



# Pseudodrusen pattern and development of late age-related macular degeneration in the fellow eye of the unilateral case

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## Abstract

**Purpose** To investigate whether the development of late age-related macular degeneration (AMD) in fellow eyes with pseudodrusen is associated with the pseudodrusen pattern in patients with unilateral exudative AMD.

**Study design** Retrospective observational study.

**Methods** A retrospective analysis was performed on 73 patients with unilateral exudative AMD showing pseudodrusen in their fellow eyes. Eyes were classified according to pseudodrusen pattern, which was determined based on maximum pseudodrusen ribbon length.

**Results** During the mean follow-up period of  $35.5 \pm 18.6$  months, 21 (28.8%) eyes developed late AMD. Among these eyes, 15 (71%) developed exudative AMD and six (29%) developed geographic atrophy (GA). Development of late AMD in fellow eyes occurred with significantly more prevalence in patients showing a ribbon-dominant type pseudodrusen pattern in their fellow eye than dot-dominant type ( $P=0.0005$ , log-rank test). Cox-regression analysis revealed that development of late AMD in fellow eyes is associated with the presence of ribbon-dominant pseudodrusen in the fellow eyes (hazard ratio 4.15, 95% confidence interval (CI) 1.59–10.8), along with older age (hazard ratio 1.10, 95% CI 1.03–1.17), a history of smoking (hazard ratio 17.2, 95% CI 1.11–263), the presence of large soft drusen in the fellow eye. (hazard ratio 5.49, 95% CI 1.29–21.1) and retinal angiomatous proliferation (hazard ratio 5.02, 95% CI 1.90–13.2)

**Conclusions** Fellow eyes with ribbon-dominant pseudodrusen in patients with unilateral exudative AMD are likely to develop late AMD.

**Keywords** Pseudodrusen pattern · Ribbon-dominant type · Dot-dominant type · Choroidal neovascularization, Geographic atrophy

## Introduction

Pseudodrusen were first described as a specific form of drusen associated with age-related macular degeneration (AMD) by Mimoun et al. in 1990 [1]. In color fundus photography, pseudodrusen appear as yellow-white lesions in the macula or superior to it. Zweifel et al. [2] used spectral-domain optical coherence tomography (SD-OCT) to

demonstrate that pseudodrusen are subretinal drusenoid deposits located above the retinal pigment epithelium (RPE).

The risk of developing late AMD, including exudative AMD and geographic atrophy (GA), is higher in the fellow eyes of patients with unilateral AMD [3]. A Japanese clinic-based study demonstrates that the incidence of developing late AMD in an unaffected fellow eye was approximately 3% in the first year and 11% in the first 5 years [4]. Several clinical studies and meta-analyses report that the incidence in patients with unilateral exudative AMD is significantly higher in eyes with pseudodrusen than in those without [5–8].

Several morphological classification criteria for pseudodrusen have been proposed based on clinical appearance in multimodal imaging. Suzuki et al. classified pseudodrusen into three groups: dot, ribbon, and peripheral [9],

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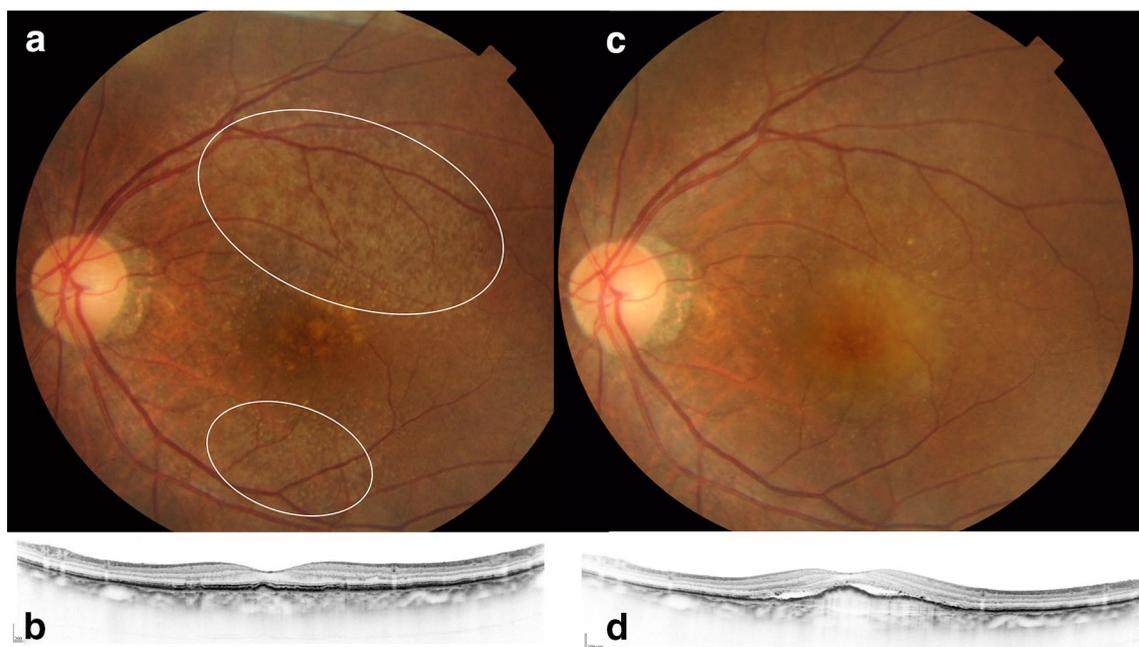
while the Comparison Age-related macular degeneration Treatment Trials (CATT) research group classified pseudodrusen into dot, ribbon, and confluent pseudodrusen. In the CATT study, the risk of developing exudative AMD in fellow eyes with pseudodrusen over 2 years was 30.7% and of GA, was 15.8% [7]. Fellow eyes with dot pseudodrusen were noted to be more likely to develop exudative AMD, and those with confluent pseudodrusen were noted to be more likely to develop GA, although the statistical analysis did not clarify this relationship between pseudodrusen subtype and the type of late AMD, exudative AMD or GA, developed in the fellow eye. This is most likely due to the coexistence of two or more pseudodrusen subtypes in the same fellow eye.

