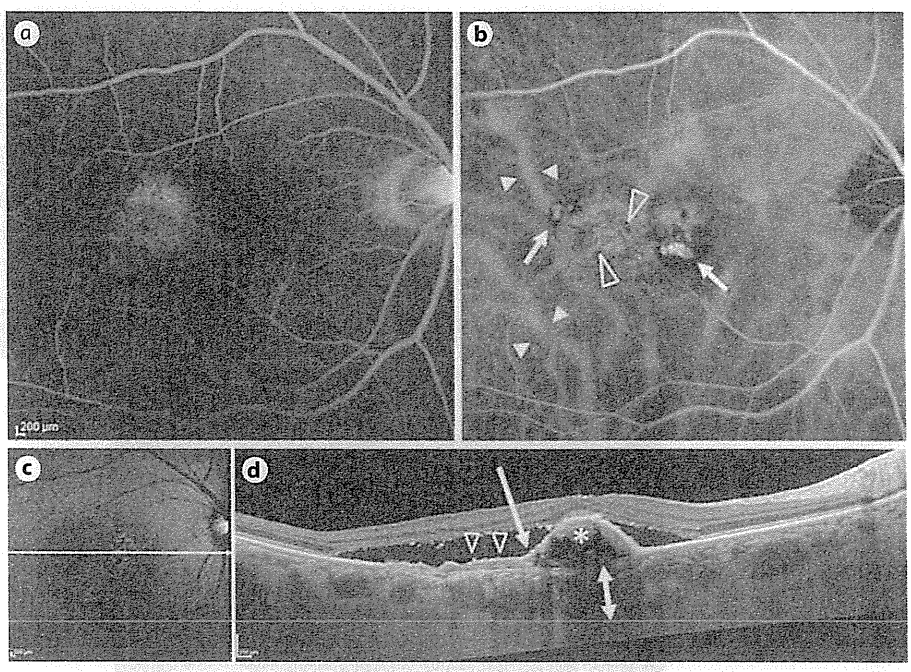

Fig. 4. Corresponding images of FA, ICGA and optical coherence tomography in a PCV case. **a** A window defect is observed in the early phase (1 min) of FA. **b** Polypoidal lesions (arrows) present inside PED are found in ICGA. BVN vessels are found (open arrowheads) in the area which shows the window defect in FA. Choroidal vessels are dilated (filled arrowheads). **c** Infrared image captured by optical coherence tomography which shows the tomographic section line of **d**. **d** A sharp-edged PED and connected lower PED exhibit the tomographic notch sign (long thin arrow). Polypoidal lesions (asterisk) are attached to the back surface of the higher PED, and a BVN exists in the lower PED which is recognized as 'double layer sign' (open arrowheads). Subfoveal choroidal thickness is remarkably increased (bidirectional arrows).

smaller polyp size on ICGA, smaller choroidal thickness [57–59] and lower response to photodynamic therapy (PDT) as compared to type 2 PCV [60].

Optical Coherence Tomography

In most PCV cases, optical coherence tomography (OCT) revealed a sharply elevated PED with/without connecting lower PEDs, which may cause the so-called 'tomographic notch sign' (fig. 4) [61]. Polypoidal lesions are likely to attach to the back surface of higher PEDs, and BVN present in the lower PED can be recognized as the 'double layer sign' by high-resolution OCT. This sign represents the BVN invading into the space between the RPE and Bruch's membrane, which is commonly found in CNV due to tAMD. Because CNV in tAMD is thought to pass through Bruch's membrane and grow under (and often over) the RPE layer, at least 1 broken site of Bruch's membrane should be detected. Using OCT, suspected broken sites of Bruch's membrane are often observed in type 1 PCV at the origin of the BVN [57]. These findings suggest that PCV is a type of CNV. However, the 'double layer sign' found in PCV may not necessarily mean the isolation of the RPE from Bruch's membrane. A recent study reported that the isolation between Bruch's membrane and the inner choroidal surface also exhibits a 'double layer sign', which means that the BVN of the PCV may remain under Bruch's membrane with polypoidal lesions [57] (fig. 6). An increase in central choroidal thickness is frequently observed by high-resolution OCT with enhanced-depth imaging or by high-permeability OCT [62, 63] (fig. 4). Several studies reported that the mean choroidal thickness of PCV patients was significantly larger than that of normal subjects [62, 64–66]. This increase in choroidal thickness was reported to be associated with increased oc-

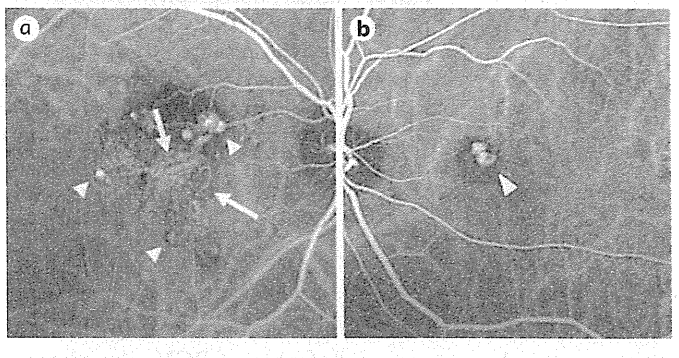

Fig. 5. Two different angiographic subtypes of PCV. Images are obtained in the early phase (up to 1 min) of ICGA. **a** Type 1 PCV shows polypoidal lesions (arrowheads) with clear BVNs (arrows). **b** Type 2 PCV shows polypoidal lesions (arrowhead) without or faint vascular networks.

