes (83%) showed pre-existing peripapillary diffuse choroidal atrophy during childhood or adolescence, and the remaining 6 (17%) eyes showed tessellation only. This suggested that the presence of peripapillary diffuse choroidal atrophy in children with high axial myopia may be an indicator for the eventual development of advanced myopic choroidal atrophy in later life. In addition, peripapillary diffuse choroidal atrophy was significantly associated with an abrupt and extreme thinning of the peripapillary choroid in OCT images [10], thus the measurement of nasal choroidal thickness in high myopic children using 56.5 μm at 3 mm nasal to fovea as a cut-off value for predicting the occurrence of myopic choroidal atrophy is warranted [11].

24.2 Progression of Diffuse Choroidal Atrophy (Myopic Maculopathy Category 2)

24.2.1 Peripapillary Diffuse Choroidal Atrophy (PDCA)

Diffuse choroidal atrophy develops initially around the optic disc, i.e., peripapillary diffuse choroidal atrophy (PDCA). Approximately half of the eyes with PDCA without plus lesions at baseline progressed, most frequently showed an enlargement of PDCA to macular diffuse choroidal atrophy (MDCA) (Table 24.1).

In the progression from PDCA to MDCA, the mean choroidal thickness was reduced by almost a half at all locations except nasal part (subfoveal choroidal thickness: from 85 μm to 50 μm; temporal choroidal thickness: from 112 μm to 62 μm; superior choroidal thickness from 112 μm to 66 μm; inferior choroidal thickness from 93 μm to 57 μm, vs. nasal choroidal thickness: from 32 μm to 21 μm). The cut-off value to differentiate the eyes with MDCA from PDCA was 62 μm at the subfovea [11]. (See Chap. 17).

24.2.2 Macular Diffuse Choroidal Atrophy (MDCA)

Approximately a half of the eyes with MDCA without plus lesions at baseline progressed, in which almost 80% of eyes developed patchy atrophies and 17% developed myopic macular neovascularization (MNV) (Table 24.1).

There was no significant difference in the subfoveal choroidal thickness between the eyes with MDCA (50 μm) and patchy atrophy (49 μm). Swept-source OCT showed that patchy atrophy was not simply an atrophy but were holes of Bruch's membrane [12, 13]. It suggested that the progression from diffuse atrophy to patchy atrophy was not due to a progressive choroidal thinning but was due to a new development of Bruch's membrane hole in the area of already thinned choroid. It was also possible that the Bruch's membrane was fragile in eyes with extremely thin choroid such as in the eyes with MDCA. Therefore, MDCA may be a prerequisite or precursor for developing Bruch's membrane holes by making Bruch's membrane more fragile in the first place. However, this is speculative and needs to be proven.

It has to be considered that approximately the remaining half of eyes with diffuse atrophy did not develop Bruch's membrane defects after a mean follow-up of 19 years [2]. This may indicate that approximately one-half of the eyes with diffuse atrophy may remain stable for a relatively long period.

24.3 Progression of Patchy Atrophy

Almost all eyes (95%) with patchy atrophy progressed, in which an enlargement of the original patchy atrophy was found predominantly in 98%, and new patchy atrophy was found in 47% followed by the development of myopic MNV in 21.7% and patchy-related macular atrophy in 8.3% (Table 24.1). Such high percentages of progression of eyes with patchy atrophy could be explained by biomechanical properties of Bruch's membrane. Once its defect is created, the Bruch's membrane defect tends to enlarge over time.

24.4 Progression of Myopic MNV

Patients with myopic MNV tend to be older (mean age, 53 years) and have relatively short axial lengths (mean, 28.9 mm) as compared to the patients with other lesions due to PM [2]. In this study population, 93% of the eyes with myopic MNV, either in the active stage or the scar phase, progressed to MNV-related macular atrophy without any treatment. Currently, anti-VEGF treatment is the first-line therapy for myopic MNV. Onishi et al. [14] reported that the incidence of MNV-related macular atrophy was lower (73.9%) in treated eyes with the intravitreal injection of ranibizumab at 5 years after MNV onset than the natural course. Chhablani et al. [15] described the 5-year outcomes after intravitreal bevacizumab monotherapy in 33 eyes with myopic MNV. In their study, the foveal atrophy was found at baseline in 5 eyes (15.2%) and in 14 eyes (42.4%) at the final visit.

24.5 Progression of Lacquer Cracks

The common progression pattern of lacquer cracks (which are linear defects of Bruch's membrane) is a progression to patchy atrophy and an increase of the number of lacquer cracks [2, 16]. Multimodal imaging is needed for the precise detection of lacquer cracks. A progression of lacquer cracks was found in 53.7% of the eyes with a mean follow-up period of 3.5 years [16]. In this study, an increase in the number of lacquer cracks was the most frequent pattern followed by a progression to patchy atrophy and an elongation of existing lacquer cracks (See more details in Chap. 13).

24.6 A Scheme Depicting the Progression Patterns of Myopic Maculopathy Suggested by OCT Findings (Fig. 24.1)

First, the progression from category 0 (no myopic maculopathy) to category 1 (fundus tessellation) is not associated with a decline of the best-corrected visual acuity. Although the tessellation is not considered as PM, a remarkable thinning of the choroid begins with the appearance of tessellation, which is the first sign of the progression of myopic maculopathy. Second, diffuse atrophy (category 2) primarily occurs in the peripapillary region (peripapillary diffuse choroidal atrophy; PDCA) and eventually extends into the macula (macular diffuse choroidal atrophy; MDCA). Third, the eyes with patchy atrophy have a hole in the macular Bruch's membrane that either forms by an enlargement of lacquer cracks or develops in the regions of advanced diffuse atrophy with a more vulnerable Bruch's membrane. Fourth, both patchy atrophy and macular atrophy (MNV-related and patchy-related) tend to enlarge with time. Fifth, macular atrophy is almost always MNV-related, although patchy-related MA can occasionally occur.