We recently proposed new classification criteria for pseudodrusen patterns consisting of a dot-dominant type and a ribbon-dominant type depending on the maximum pseudodrusen ribbon length evaluated in the eye [10]. This allows for a clear differentiation of eyes containing several types of pseudodrusen. In the present study, we report the long-term follow-up results from cases of unilateral exudative AMD with unaffected fellow eyes showing pseudodrusen and report an investigation into the risk of developing late AMD by comparing dot-dominant and ribbon-dominant pseudodrusen types in the unaffected fellow eyes.

## Methods

We retrospectively reviewed the medical records of 73 consecutive unilateral exudative AMD patients who initially visited the Macula Clinic in the Department of Ophthalmology at the University of Yamanashi between August 2011 and January 2017 showing pseudodrusen in their fellow eye and were followed up for at least 6 months. This study adhered to the tenets of the Declaration of Helsinki. This retrospective study was approved by Institutional Review Board/Ethics committee in University of Yamanashi.

At initial presentation, all patients underwent comprehensive examinations, including measuring best-corrected visual acuity (BCVA) and intraocular pressure as well as using slit-lamp biomicroscopy, color fundus photography, fundus autofluorescence (FAF), near-infrared reflectance (NIR), fluorescein angiography (FA), indocyanine green angiography (ICGA) using a confocal laser scanning ophthalmoscope (HRA2 Spectralis.), and SD-OCT (Spectralis). A pseudodrusen diagnosis was made based on peculiar reticular patterns around the macula visualized by NIR or FAF enhancement and SD-OCT findings of subretinal hyper-reflective deposits localized above the RPE layer. The presence and type of pseudodrusen were



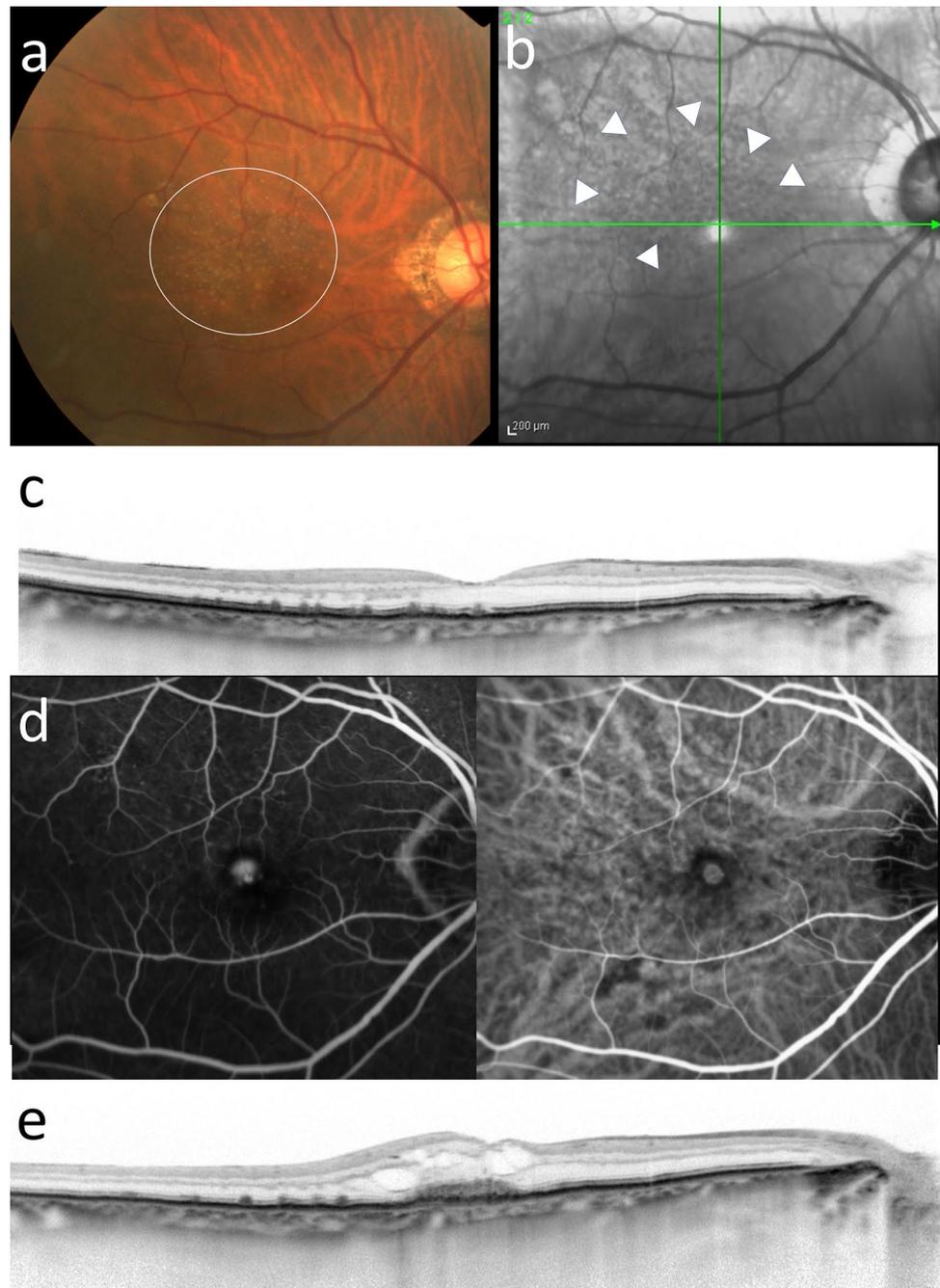
**Fig. 1** Development of exudative age-related macular degeneration (AMD) in fellow eye with a ribbon-dominant type of pseudodrusen pattern. **a** A 77-year-old woman was diagnosed with typical neovascular AMD in the right eye. **a** A color fundus photograph at the initial visit clearly demonstrates soft drusen and a ribbon-dominant type of pseudodrusen pattern OS. The areas surrounded by white ovals are