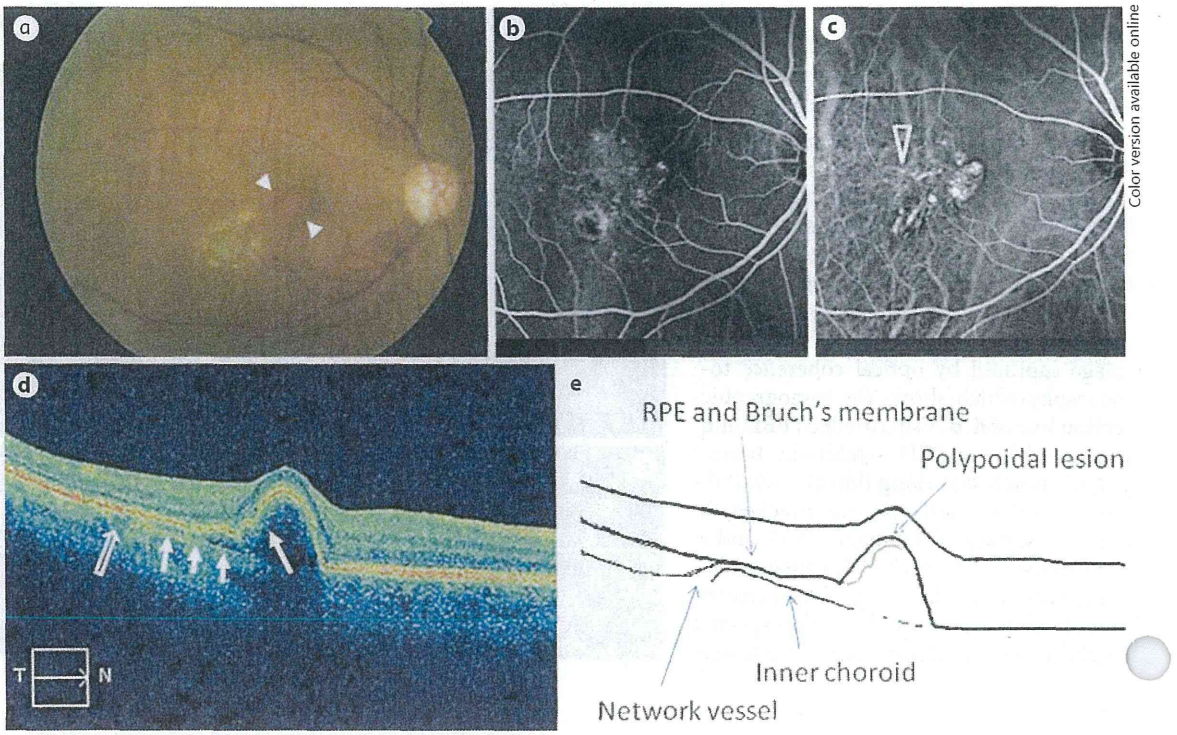

Fig. 6. Fundus photography, FA, ICGA and OCT images of type 2 PCV. **a** An orange-red lesion (arrowheads) is found at the fovea. **b** An occult with no classic lesion is observed by FA. **c** Distinct polypoidal lesions with a faint network vessel (open arrowhead) are found in ICGA. **d** The origin of a network vessel is indicated with an open arrow. The suspected isolation between Bruch's membrane and the inner choroidal surface (short arrows) exhibits the 'double layer sign' in OCT. Polypoidal lesions (long arrow) are located on the back surface of the detached RPE with underlying Bruch's membrane. **e** Explanatory illustration of **d**.

ular perfusion pressure and an engorgement of the vortex vein [67, 68]. It is interesting that central serous chorioretinopathy, known as a risk factor of PCV, also shows a remarkable increase in choroidal thickness [62, 64].

Fundus Autofluorescence

Fundus autofluorescence studies performed for PCV have been recently reported. In the affected eyes with PCV, confluent hypoautofluorescence at the polypoidal lesions surrounded by a hyperautofluorescent ring was seen in 80.4% of PCV cases, and granular hypoautofluorescence at the BVN was seen in 98.9% of PCV cases. In addition, 42.4% of eyes with PCV showed hypoautofluorescence outside the macular area. In the unaffected fellow eyes, hypoautofluorescence was observed inside the macular area (58.1%) and in the entire fundus autofluorescence image (62.8%) in patients with PCV [69, 70].

Histopathology

Histopathological studies of PCV using human specimens were conducted by obtaining subretinal tissues during vitreoretinal surgeries [55, 71–75]. One report noted that polypoidal structures were located within Bruch's space. They were composed of clusters of dilated, thin-walled blood vessels surrounded by macrophages and fibrin material [71]. Kuroiwa et al. [72] reported that 4 of their 5 cases demonstrated large choroidal arterioles with an inner elastic layer; disruption of the inner elastic layer and arteriosclerotic changes of the vessels were identified. Increased deposition of basement membrane-like material, together with collagen fibers, arterioles and venules, can be found in excised specimens from patients with PCV, and arteriosclerosis was an important pathological feature [72]. Another histopathological examination revealed that the specimen consisted of a degenerated RPE-Bruch's membrane-choriocapillaris complex and an in-

ner choroid. A tortuous, unusually dilated venule was present adjacent to an arteriole with marked sclerotic changes, appearing to form an arteriovenous crossing. These vessels seemed to represent native inner choroidal vessels, and had hemorrhage per diapedesis. Blood cells and fibrin filled the lumina of these vessels, and accumulated in the extravascular spaces, thus indicating vascular stasis [55]. Hyperpermeability and hemorrhage due to stasis of a dilated venule and an arteriole involved by sclerosis at the site where they crossed in the inner choroid might cause edema and degeneration of the tissue. A voluminous accumulation of blood cells and fibrin might generate an elevation of tissue pressure sufficient to displace the weakened lesion anteriorly. These results suggest that the polypoidal vessels in this case represent an abnormality in the inner choroidal vasculature. Another study reported positive immunohistochemical staining for vascular endothelial growth factor (VEGF) in the RPE and the vascular endothelial cells in the specimen, which suggested that the fibrovascular complex was a subretinal CNV [73]. In a recent study, hyalinization of the choroidal vessels and a massive exudation of fibrin and blood plasma with a change in the arteriosclerosis were observed in all of the specimens from PCV lesions. Some blood vessels were located above the RPE in 2 of the 5 eyes analyzed [74]. Immunohistochemically, CD68-positive cells were detected around the hyalinized vessels. There were no smooth muscle actin-positive cells in the vessels in the PCV. CD34 staining showed endothelial discontinuity. Vascular endothelial cells within the PCV specimens were immunonegative for VEGF. Hypoxia inducible factor-1-immunopositive inflammatory cells were located in the stroma of specimens [74].

Genetic Factors

The molecular mechanisms responsible for the onset of disease, for the outcomes of the natural course, or any interventions, are not understood in PCV. Genetic association analysis was thought to be a useful tool to find those molecules which may be involved in the pathogenesis of this disease. For example, genetic variants in the complement factor H (CFH) gene on chromosome 1q32 [75–79] and in 2 tightly linked genes, age-related maculopathy susceptibility 2 (ARMS2), also known as LOC387715, and high-temperature requirement factor A1 (HTRA1) on 10q26 [80–83] are well known as major contributors to AMD. In particular, the single-nucleotide polymorphism (SNP) at rs1061170 (coding variant Y402H) in the CFH gene is presumed to have functional consequences consistent with AMD pathology [84]. However, the CFH Y402H variant shows apparent ethnic differences in its association with AMD because of the frequency of the risk allele (C allele); the risk allele frequency is 0.38 in Caucasians in the HapMap database [85], but it is 0.057 in the Japanese population and 0.067 in the Chinese population. Hence, CFH Y402H shows a strong association with AMD in Caucasians, but it was difficult to detect a positive association with Asian AMD cases owing to a limitation in statistical power [86–89]. Recently, large population studies and meta-analyses came to identify the CFH Y402H variant as a significant genetic risk factor in Asian AMD [20, 90], although the susceptibility conferred by the Y402H variant may not translate across ethnic lines. However, other multiple CFH variants have been shown to be associated with AMD in Asians [89, 91–93]. In particular, the CFH I62V variant was significantly associated with AMD (allelic OR = 1.85, 95% CI = 1.63–2.09) in a meta-analysis of Asian cohorts although no significant association of this SNP was established with AMD in Caucasian populations [91]. These reports suggested that variations in the CFH gene universally influence AMD susceptibility, but causal SNPs in the CFH region may vary among races.