24.7 Risk Factors for Progression of Myopic Maculopathy

Risk factors for progression of myopic maculopathy include older age, longer axial length, greater increase in axial length, a presence or enlargement of parapapillary diffuse choroidal atrophy (PDCA) [2], and eyes with diffuse atrophy or a greater category of baseline myopic maculopathy [6] (Fig. 24.2).

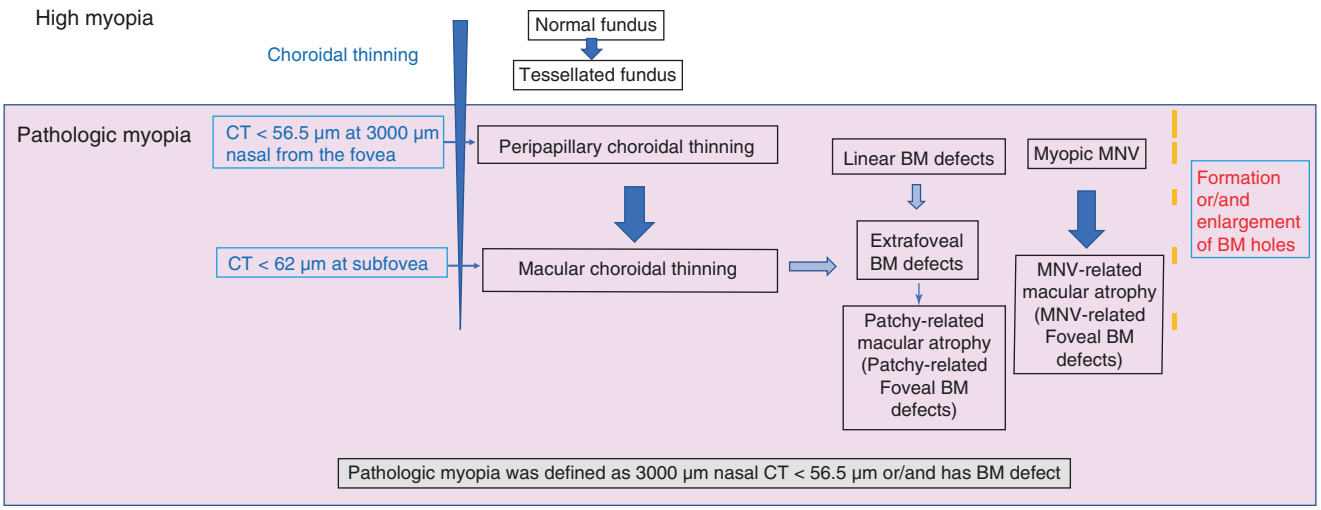

Fig. 24.1 A scheme depicting the progression patterns of myopic maculopathy and corresponding characteristics of OCT findings. *BM* Bruch's membrane, *MNV* macular neovascularization, *CT* choroidal thickness

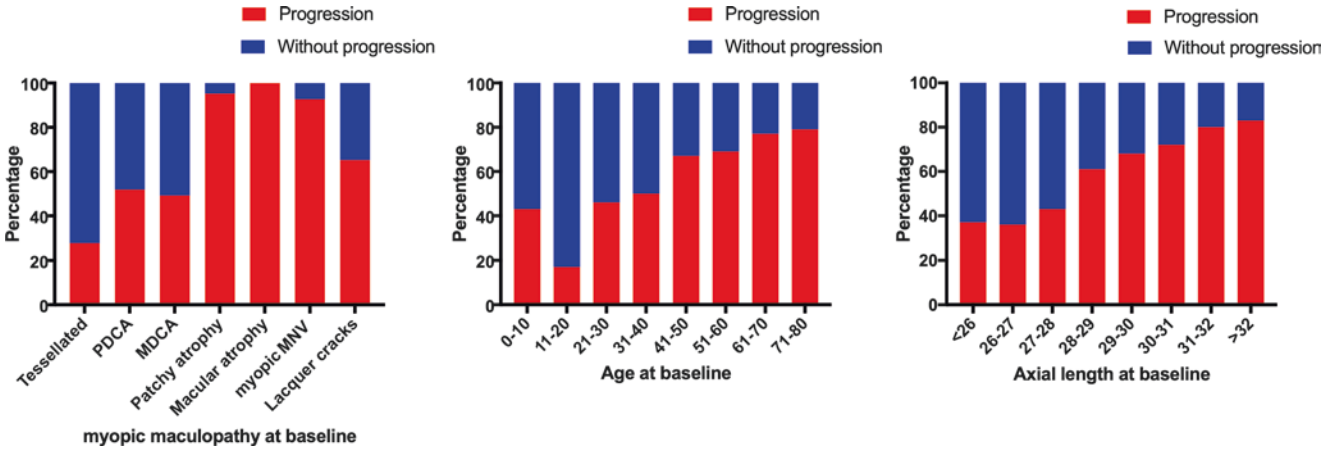

Fig. 24.2 Proportion of progression of myopic maculopathy by myopic maculopathy lesion, age and axial length at baseline. *PDCA* peripapillary diffuse choroidal atrophy, *MDCA* macular diffuse choroidal atrophy, *MNV* macular neovascularization

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