ribbon pseudodrusen. **b** The subfoveal choroidal thickness was determined as 225  $\mu\text{m}$  using spectral-domain optical coherence tomography (SD-OCT). **c** Pseudodrusen were indistinguishable using color fundus photography 48 months after the initial visit. **d** SD-OCT revealed the presence of subretinal fluid

defined when confirmed by at least one imaging modality. Different types of pseudodrusen pattern (dot, ribbon, and confluent) often coexist in an eye, so two pseudodrusen patterns in fellow eyes were defined as follows: a ribbon-dominant type when ribbon pseudodrusen of 1500  $\mu\text{m}$  or longer with or without confluent pseudodrusen was observed, and a dot-dominant type when only dot pseudodrusen were exhibited, or when dot pseudodrusen or ribbon pseudodrusen were shorter than 1500  $\mu\text{m}$  along

the long axis [10]. The pseudodrusen pattern diagnosis was made by two independent evaluators (YS and SY). If the judgment of the two evaluators differed, a third evaluator (HI) made the final decision. Subfoveal choroidal thickness in fellow eyes was measured as the vertical distance between the outer border of the RPE and the choriocleral border using the enhanced depth-imaging mode equipped with HRA2 Spectralis ver. 5.4. Soft drusen were differentiated from pseudodrusen using SD-OCT and FA, and the

**Fig. 2** Development of exudative AMD in fellow eye with a dot-dominant type of pseudodrusen pattern. A 80-year-old man was diagnosed with typical neovascular age-related macular degeneration (AMD) in the left eye. **a** A dot-dominant type of pseudodrusen pattern (surrounded by a white oval) was found OD using color fundus photography at the initial visit. **b** Reticular pattern (as indicated by white arrow heads) was observed on a near-infrared reflectance image OD. **c** A horizontal spectral-domain optical coherence tomography (SD-OCT) scan through the fovea revealed the presence of several subretinal drusenoid deposits. **d** Fluorescein angiography (left image) demonstrates active leakage from the fovea and indocyanine green angiography (right image) also showed mesh-like pattern on the macula 19 months after the initial visit. **e** A horizontal SD-OCT scan through the fovea reveals the presence of macular edema and subretinal hyper-reflective materials



presence of large soft drusen with a diameter of at least 125  $\mu\text{m}$  [11] was evaluated.

Patients received comprehensive examinations without FA and ICGA at each follow-up visit, the interval of which ranged from four to eight weeks, according to the treatment regimen in the affected eye. The development of late AMD in fellow eyes, including exudative AMD and GA, as well as its latent period, was investigated. Exudative AMD in fellow eyes was diagnosed when exudative changes including intra- or subretinal hemorrhages or fluid were observed using SD-OCT in association with intra-, subretinal, or sub-RPE neovascularization confirmed by FA and ICGA (Figs 1, 2). The development of GA in fellow eyes was diagnosed when a hypofluorescent area larger than 175  $\mu\text{m}$  was observed in an FAF image, corresponding with RPE defects in the SD-OCT image [12] (Fig. 3). The follow-up period ranged between 6 and 60 months.