Although limited information is available on the genetic basis of PCV, several studies demonstrated how genetics play an important role in the pathogenesis of PCV. The 2 major AMD susceptibility loci (CFH and ARMS2/HTRA1) have been shown to influence the risk of PCV [18–20, 94–100]. In particular, SNPs in the ARMS2/HTRA1 locus, rs10490924 (A69S) and rs11200638, are significantly associated with PCV [18, 20, 22–24]. Moreover, recent transgenic mouse studies demonstrated that the overexpression of HTRA1 displayed the cardinal features of PCV, including branching networks of choroidal vessels, polypoidal lesions and severe degeneration of the elastic laminae and tunica media of the choroidal vessels [101, 102]. However, all genetic association studies showed a weaker association of ARMS2/HTRA1 with PCV than with tAMD, although the reasons were unknown (table 1). Those results raised the question whether other susceptible genes which are specific for PCV pathogenesis may exist. A previous report showed that coding variants of the elastin gene (rs2301995 and rs2856728) were associated with PCV, but not with tAMD [103]. However, two subsequent reports with larger cohorts showed the opposite results: the elastin gene polymorphism was associated with tAMD but not with PCV [22, 104], which made the association of elastin gene vari-

Table 1. Genetic association analysis studies for ARMS2 rs10490924 (A69S) in tAMD and PCV

Study	Year	Ethnicity	Number of genotypes (GG/GT/TT)			Risk allele frequency		
			tAMD	PCV	control	tAMD	PCV	control
Sakurada et al. [109]	2008	Japanese	NA	15/49/45	39/32/14	NA	0.64	0.35
Lee et al. [102]	2008	Chinese	NA	17/30/25	33/48/12	NA	0.56	0.39
Gotoh et al. [19]	2009	Japanese	18/30/52	18/50/32	85/84/20	0.67	0.57	0.33
Hayashi et al. [20]	2010	Japanese	67/155/183	122/216/171	502/638/196	0.64	0.55	0.39
Fuse et al. [21]	2011	Japanese	6/20/24	22/20/18	64/58/16	0.68	0.47	0.33
Tanaka et al. [22]	2011	Japanese	46/81/126	94/162/125	99/142/36	0.66	0.54	0.39
Yanagisawa et al. [23]	2011	Japanese	26/81/74	42/77/79	79/94/30	0.63	0.59	0.38
Liang et al. [24]	2012	Chinese	15/46/90	23/79/60	90/117/40	0.75	0.61	0.40

NA = Not assessed.

ants with tAMD and PCV inconclusive. Those results might have occurred due to statistical type 1 and type 2 errors, but it is also possible that PCV is not a genetically homogeneous pathology. Another study reported that a missense variant at rs5882 in the cholesteryl ester transfer protein gene, a key regulator of high-density lipoprotein metabolism, was significantly associated with PCV ($p = 2.73 \times 10^{-4}$), although it was not associated with tAMD [25]. The rs5882 GG genotype had a 3.53-fold (95% CI = 1.93–6.45) increased risk for PCV, and conferred a significantly lower serum high-density lipoprotein cholesterol level in PCV patients than the AA genotype ($p = 0.048$). On chromosome 9p21, which is well known to be associated with coronary artery disease and type 2 diabetes, rs10757278 was significantly associated with PCV (risk allele: A, allelic $p = 0.014$; OR = 1.44; 95% CI = 1.08–1.94), but was not associated with tAMD [105].

Recently, two studies demonstrated a difference in the association of the rs10490924 (A69S) variant in ARMS2 between the two angiographic phenotypes of PCV, type 1 PCV and type 2 PCV [27, 58] (fig. 5). In those studies, no association of the ARMS2 A69S polymorphism with type 2 PCV was detected, whereas type 1 PCV showed a strong association with the ARMS2 A69S variant. Since the ARMS2 polymorphism is widely known to associate with AMD, their report indicates the existence of heterogenic susceptibility within PCV phenotypes, which may contribute to the different characteristics of PCV versus tAMD. This dissociation between the two angiographic phenotypes might suggest a correlation of ARMS2 with the formation of the BVN in PCV. In addition, this genetic heterogeneity in PCV may be a reason for the lower association of ARMS2/HTRA1 with PCV, including both phenotypes (types 1 and 2), than with tAMD.

Natural Course

Previous studies have reported that the natural course of PCV is favorable, since it often shows spontaneous regression [10–12, 28]. However, on the other hand, it often causes severe hemorrhagic and exudative changes that result in a poor visual prognosis [12, 13]. The clinical risk factors for a poor prognosis in PCV have been previously evaluated [11–13]. Bessho et al. [13] investigated the natural course of PCV in terms of the changes in the best-corrected VA (BCVA) after 12 months of observation, and found that the mean BCVA of PCV patients worsened significantly over the natural course. The clustered polypoidal choroidal lesions detected by ICGA were associated with a poor prognosis over the natural course. In this report, over 20% of PCV patients gained VAs of more than 0.2 logMAR, whereas about 50% of the patients lost their VA by more than 0.2 logMAR during the 12 months after the initial visit. The presence of serous PED is a suspected risk factor, whereas the presence of subretinal fibrinous material is a possible beneficial factor for the 12-month BCVA in PCV patients. Since polyp lesions are mostly present at the margin and inside the PED, and serous PED suggests strong infiltrating activity of the PCV [106], the accelerated infiltration from the polyp lesions into the subretinal pigment epithelial space may increase the tension on the PED flap, and thus cause PED microrips followed by acute decompression of the PED and increased blood flow in the polyp lesions. This then results in the rupture of these polyp lesions, and acute severe hemorrhage. In fact, PCV is often associated with systemic hypertension [38–40]. Subretinal fibrinous material, often observed on the PED in PCV patients, may be a beneficial factor for the visual prognosis over the natural

course or after treatment [13, 44, 45]. Although the detailed mechanism of how this subretinal fibrinous material contributes to a better prognosis for PCV over its natural course is unknown, the involvement of an acute inflammatory pathway to produce this fibrinous material was suspected in certain cases of PCV [74, 107, 108], which often resolve spontaneously like common inflammatory conditions.

The clustered lesions found by ICGA induced a disadvantage to the visual outcome in PCV [12, 13]. As a genetic risk factor, the risk alleles at rs10490924 and rs11200638 in the ARMS2/HTRA1 locus were reported to be significantly associated with a larger lesion size, a higher risk of vitreous hemorrhage, an earlier onset and a bilateral involvement, as compared to nonrisk allele holders in PCV cases [19, 109–111].

Response to Treatment

Photodynamic Therapy

Evidence is accumulating that PCV shows a better response to PDT than tAMD [14, 15, 112]. Most studies reported that the mean posttreatment VA was improved in PCV over a short-term follow-up (up to 1 year). In particular, most polypoidal lesions regressed by PDT whereas the BVN remains after PDT [113–116]. A recent multicenter randomized controlled trial revealed that polyp lesions disappeared in more than 70% of the PCV cases within 6 months after PDT [117]. However, several reports suggested some heterogeneity in the response to PDT among PCV patients [15, 52]. Tamura et al. [45] reported better outcomes for PCV cases with subretinal fibrinous material adjacent to the polypoidal lesions treated with PDT. In accordance with the literature, PCV cases with grape-shaped polyp lesions showed poorer outcomes than other PCV cases. In view of the angiographic subtypes of PCV, type 1 PCV is considered to be more refractory to PDT than type 2 PCV [60]. Although the mean VA was improved and maintained up to 12 months after PDT in most reports [14, 15, 112–119], longer observational studies revealed that the merit of therapy was reduced 12 months after the initial PDT, mainly due to recurrences of the lesions [14, 120–122]. Consequently, the improvement in the mean VA of the PCV patients was not significant anymore 30–36 months after the initial PDT [14, 121, 122]. Moreover, it could be below the baseline value 5 years after the treatment [123–125]. Persistent BVN may be the origin of new polypoidal lesions [126]. In a recent prospective cohort study, 56 out of 139 eyes (40%) in the tAMD cases and 52 out of 107 eyes (49%) in the PCV cases were recurrent during the 60 months of follow-up after the initial PDT [123]. In particular, 44 eyes (32%) in the tAMD and 27 eyes (25%) in the PCV cases were recurrent within 12 months after the initial resolution of the lesions obtained by PDT. The mean recurrence period during the 60 months of follow-up was 15.7 ± 13.5 months (mean ± SD) in the PCV group, which was significantly longer than in the tAMD group (8.6 ± 9.3 months). The mean VA was maintained for 60 months in the tAMD and PCV patients who showed no recurrence of their lesions.

Recently, genetic variants in the CFH gene have been tested to explain the response to PDT. In particular, the Y402H coding variant (rs1061170) in CFH is presumed to have functional consequences consistent with AMD pathology [84], and most studies were performed to determine whether CFH Y402H correlates with the outcome of PDT [127–131]. In tAMD, Brantley et al. [129] reported an association of the CFH Y402H variant with the visual outcome after PDT. In that study, the C allele was beneficial for the patients. Goverdhan et al. [131] also reported the positive association of CFH Y402H with the outcome of PDT in tAMD, but discovered the C allele as the risk allele for a better VA. On the other hand, other studies failed to demonstrate any association of this variant with the outcome of PDT [127, 128, 130]. In PCV cases, one study demonstrated that the SNPs rs1061170 (Y402H) and rs1410996 in the CFH region were significantly associated with an anatomical response to PDT [132]. Two studies found that the genotype at rs10490924 (A69S) in ARMS2 was significantly associated with the lesion size in PCV patients, as well as the visual outcome in tAMD and PCV patients 12 months after their first PDT [110, 133]. Therefore, patients with more G alleles at rs10490924 showed better BCVA values until 12 months after their first PDT. Nakata et al. [134] reported that a variant at rs12603825 in the pigment epithelium-derived factor gene was associated with the recurrence-free period, and our own study revealed a significant association of the SNP at rs3173798 in the CD36 gene with the visual outcome of PDT in a dominant model. The presence of the C allele in rs3173798 was significantly associated with a poor response to PDT after multivariate logistic regression analysis with clinical pre-PDT parameters. The mean BCVA in the group with the TT genotype of rs3173798 was significantly improved over the 12 months of follow-up after the initial PDT [135].

Table 2. CFH Y402H variants and their influence on the outcome of anti-VEGF therapy

Authors	Anti-VEGF agent	Cases, n	Main outcome measures	Genotypes with beneficial effects
Smailhodzic et al. [155]	Ranibizumab	420	Posttreatment VA at 3 months (logMAR)	TT > CC
Kloeckener-Gruissem et al. [151]	Ranibizumab	243 (63/63 eyes)	Change in VA at 12 months from baseline (upper 25%/lower 25%)	TT, CT > CC
Lee et al. [153]	Ranibizumab	156	Number of retreatments during 9 months	TT > CC
Orlin et al. [150]	Ranibizumab, bevacizumab	150	Posttreatment VA deterioration +/–)	NS
McKibbin et al. [152]	Ranibizumab	104	Change in VA at 6 months from baseline (more than 5-letter improvements +/–)	CC, CT > TT
Chang et al. [158]	Ranibizumab	102	Posttreatment VA at 3 and 6 months (logMAR)	CC > CT > TT (tendency, NS)
Yamashiro et al. [147]	Ranibizumab	75	Posttreatment VA at 3 and 12 months (logMAR)	NS

NS = Not significant.

Table 3. SNPs in the VEGF-A region and the effects on the outcome of anti-VEGF therapy

SNP ID	Location	Major/minor allele	Main outcome measures	Genotypes with beneficial effects
rs1413711	Intron 1	C/T	Change in VA at 6 months from baseline (more than 5-letter improvements +/–)	CC, CT > TT [152]
rs833069	Intron 2	A/G	Change in CRT at 3 months from baseline Change in VA (logMAR) at 3 months from baseline	GG > AA [158] NS [155]
rs3025000	Intron 3	C/T	Change in ETDRS letters at 6 months from baseline	CC < CT, TT [159]
rs699947	Promoter	C/A	Change in VA (logMAR) at 3 months from baseline Change in VA (logMAR) at 12 months from baseline	NS [155] NS [160]
rs699946	Promoter	G/A	Change in VA (logMAR) at 12 months from baseline	GG > GA > AA [160]

CRT = Central retinal thickness; NS = not significant; ETDRS = Early Treatment Diabetic Retinopathy Study.

Anti-VEGF Therapy

The intravitreal injection of anti-VEGF agents is currently the primary treatment for exudative AMD. Studies from Western countries have reported significantly better visual outcomes with monthly intravitreal injections of ranibizumab (IVR) than PDT in exudative AMD patients [136, 137], but these studies did not distinguish between the phenotypes of AMD, and the effects of anti-VEGF therapy for PCV may differ from those for tAMD. Overall, the effects of IVR monotherapy against PCV are currently contentious, and no consensus has been reached to date. Some studies reported that the polypoidal lesions of PCV were barely resolved by anti-VEGF monotherapy, which might explain the limited efficacy of IVR against PCV [138–140]. However, Song et al. [141] reported that IVR without PDT for PCV in Korean patients resulted in significant visual and anatomical improvements over a 1-year follow-up period, and other

reports suggested that the disappearance of the polypoidal lesions occurred at a high rate in PCV cases after anti-VEGF monotherapy [74, 142, 143]. A recent review suggested an overall improvement of the VA of PCV patients using IVR [144], and a most recent multicenter randomized controlled trial (LAPTOP study) revealed that IVR monotherapy achieved a significantly better visual prognosis than PDT monotherapy in PCV patients [145]. However, Matsumiya et al. [16, 17] reported that the degree of improvement in the VA in PCV patients was lower than that of tAMD patients treated by anti-VEGF monotherapy. Some reports demonstrated that several pretreatment factors influenced the outcome of IVR [16, 17, 146], which might be useful to predict the visual and anatomical consequences for PCV patients who undergo IVR.

Although very little has been studied about the genetic factors associated with the outcome of IVR in PCV patients [147], a number of recent studies assessed the possible genetic factors associated with the outcome of IVR in tAMD patients [147–160]. Most studies focused on the SNPs in the CFH, ARMS2 and VEGF-A genes, since these genes were reported to be associated with the pathogenesis of exudative AMD, but a consistent conclusion has not been made to date (tables 2, 3). In particular, CFH Y402H was the most studied SNP and many reports demonstrated that the C allele in CFH Y402H was associated with the reduced response to anti-VEGF therapy [151, 154, 155]. Since the C allele in CFH Y402H is known to be a risk allele for the incidence of exudative AMD, C allele-rich cases likely have more active lesions than the others, and hence those cases are likely more refractory to the treatment. A recent meta-analysis demonstrated the association of CFH Y402H with the visual outcome of IVR in Caucasians (the CC genotype showed a decreased response to anti-VEGF therapy compared to the TT genotype) [148]. However, more recent reports described that the C allele was beneficial for the posttreatment BCVA in British and Korean populations over shorter (3 and 6 months) follow-up periods [152, 158]. The risk/benefit effects of CFH Y402H regarding the treatment outcome might be changed by the proportion of AMD phenotypes at baseline or by the duration of the follow-up period. Moreover, the association of CFH Y402H with the outcome of IVR might be different between Caucasians and Asians, since the frequency of the C allele is very low in Asian populations [90]. Although Chang et al. [158] and Yamashiro et al. [147] reported a relatively better visual outcome (though not significantly better) in the C-rich genotypes than the others for CFH Y402H in the Asian populations, additional meta-analyses will be required to conclude the association of CFH Y402H with the visual outcome of IVR in Asians, particularly in PCV cases.