Statistical analyses were performed using DR. SPSS (IBM Inc.). Baseline characteristics of the two groups were compared using the Mann-Whitney U test and the chi-square test for continuous and categorical variables. Cox-regression analysis was performed to determine baseline factors associated with the development of late AMD in the fellow eye. P values less than 0.05 were considered statistically significant.

## Results

Seventy-three patients (36 men; 37 women; mean age,  $79.2 \pm 7.3$  years) were enrolled in the present study. Table 1 shows the demographic data of the subjects with dot-dominant and ribbon-dominant types of pseudodrusen patterns in their fellow eyes. Greatest length of ribbon pseudodrusen was significantly longer in ribbon-dominant pseudodrusen than in dot-dominant pseudodrusen.

During the mean follow-up period of  $35.5 \pm 18.6$  months, 21 (28.8%) fellow eyes developed late AMD, including GA (n=6) and exudative AMD (n=15).

During the study period, pseudodrusen pattern did not change in either group. However, complete regression (n=2) or partial regression (n=7) of pseudodrusen was seen only when eyes with pseudodrusen were converted to late AMD including exudative AMD (n=6) and GA (n=3).

GA developed in the fellow eyes of five patients with neovascular AMD in their affected eye and in a patient with polypoidal choroidal vasculopathy (PCV) in the affected eye. Typical neovascular AMD developed in the fellow eyes of seven patients with typical neovascular AMD in the affected eye, and RAP developed in the fellow eyes of eight patients with RAP in the affected eye.

The Kaplan-Meier curve in Fig. 4 demonstrates that the cumulative incidence of developing late AMD in the fellow

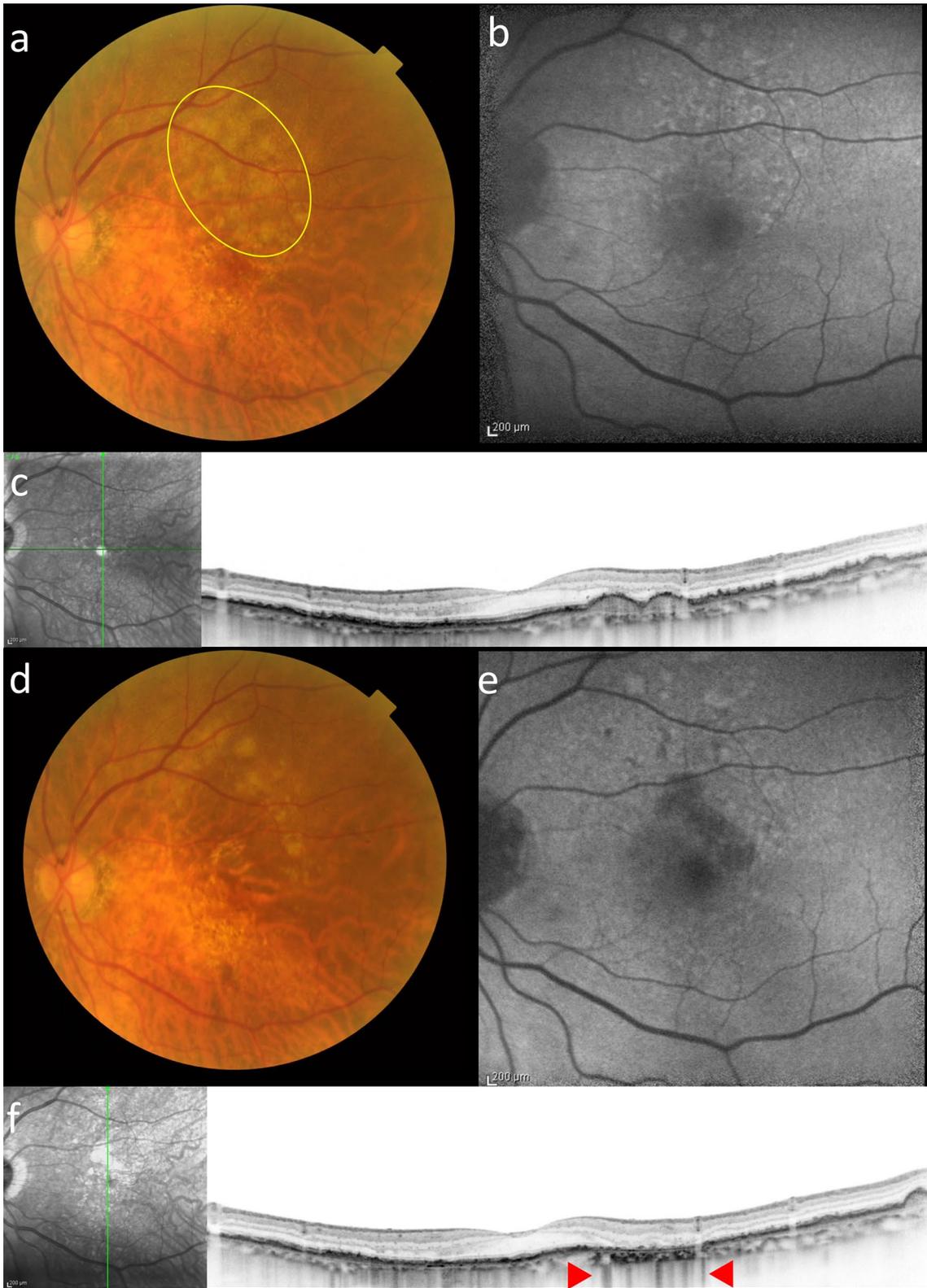
**Fig. 3** Development of geographic atrophy in fellow eye with a ribbon-dominant type of pseudodrusen pattern. A 82-year-old man was diagnosed with typical neovascular age-related macular degeneration (AMD) OD. **a** A ribbon-dominant type of pseudodrusen pattern (surrounded by a yellow oval) was found OS using color fundus photography at the initial visit. **b** Reticular pattern was not observed on a fundus autofluorescence (FAF) OS. **c** A vertical spectral-domain optical coherence tomography (SD-OCT) scan through the fovea revealed the presence of several subretinal drusenoid deposits. **d** Ribbon dominant pseudodrusen were indistinguishable on color fundus photography 33 months after the initial visit. **e** FAF showed hypoautofluorescence corresponding to retinal pigment epithelial atrophy. **f** A horizontal SD-OCT scan through the fovea revealed the defect of retinal pigment epithelium and choroidal hypertransmission (between red arrowheads)

eye was 3%, 13%, 23%, 36%, and 45% at 12, 24, 36, 48, and 60 months, respectively. It is estimated that nearly half of the patients would develop late AMD in their fellow eye within 5 years.

During the study period, exudative AMD developed in 15 eyes and GA in 6 eyes. Of 15 eyes developing exudative AMD, ribbon-dominant type was seen in 8 (53.3%) eyes and dot-dominant type in 7 (46.7%) eyes. Of 6 eyes developing GA, 5 (83.3) eyes were ribbon-dominant and 1 eye (16.7%) was dot-dominant. Exudative AMD developed at 3 months (1 eye), 8 months (1 eye), 17 months (1 eye), 19 months (2 eyes), 25 months (1 eye), 32 months (1 eye), 33 months (1 eye), 39 months (1 eye), 41 months (1 eye), 42 months (1 eye), 48 months (1 eye), 50 months (1 eye), 56 months (1 eye), and 60 months (1 eye) after first-eye involvement; and GA developed at 17 months (2 eyes), 18 months (1 eye), 29 months (1 eye), 36 months (1 eye) and 44 months (1 eye) after first-eye involvement.

Kaplan-Meier curves shown in Fig. 5 have been subdivided according to the development of exudative AMD, GA, or late AMD including exudative AMD or GA, and each is stratified by the two pseudodrusen patterns in fellow eyes. The cumulative proportion of patients developing exudative AMD (Fig. 5a), GA (Fig. 5b), or late AMD including exudative AMD or GA (Fig. 5c) in the fellow eye was significantly higher in patients with the ribbon-dominant type of pseudodrusen pattern compared with those exhibiting the dot-dominant type ( $P=0.029$ ,  $P=0.0026$ , and  $P=0.0005$ , respectively; log-rank test).

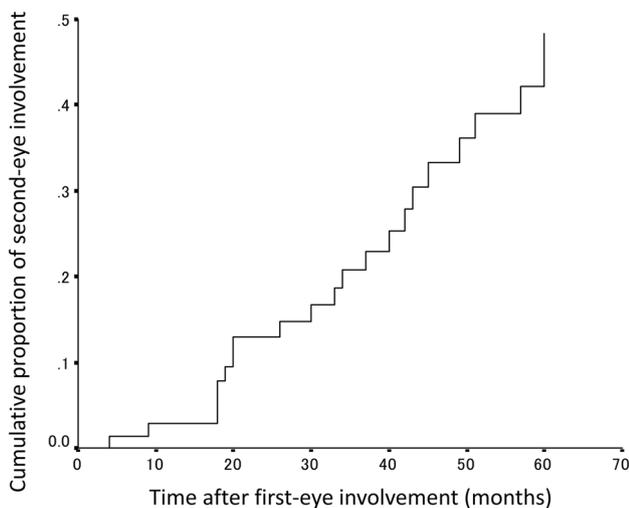
Table 2 shows the results of the Cox-regression analysis model evaluating the development of late AMD in fellow eyes in the patients with unilateral exudative AMD at baseline. Ribbon-dominant type pseudodrusen in fellow eyes had a significantly higher hazard ratio, along with older age, a history of smoking, large soft drusen in the fellow eye, and RAP in the affected eye.