Combination Therapy

Recently, a multicenter randomized controlled trial (EVEREST study) was conducted to compare the effects of PDT monotherapy, IVR monotherapy and their combination (PDT + IVR) in patients with PCV. It reported that all therapies resulted in improvements of the patients' VAs 6 months after treatment [117]. In addition, PDT monotherapy and combination therapy achieved a significantly higher proportion of patients with complete polyp regression (more than 70%) at 6 months than IVR monotherapy (less than 30%). Similar results were reported in other studies with different populations [113, 116, 139, 143, 146, 161]. Considering the results from recent publications, combination therapy is likely the most effective modality for treating PCV. However, the cost-effectiveness of combination therapy should be carefully assessed, and a strategy to select the appropriate candidates for this therapy should be established because of its expense.

In the future, it will be important to evaluate the long-term results of each modality with a large number of subjects to determine the efficacy and durability of this therapy, particularly in PCV patients.

Conclusions

As described above, PCV is a unique phenotype of AMD which should be handled with a different strategy from tAMD. In particular, the effects of various treatment modalities may be different between tAMD and PCV, which necessitate further investigation to determine the correct indications for PDT, anti-VEGF therapy and combination therapy for PCV. Moreover, genetic association analyses may disclose the difference in the pathogenesis between tAMD and PCV, and may indicate how to choose the appropriate interventions for each PCV patient.

Disclosure Statement

The authors report no conflicts of interest.

References

1 Yannuzzi LA, Sorenson J, Spaide RF, et al: Idiopathic polypoidal choroidal vasculopathy (IPCV). Retina 1990;10:1–8.
2 Kleiner RC, Brucker AJ, Johnston RL: The posterior uveal bleeding syndrome. Retina 1990;10:9–17.
3 Stern RM, Zakov ZN, Zegarra H, Gutman FA: Multiple recurrent serosanguineous retinal pigment epithelial detachments in black women. Am J Ophthalmol 1985;100:560–569.
4 Yannuzzi LA, Ciardella A, Spaide RF, et al: The expanding clinical spectrum of idiopathic polypoidal choroidal vasculopathy. Arch Ophthalmol 1997;115:478–485.
5 Yannuzzi LA, Wong DW, Sforzolini BS, Goldbaum M, Tang KC, Spaide RF, Freund KB, Slakter JS, Guyer DR, Sorenson JA, Fisher Y, Maberley D, Orlock DA: Polypoidal choroidal vasculopathy and neovascularized age-related macular degeneration. Arch Ophthalmol 1999;117:1503–1510.
6 Lim TH, Laude A, Tan CS: Polypoidal choroidal vasculopathy: an angiographic discussion. Eye (Lond) 2010;24:483–490.
7 Goldman DR, Freund KB, McCannel CA, Sarraf D: Peripheral polypoidal choroidal vasculopathy as a cause of peripheral exudative hemorrhagic chorioretinopathy: a report of 10 eyes. Retina 2013;33:48–55.
8 Mantel I, Schalenbourg A, Zografos L: Peripheral exudative hemorrhagic chorioretinopathy: polypoidal choroidal vasculopathy and hemodynamic modifications. Am J Ophthalmol 2012;153:910–922.
9 Laude A, Cackett PD, Vithana EN, Yeo IY, Wong D, Koh AH, Wong TY, Aung T: Polypoidal choroidal vasculopathy and neovascular age-related macular degeneration: same or different disease? Prog Retin Eye Res 2010;29:19–29.
10 Uyama M, Matsubara T, Fukushima I, et al: Idiopathic polypoidal choroidal vasculopathy in Japanese patients. Arch Ophthalmol 1999;117:1035–1042.
11 Sho K, Takahashi K, Yamada H, et al: Polypoidal choroidal vasculopathy: incidence, demographic features, and clinical characteristics. Arch Ophthalmol 2003;121:1392–1396.
12 Uyama M, Wada M, Nagai Y, et al: Polypoidal choroidal vasculopathy: natural history. Am J Ophthalmol 2002;133:639–648.
13 Bessho H, Honda S, Imai H, Negi A: Natural course and funduscopic findings of polypoidal choroidal vasculopathy in a Japanese population over one year of follow-up. Retina 2011;31:1598–1602.
14 Honda S, Kurimoto Y, Kagotani Y, et al: Photodynamic therapy for typical age-related macular degeneration and polypoidal choroidal vasculopathy: a 30-month multicenter study in Hyogo, Japan. Jpn J Ophthalmol 2009;53:593–597.
15 Honda S, Imai H, Yamashiro K, et al: Comparative assessment of photodynamic therapy for typical age-related macular degeneration and polypoidal choroidal vasculopathy: a multicenter study in Hyogo prefecture, Japan. Ophthalmologica 2009;223:333–338.
16 Matsumiya W, Honda S, Kusuhara S, Tsukahara Y, Negi A: Effectiveness of intravitreal ranibizumab in exudative age-related macular degeneration (AMD): comparison between typical neovascular AMD and polypoidal choroidal vasculopathy over a 1 year follow-up. BMC Ophthalmol 2013;13:10.
17 Matsumiya W, Honda S, Bessho H, Kusuhara S, Tsukahara Y, Negi A: Early responses to intravitreal ranibizumab in typical neovascular age-related macular degeneration and polypoidal choroidal vasculopathy. J Ophthalmol 2011;2011:742020.
18 Kondo N, Honda S, Ishibashi K, Tsukahara Y, Negi A: LOC387715/HTRA1 variants in polypoidal choroidal vasculopathy and age-related macular degeneration in a Japanese population. Am J Ophthalmol 2007;144:608–612.
19 Gotoh N, Nakanishi H, Hayashi H, Yamada R, Otani A, Tsujikawa A, Yamashiro K, Tamura H, Saito M, Saito K, Iida T, Matsuda F, Yoshimura N: ARMS2 (LOC387715) variants in Japanese patients with exudative age-related macular degeneration and polypoidal choroidal vasculopathy. Am J Ophthalmol 2009;147:1037–1041.
20 Hayashi H, Yamashiro K, Gotoh N, Nakanishi H, Nakata I, Tsujikawa A, Otani A, Saito M, Iida T, Matsuo K, Tajima K, Yamada R, Yoshimura N: CFH and ARMS2 variations in age-related macular degeneration, polypoidal choroidal vasculopathy, and retinal angiomatous proliferation. Invest Ophthalmol Vis Sci 2010;51:5914–5919.
21 Fuse N, Mengkegale M, Miyazawa A, Abe T, Nakazawa T, Wakusawa R, Nishida K: Polymorphisms in ARMS2 (LOC387715) and LOXL1 genes in the Japanese with age-related macular degeneration. Am J Ophthalmol 2011;151:550–556.
22 Tanaka K, Nakayama T, Yuzawa M, Wang Z, Kawamura A, Mori R, Nakashizuka H, Sato N, Mizutani Y: Analysis of candidate genes for age-related macular degeneration subtypes in the Japanese population. Mol Vis 2011;17:2751–2758.
23 Yanagisawa S, Kondo N, Miki A, Matsumiya W, Kusuhara S, Tsukahara Y, Honda S, Negi A: Difference between age-related macular degeneration and polypoidal choroidal vasculopathy in the hereditary contribution of the A69S variant of the age-related maculopathy susceptibility 2 gene (ARMS2). Mol Vis 2011;17:3574–3582.
24 Liang XY, Lai TY, Liu DT, Fan AH, Chen LJ, Tam PO, Chiang SW, Ng TK, Lam DS, Pang CP: Differentiation of exudative age-related macular degeneration and polypoidal choroidal vasculopathy in the ARMS2/HTRA1 locus. Invest Ophthalmol Vis Sci 2012;53:3175–3182.
25 Zhang X, Li M, Wen F, Zuo C, Chen H, Wu K, Zeng R: Different impact of high-density lipoprotein-related genetic variants on polypoidal choroidal vasculopathy and neovascular age-related macular degeneration in a Chinese Han population. Exp Eye Res 2013;108:16–22.
26 Tsujikawa A, Ojima Y, Yamashiro K, Nakata I, Ooto S, Tamura H, Nakanishi H, Hayashi H, Otani A, Yoshimura N: Association of lesion size and visual prognosis to polypoidal choroidal vasculopathy. Am J Ophthalmol 2011;151:961–972.
27 Miki A, Honda S, Kondo N, Negi A: The association of age-related maculopathy susceptibility 2 (ARMS2) and complement factor H (CFH) variants with two angiographic subtypes of polypoidal choroidal vasculopathy. Ophthalmic Genet 2013;34:146–150.
28 Imamura Y, Engelbert M, Iida T, Freund KB, Yannuzzi LA: Polypoidal choroidal vasculopathy: a review. Surv Ophthalmol 2010;55:501–515.
29 Al-Rashaed S: Idiopathic polypoidal choroidal vasculopathy in a young man: case report and literature review. Middle East Afr J Ophthalmol 2008;15:90–93.
30 Maruko I, Iida T, Saito M, Nagayama D, Saito K: Clinical characteristics of exudative age-related macular degeneration in Japanese patients. Am J Ophthalmol 2007;144:15–22.
31 Chang YC, Wu WC: Polypoidal choroidal vasculopathy in Taiwanese patients. Ophthalmic Surg Lasers Imaging 2009;40:576–81.
32 Wen F, Chen C, Wu D, Li H: Polypoidal choroidal vasculopathy in elderly Chinese patients. Graefes Arch Clin Exp Ophthalmol 2004;242:625–629.
33 Liu Y, Wen F, Huang S, Luo G, Yan H, Sun Z, Wu D: Subtype lesions of neovascular age-related macular degeneration in Chinese patients. Graefes Arch Clin Exp Ophthalmol 2007;245:1441–1445.
34 Song SJ, Youm DJ, Chang Y, Yu HG: Age-related macular degeneration in a screened South Korean population: prevalence, risk factors, and subtypes. Ophthalmic Epidemiol 2009;16:304–310.
35 Byeon SH, Lee SC, Oh HS, Kim SS, Koh HJ, Kwon OW: Incidence and clinical patterns of polypoidal choroidal vasculopathy in Korean patients. Jpn J Ophthalmol 2008;52:57–62.
36 Ciardella AP, Donsoff IM, Huang SJ, Costa DL, Yannuzzi LA: Polypoidal choroidal vasculopathy. Surv Ophthalmol 2004;49:25–37.
37 Tsujikawa A, Nakanishi H, Ojima Y, Iwama D, Tamura H, Otani A, Yoshimura N: Macular polypoidal choroidal vasculopathy with a remote lesion. Clin Experiment Ophthalmol 2008;36:817–823.
38 Ueta T, Obata R, Inoue Y, et al: Background comparison of typical age-related macular degeneration and polypoidal choroidal vasculopathy in Japanese patients. Ophthalmology 2009;116:2400–2406.