**Table 1** Baseline characteristics of patients with unilateral exudative age-related macular degeneration (AMD) with pseudodrusen in the fellow eye

	Dot-dominant (n=49)	Ribbon-dominant (n=24)	P value
Age (years)	79.1±7.0	79.4±7.9	0.91
Male	25 (51%)	11 (45.8%)	0.81
History of never smoking	27 (55.1%)	14 (58.3%)	1.0
Presence of large soft drusen (>125 μm)	28 (57.1%)	19 (79.2%)	0.08
Subfoveal choroidal thickness(μm)	153±58	144±52	0.80
Greatest length of ribbon pseudodrusen(μm)	447±1390	3750±1823	<0.001
Exudative AMD subtype in the affected eye			0.57
Typical neovascular AMD	36 (73.4%)	15 (62.5%)	
PCV	4 (8.2%)	2 (8.3%)	
RAP	9 (18.4%)	7 (29.2%)	
Follow-up period (months)	37.8±17.8	30.7±20.5	0.10

AMD age-related macular degeneration, PCV polypoidal choroidal vasculopathy, RAP retinal angiomatous proliferation



**Fig. 4** Kaplan–Meier survival curve of unilateral exudative age-related macular degeneration (AMD) cases showing the development of late AMD in fellow eyes with pseudodrusen

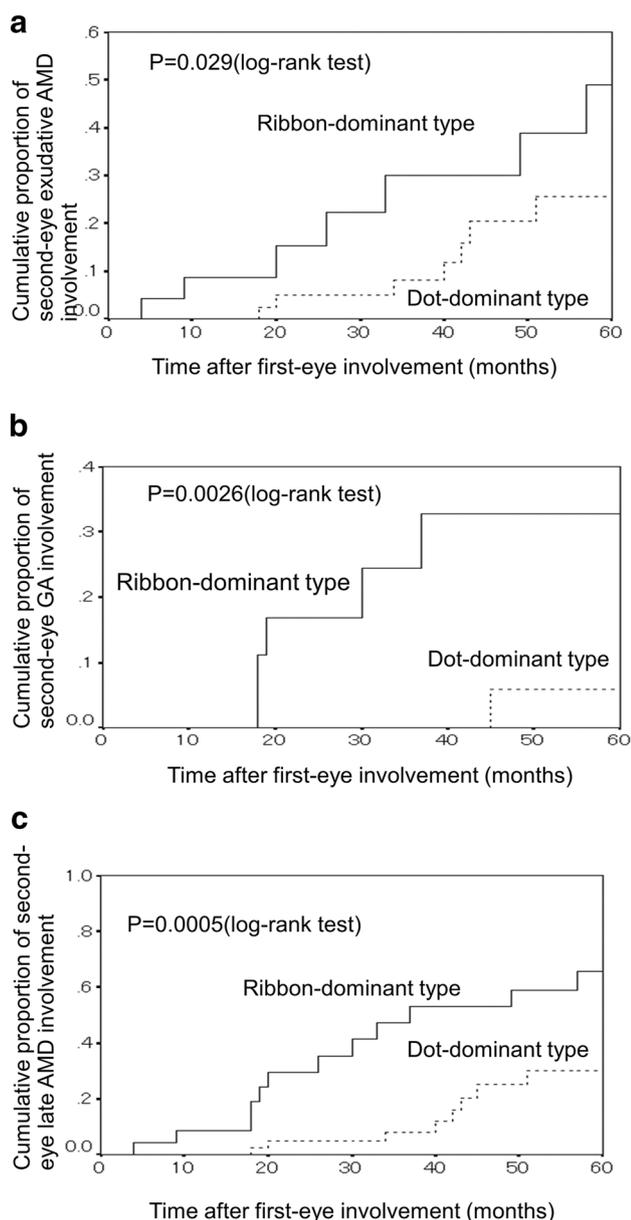
## Discussion

The CATT study demonstrated that late AMD developed in 73 out of 176 (41.5%) fellow eyes with pseudodrusen during the 2-year treatment period for the affected eyes, significantly more prevalent compared with 101 out of 446 (22.8%) fellow eyes without pseudodrusen ( $P < 0.0001$ ) [7]. In the present study, we investigated 73 fellow eyes with pseudodrusen in unilateral exudative AMD patients and found that 13% developed late AMD within two years. This figure appears to be much smaller compared with the 41.5%

reported by the CATT study. A meta-analysis of Caucasian eyes reports that incidence of late AMD in fellow eyes was 12.2% at 1 year and 26.8% at 4 years [13]. In comparison, a Japanese clinic-based study reports that incidence of developing exudative AMD in fellow eyes was 3.4% at 1 year and 11.3% at 5 years [4]. Thus, the risk of developing late AMD in fellow eyes might be lower in Japanese compared with Caucasian patients.

Dot pseudodrusen have been reported in almost 100% of exudative AMD eyes with pseudodrusen in an Asian cohort [14, 15]. Therefore, Elfandi et al. classified eyes with pseudodrusen into two subtypes, dot-dominant and dot-ribbon type, based on the findings in Japanese patients. As in our previous report, we classified pseudodrusen patterns in the present study into two types, dot-dominant and ribbon-dominant types, based on the maximum length of the ribbon pseudodrusen [10]. We also compared the frequency of developing late AMD in fellow eyes with the two types of pseudodrusen pattern in cases of unilateral exudative AMD.