39 Sakurada Y, Yoneyama S, Imasawa M, Iijima H: Systemic risk factors associated with polypoidal choroidal vasculopathy and neovascular age-related macular degeneration. Retina 2013;33:841–845.

40 Hirami Y, Tsujikawa A, Otani A, Yodoi Y, Aikawa H, Mandai M, Yoshimura N: Hemorrhagic complications after photodynamic therapy for polypoidal choroidal vasculopathy. Retina 2007;27:335–341.

41 Kikuchi M, Nakamura M, Ishikawa K, et al: Elevated C-reactive protein levels in patients with polypoidal choroidal vasculopathy and patients with neovascular age-related macular degeneration. Ophthalmology 2007;114:1722–1727.

42 Cackett P, Yeo I, Cheung CM, Vithana EN, Wong D, Tay WT, Tai ES, Aung T, Wong TY: Relationship of smoking and cardiovascular risk factors with polypoidal choroidal vasculopathy and age-related macular degeneration in Chinese persons. Ophthalmology 2011;118:846–852.

43 Japanese Study Group of Polypoidal Choroidal Vasculopathy: Criteria for diagnosis of polypoidal choroidal vasculopathy (in Japanese). Nippon Ganka Gakkai Zasshi 2005;109:417–427.

44 Otsuji T, Tsumura A, Takahashi K, et al: Evaluation of cases of polypoidal choroidal vasculopathy showing classic choroidal neovascularisation in their natural course. J Jpn Ophthalmol Soc 2006;110:454–461.

45 Tamura H, Tsujikawa A, Otani A, et al: Polypoidal choroidal vasculopathy appearing as classic choroidal neovascularisation on fluorescein angiography. Br J Ophthalmol 2007;91:1152–1159, erratum in Br J Ophthalmol 2007;91:1572.

46 Musashi K, Tsujikawa A, Hirami Y, Otani A, Yodoi Y, Tamura H, Yoshimura N: Microrips of the retinal pigment epithelium in polypoidal choroidal vasculopathy. Am J Ophthalmol 2007;143:883–885.

47 Tsujikawa A, Hirami Y, Nakanishi H, Ojima Y, Aikawa H, Tamura H, Otani A, Yoshimura N: Retinal pigment epithelial tear in polypoidal choroidal vasculopathy. Retina 2007;27:832–838.

48 Cackett P, Wong D, Yeo I: A classification system for polypoidal choroidal vasculopathy. Retina 2009;29:187–191.

49 Hirami Y, Mandai M, Takahashi M, Teramukai S, Tada H, Yoshimura N: Association of clinical characteristics with disease subtypes, initial visual acuity, and visual prognosis in neovascular age-related macular degeneration. Jpn J Ophthalmol 2009;53:396–407.

50 Yuzawa M, Mori R, Kawamura A: The origins of polypoidal choroidal vasculopathy. Br J Ophthalmol 2005;89:602–607.

51 Okubo A, Ito M, Sameshima M, Uemura A, Sakamoto T: Pulsatile blood flow in the polypoidal choroidal vasculopathy. Ophthalmology 2005;112:1436–1441.

52 Byeon SH, Lew YJ, Lee SC, Kwon OW: Clinical features and follow-up results of pulsating polypoidal choroidal vasculopathy treated with photodynamic therapy. Acta Ophthalmol 2010;88:660–668.

53 Sasahara M, Tsujikawa A, Musashi K, Gotoh N, Otani A, Mandai M, Yoshimura N: Polypoidal choroidal vasculopathy with choroidal vascular hyperpermeability. Am J Ophthalmol 2006;142:601–607.

54 Koizumi H, Yamagishi T, Yamazaki T, Kinoshita S: Relationship between clinical characteristics of polypoidal choroidal vasculopathy and choroidal vascular hyperpermeability. Am J Ophthalmol 2013;155:305–313.

55 Okubo A, Sameshima M, Uemura A, Kanda S, Ohba N: Clinicopathological correlation of polypoidal choroidal vasculopathy revealed by ultrastructural study. Br J Ophthalmol 2002;86:1093–1098.

56 Okubo A, Hirakawa M, Ito M, Sameshima M, Sakamoto T: Clinical features of early and late stage polypoidal choroidal vasculopathy characterized by lesion size and disease duration. Graefes Arch Clin Exp Ophthalmol 2008;246:491–499.

57 Kawamura A, Yuzawa M, Mori R, Haruyama M, Tanaka K: Indocyanine green angiographic and optical coherence tomographic findings support classification of polypoidal choroidal vasculopathy into two types. Acta Ophthalmol 2013;91:e474–e481.

58 Tanaka K, Nakayama T, Mori R, Sato N, Kawamura A, Mizutani Y, Yuzawa M: Associations of complement factor H (CFH) and age-related maculopathy susceptibility 2 (ARMS2) genotypes with subtypes of polypoidal choroidal vasculopathy. Invest Ophthalmol Vis Sci 2011;52:7441–7444.

59 Miki A, Honda S, Kondo N, Negi A: The association of age-related maculopathy susceptibility 2 (ARMS2) and complement factor H (CFH) variants with two angiographic subtypes of polypoidal choroidal vasculopathy. Ophthalmic Genet 2013;34:146–150.

60 Yuzawa M: Polypoidal choroidal vasculopathy (in Japanese). Nihon Ganka Gakkai Zasshi 2012;116:200–231, discussion 232.

61 Tsujikawa A: Usefulness of optical coherence tomography for differential diagnosis: polypoidal lesions and type 2 choroidal neovascularization (in Japanese). Jpn J Clin Ophthalmol (Rinsho Ganka) 2013;67:1058–1063.

62 Yang LH, Jonas JB, Wei WB: Optical coherence tomographic enhanced depth imaging of polypoidal choroidal vasculopathy. Retina 2013;33:1584–1589.

63 Nagase S, Miura M, Makita S, Iwasaki T, Goto H, Yasuno Y: High-penetration optical coherence tomography with enhanced depth imaging of polypoidal choroidal vasculopathy. Ophthalmic Surg Lasers Imaging 2012;43:e5–e39.

64 Kim SW, Oh J, Kwon SS, Yoo J, Huh K: Comparison of choroidal thickness among patients with healthy eyes, early age-related maculopathy, neovascular age-related macular degeneration, central serous chorioretinopathy, and polypoidal choroidal vasculopathy. Retina 2011;31:1904–1911.

65 Koizumi H, Yamagishi T, Yamazaki T, Kawasaki R, Kinoshita S: Subfoveal choroidal thickness in typical age-related macular degeneration and polypoidal choroidal vasculopathy. Graefes Arch Clin Exp Ophthalmol 2011;249:1123–1128.

66 Chung SE, Kang SW, Lee JH, Kim YT: Choroidal thickness in polypoidal choroidal vasculopathy and exudative age-related macular degeneration. Ophthalmology 2011;118:840–845.

67 Rishi P, Rishi E, Mathur G, Raval V: Ocular perfusion pressure and choroidal thickness in eyes with polypoidal choroidal vasculopathy, wet-age-related macular degeneration, and normals. Eye (Lond) 2013;27:1038–1043.

68 Chung SE, Kang SW, Kim JH, Kim YT, Park Y: Engorgement of vortex vein and polypoidal choroidal vasculopathy. Retina 2013;33:834–840.

69 Yamagishi T, Koizumi H, Yamazaki T, Kinoshita S: Fundus autofluorescence in polypoidal choroidal vasculopathy. Ophthalmology 2012;119:1650–1657.

70 Suzuki M, Gomi F, Sawa M, Ueno C, Nishida K: Changes in fundus autofluorescence in polypoidal choroidal vasculopathy during 3 years of follow-up. Graefes Arch Clin Exp Ophthalmol 2013;251:2331–2337.

71 Terasaki H, Miyake Y, Suzuki T, Nakamura M, Nagasaka T: Polypoidal choroidal vasculopathy treated with macular translocation: clinical pathological correlation. Br J Ophthalmol 2002;86:321–327.

72 Kuroiwa S, Tateiwa H, Hisatomi T, Ishibashi T, Yoshimura N: Pathological features of surgically excised polypoidal choroidal vasculopathy membranes. Clin Exp Ophthalmol 2004;32:297–302.

73 Nakajima M, Yuzawa M, Shimada H, Mori R: Correlation between indocyanine green angiographic findings and histopathology of polypoidal choroidal vasculopathy. Jpn J Ophthalmol 2004;48:249–255.

74 Nakashizuka H, Mitsumata M, Okisaka S, Shimada H, Kawamura A, Mori R, Yuzawa M: Clinicopathologic findings in polypoidal choroidal vasculopathy. Invest Ophthalmol Vis Sci 2008;49:4729–4737.

75 Klein RJ, Zeiss C, Chew EY, et al: Complement factor H polymorphism in age-related macular degeneration. Science 2005;308:385–389.

76 Edwards AO, Ritter R III, Abel KJ, et al: Complement factor H polymorphism and age-related macular degeneration. Science 2005;308:421–424.

77 Haines JL, Hauser MA, Schmidt S, et al: Complement factor H variant increases the risk of age-related macular degeneration. Science 2005;308:419–421.