The Cox proportional hazard analysis in the present study demonstrates that older age, a history of smoking, the presence of large soft drusen in the fellow eye, exhibiting the ribbon-dominant type of pseudodrusen pattern in the fellow eye, and RAP in the affected eye are associated with the development of late AMD in fellow eyes. In the CATT study, reticular or confluent pseudodrusen, which roughly corresponds to the ribbon-dominant type pattern in this study, was associated with the development of GA rather than exudative AMD, and dot pseudodrusen, which corresponds to the dot-dominant type pattern in this study, was associated with the development of exudative AMD. These findings differ from the present results, which show that the



**Fig. 5** Kaplan-Meier survival curves of unilateral exudative age-related macular degeneration (AMD) cases showing the development of **a** exudative AMD, **b** geographic atrophy (GA), or **c** late AMD including exudative AMD or GA in fellow eyes with pseudodrusen, stratified according to the pseudodrusen pattern observed in the fellow eye

development of exudative AMD in fellow eyes was more prevalent in patients with the ribbon-dominant type of pseudodrusen pattern compared to those with the dot-dominant type (Fig. 5a). The area affected with pseudodrusen in eyes

with the ribbon-dominant type tends to be larger than in eyes with the dot-dominant type, which might be related to the higher incidence of developing late AMD, including GA and exudative AMD, in eyes with the ribbon-dominant type pseudodrusen pattern in this study, although a statistical assessment was not performed. Another possible reason for the difference from the previous report is an ethnic difference. In the Japanese, the prevalence of GA is lower compared with Caucasians [16]. Differences of pigmentation of retinal pigment epithelium between Asians and Caucasians might be responsible for the different results.

In the present study, RAP is an independent risk factor for developing late AMD among eyes with pseudodrusen. It is well known that RAP has greater soft drusen than typical AMD [17]. It is reported that drusen load is a predictive factor for development of advanced AMD [18]. Although we classified soft drusen size into 2 groups (larger or smaller than 125  $\mu\text{m}$ ), soft drusen size in eyes with RAP was much greater than 125  $\mu\text{m}$  in the current study. This might be why RAP is an independent risk factor for development of late AMD including exudative AMD or GA in eyes with pseudodrusen.

Of 21 eyes developing late AMD including exudative AMD ( $n=15$ ) and GA ( $n=6$ ), there was no change in the pseudodrusen pattern in either group during the study period. However, complete regression ( $n=2$ ) or partial regression ( $n=7$ ) of pseudodrusen was seen only when eyes with pseudodrusen were converted to late AMD including exudative AMD ( $n=6$ , 40%) and GA ( $n=3$ , 50%). Subretinal or sub-RPE exudation might cause regression of pseudodrusen in eyes developing exudative AMD. Since pseudodrusen were located above RPE layer, RPE attenuation might cause the regression of pseudodrusen in eyes developing GA.

The limitations of this study include the retrospective nature of the analysis and the small sample size; the latter is due to the low prevalence (10–16%) of pseudodrusen in Asian patients with exudative AMD [19, 20]. In addition, the number of eyes developing GA is small, so it might be difficult to draw a definitive conclusion regarding the association between pseudodrusen pattern and development of GA. It is necessary to perform a large-scale, multi-center study to clarify the relationship between pseudodrusen pattern and the development of late AMD in the fellow eyes of Asian patients with unilateral exudative AMD.

In conclusion, a ribbon-dominant type of pseudodrusen pattern is associated with a higher risk of developing late AMD compared with a dot-dominant type in fellow eyes of unilateral exudative AMD patients.

**Table 2** Cox regression analysis of developing late age-related macular degeneration (AMD) in fellow eyes with pseudodrusen in patients with unilateral exudative AMD

	P-value	Hazard ratio	95% CI
Age (years)	0.005	1.10	1.03–1.17
Male	0.12	0.12	0.009–1.67
History of smoking	0.041	17.2	1.11–263
Subfoveal choroidal thickness ( $\mu\text{m}$ )	0.33	0.996	0.987–1.004
RAP (1: RAP; 0: neovascular AMD or PCV)	0.001	5.02	1.90–13.2
Presence of large soft drusen ( $>125 \mu\text{m}$ )	0.021	5.49	1.29–21.1
Pseudodrusen subtype (1: ribbon-dominant; 0: dot-dominant)	0.004	4.15	1.59–10.8

AMD age-related macular degeneration, PCV polypoidal choroidal vasculopathy, RAP retinal angiomatous proliferation, 95% CI 95% confidence interval

**Conflicts of interest** Y Sakurada, Lecture fees (Santen, Bayer, Novartis); A. Sugiyama, None; W. Kikushima, None; S. Yoneyama, None; N. Tanabe, None; M. Matsubara, None; H. Iijima, Speaker fees (Bayer, Santen, Novartis, Shionogi), Lecture fee (Novartis).

## References

- Mimoun G, Soubrane G, Coscas G. Macular drusen. *J Fr Ophthalmol.* 1990;13:511–30 (in French).
- Zweifel SA, Spaide RF, Curcio CA, Malek G, Imamura Y. Reticular pseudodrusen are subretinal drusenoid deposits. *Ophthalmology.* 2010;117(303–12):e301.
- Solomon SD, Jefferys JL, Hawkins BS, Bressler NM, Submacular Surgery Trials Research G. Incident choroidal neovascularization in fellow eyes of patients with unilateral subfoveal choroidal neovascularization secondary to age-related macular degeneration: SST report No. 20 from the submacular surgery trials research group. *Arch Ophthalmol.* 2007;125:1323–30.
- Ueta T, Iriyama A, Francis J, Takahashi H, Adachi T, Obata R, et al. Development of typical age-related macular degeneration and polypoidal choroidal vasculopathy in fellow eyes of Japanese patients with exudative age-related macular degeneration. *Am J Ophthalmol.* 2008;146:96–101.
- Finger RP, Wu Z, Luu CD, Kearney F, Ayton LN, Lucci LM, et al. Reticular pseudodrusen: a risk factor for geographic atrophy in fellow eyes of individuals with unilateral choroidal neovascularization. *Ophthalmology.* 2014;121:1252–6.
- Hogg RE, Silva R, Staurengi G, Murphy G, Santos AR, Rosina C, et al. Clinical characteristics of reticular pseudodrusen in the fellow eye of patients with unilateral neovascular age-related macular degeneration. *Ophthalmology.* 2014;121:1748–55.
- Zhou Q, Daniel E, Maguire MG, Grunwald JE, Martin ER, Martin DF, et al. Pseudodrusen and Incidence of late age-related macular degeneration in fellow eyes in the comparison of age-related macular degeneration treatments trials. *Ophthalmology.* 2016;123:1530–40.
- Zhou Q, Shaffer J, Ying GS. Pseudodrusen in the fellow eye of patients with unilateral neovascular age-related macular degeneration: a meta-analysis. *PLoS One.* 2016;11:e0149030.
- Suzuki M, Sato T, Spaide RF. Pseudodrusen subtypes as delineated by multimodal imaging of the fundus. *Am J Ophthalmol.* 2014;157:1005–12.
- Shijo T, Sakurada Y, Yoneyama S, Sugiyama A, Kikushima W, Tanabe N, et al. Prevalence and characteristics of pseudodrusen subtypes in advanced age-related macular degeneration. *Graefes Arch Clin Exp Ophthalmol.* 2017;255:1125–31.
- Ferris FL, Davis MD, Clemons TE, Lee LY, Chew EY, Lindblad AS, et al. A simplified severity scale for age-related macular degeneration: AREDS Report No. 18. *Arch Ophthalmol.* 2005;123:1570–4.
- Sakurada Y, Yoneyama S, Sugiyama A, Tanabe N, Kikushima W, Mabuchi F, et al. Prevalence and genetic characteristics of geographic atrophy among elderly Japanese with age-related macular degeneration. *PLoS One.* 2016;11:e0149978.
- Wong TY, Chakravarthy U, Klein R, Mitchell P, Zlateva G, Buggege R, et al. The natural history and prognosis of neovascular age-related macular degeneration: a systematic review of the literature and meta-analysis. *Ophthalmology.* 2008;115:116–26.
- Kim JH, Chang YS, Kim JW, Lee TG, Kim CG. Prevalence of subtypes of reticular pseudodrusen in newly diagnosed exudative age-related macular degeneration and polypoidal choroidal vasculopathy in Korean patients. *Retina.* 2015;35:2604–12.
- Elfandi S, Ooto S, Ueda-Arakawa N, Takahashi A, Yoshikawa M, Nakanishi H, et al. Clinical and genetic characteristics of Japanese patients with age-related macular degeneration and pseudodrusen. *Ophthalmology.* 2016;123:2205–12.
- Oshima Y, Ishibashi T, Murata T, Tahara Y, Kiyohara Y, Kubota T. Prevalence of age related maculopathy in a representative Japanese population: the Hisayama study. *Br J Ophthalmol.* 2001;85:1153–7.
- Kim JH, Kim JR, Kang SW, Kim SJ, Ha HS. Thinner choroid and greater drusen extent in retinal angiomatous proliferation than in typical exudative age-related macular degeneration. *Am J Ophthalmol.* 2013;155:743–9.
- Nathoo NA, Or C, Young M, Chui L, Fallah N, Kirker AW, et al. Optical coherence tomography-based measurement of drusen load predicts development of advanced age-related macular degeneration. *Am J Ophthalmol.* 2014;158:757–61.
- Ueda-Arakawa N, Ooto S, Nakata I, Yamashiro K, Tsujikawa A, Oishi A, et al. Prevalence and genomic association of reticular pseudodrusen in age-related macular degeneration. *Am J Ophthalmol.* 2013;155:260–9.
- Yoneyama S, Sakurada Y, Mabuchi F, Imasawa M, Sugiyama A, Kubota T, et al. Genetic and clinical factors associated with reticular pseudodrusen in exudative age-related macular degeneration. *Graefes Arch Clin Exp Ophthalmol.* 2014;252:1435–41.

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