78 Maller J, George S, Purcell S, et al: Common variation in three genes, including a noncoding variant in CFH, strongly influences risk of age-related macular degeneration. Nat Genet 2006;38:1055–1059.
79 Li M, Atmaca-Sonmez P, Othman M, et al: CFH haplotypes without the Y402H coding variant show strong association with susceptibility to age-related macular degeneration. Nat Genet 2006;38:1049–1054.
80 Dewan A, Liu M, Hartman S, et al: HTRA1 promoter polymorphism in wet age-related macular degeneration. Science 2006;314:989–992.
81 Yang Z, Camp NJ, Sun H, et al: A variant of the HTRA1 gene increases susceptibility to age-related macular degeneration. Science 2006;314:992–993.
82 Fritsche LG, Loenhardt T, Janssen A, et al: Age-related macular degeneration is associated with an unstable ARMS2 (LOC387715) mRNA. Nat Genet 2008;40:892–896.
83 Kanda A, Chen W, Othman M, et al: A variant of mitochondrial protein LOC387715/ARMS2, not HTRA1, is strongly associated with age-related macular degeneration. Proc Natl Acad Sci USA 2007;104:16227–16232.
84 Ormsby RJ, Ranganathan S, Tong JC, et al: Functional and structural implications of the complement factor H Y402H polymorphism associated with age-related macular degeneration. Invest Ophthalmol Vis Sci 2008;49:1763–1770.
85 The International HapMap Consortium: The International HapMap Project. Nature 2003;426:789–796.
86 Okamoto H, Umeda S, Obazawa M, et al: Complement factor H polymorphisms in Japanese population with age-related macular degeneration. Mol Vis 2006;12:156–158.
87 Gotoh N, Yamada R, Hiratani H, et al: No association between complement factor H gene polymorphism and exudative age-related macular degeneration in Japanese. Hum Genet 2006;120:139–143.
88 Fuse N, Miyazawa A, Mengkegale M, et al: Polymorphisms in complement factor H and hemicentin-1 genes in a Japanese population with dry-type age-related macular degeneration. Am J Ophthalmol 2006;142:1074–1076.
89 Mori K, Gehlbach PL, Kabasawa S, et al: Coding and noncoding variants in the CFH gene and cigarette smoking influence the risk of age-related macular degeneration in a Japanese population. Invest Ophthalmol Vis Sci 2007;48:5315–5319.
90 Kondo N, Bessho H, Honda S, Negi A: Complement factor H Y402H variant and risk of age-related macular degeneration in Asians: a systematic review and meta-analysis. Ophthalmology 2011;118:339–344.
91 Yuan D, Yang Q, Liu X, Yuan D, Yuan S, Xie P, Liu Q: Complement factor H Val62Ile variant and risk of age-related macular degeneration: a meta-analysis. Mol Vis 2013;19:374–383.
92 Ng TK, Chen LJ, Liu DT, et al: Multiple gene polymorphisms in the complement factor H gene are associated with exudative age-related macular degeneration in Chinese. Invest Ophthalmol Vis Sci 2008;49:3312–3317.
93 Kim NR, Kang JH, Kwon OW, et al: Association between complement factor H gene polymorphisms and neovascular age-related macular degeneration in Koreans. Invest Ophthalmol Vis Sci 2008;49:2071–2076.
94 Chen H, Liu K, Chen LJ, Hou P, Chen W, Pang CP: Genetic associations in polypoidal choroidal vasculopathy: a systematic review and meta-analysis. Mol Vis 2012;18:816–829.
95 Yuan D, Yuan D, Yuan S, Liu Q: The age-related maculopathy susceptibility 2 polymorphism and polypoidal choroidal vasculopathy in Asian populations: a meta-analysis. Ophthalmology 2013;120:2051–2057.
96 Cheng Y, Huang L, Li X, Zhou P, Zeng W, Zhang C: Genetic and functional dissection of ARMS2 in age-related macular degeneration and polypoidal choroidal vasculopathy. PLoS One 2013;8:e53665.
97 Jiang JJ, Wu X, Zhou P, Yu WZ, Huang LZ, Li XX: Meta-analysis of the relationship between the LOC387715/ARMS2 polymorphism and polypoidal choroidal vasculopathy. Genet Mol Res 2012;11:4256–4267.
98 Lima LH, Schubert C, Ferrara DC, Merriam JE, Imamura Y, Freund KB, Spaide RF, Yannuzzi LA, Allikmets R: Three major loci involved in age-related macular degeneration are also associated with polypoidal choroidal vasculopathy. Ophthalmology 2010;117:1567–1570.
99 Kondo N, Honda S, Kuno S, Negi A: Coding variant I62V in the complement factor H gene is strongly associated with polypoidal choroidal vasculopathy. Ophthalmology 2009;116:304–310.
100 Jones A, Kumar S, Zhang N, Tong Z, Yang JH, Watt C, Anderson J, Amrita, Fillerup H, McCloskey M, Luo L, Yang Z, Ambati B, Marc R, Oka C, Zhang K, Fu Y: Increased expression of multifunctional serine protease, HTRA1, in retinal pigment epithelium induces polypoidal choroidal vasculopathy in mice. Proc Natl Acad Sci USA 2011;108:14578–14583.
101 Vierkotten S, Muether PS, Fauser S: Overexpression of HTRA1 leads to ultrastructural changes in the elastic layer of Bruch's membrane via cleavage of extracellular matrix components. PLoS One 2011;6:e22959.
102 Lee KY, Vithana EN, Mathur R, et al: Association analysis of CFH, C2, BF, and HTRA1 gene polymorphisms in Chinese patients with polypoidal choroidal vasculopathy. Invest Ophthalmol Vis Sci 2008;49:2613–2619.
103 Kondo N, Honda S, Ishibashi K, et al: Elastin gene polymorphisms in neovascular age-related macular degeneration and polypoidal choroidal vasculopathy. Invest Ophthalmol Vis Sci 2008;49:1101–1105.
104 Yamashiro K, Mori K, Nakata I, Tsuchihashi T, Horie-Inoue K, Nakanishi H, Tsujikawa A, Saito M, Iida T, Yamada R, Matsuda F, Inoue S, Awata T, Yoneya S, Yoshimura N: Association of elastin gene polymorphism to age-related macular degeneration and polypoidal choroidal vasculopathy. Invest Ophthalmol Vis Sci 2011;52:8780–8784.
105 Zhang X, Wen F, Zuo C, Li M, Chen H, Wu K: Association of genetic variation on chromosome 9p21 with polypoidal choroidal vasculopathy and neovascular age-related macular degeneration. Invest Ophthalmol Vis Sci 2011;52:8063–8067.
106 Tsujikawa A, Sasahara M, Otani A, et al: Pigment epithelial detachment in polypoidal choroidal vasculopathy. Am J Ophthalmol 2007;143:102–111.
107 Ciardella AP, Donsoff IM, Huang SJ, et al: Polypoidal choroidal vasculopathy. Surv Ophthalmol 2004;49:25–37.
108 Kikuchi M, Nakamura M, Ishikawa K, et al: Elevated C-reactive protein levels in patients with polypoidal choroidal vasculopathy and patients with neovascular age-related macular degeneration. Ophthalmology 2007;114:1722–1727.
109 Sakurada Y, Kubota T, Imasawa M, Tsumura T, Mabuchi F, Tanabe N, Iijima H: Angiographic lesion size associated with LOC387715 A69S genotype in subfoveal polypoidal choroidal vasculopathy. Retina 2009;29:1522–1526.
110 Bessho H, Honda S, Kondo N, Negi A: The association of ARMS2 polymorphisms with phenotype in typical neovascular age-related macular degeneration and polypoidal choroidal vasculopathy. Mol Vis 2011;17:977–982.
111 Sakurada Y, Kubota T, Mabuchi F, et al: Association of LOC387715 A69S with vitreous hemorrhage in polypoidal choroidal vasculopathy. Am J Ophthalmol 2008;145:1058–1062.
112 Gomi F, Ohji M, Sayanagi K, Sawa M, Sakaguchi H, Oshima Y, et al: One-year outcomes of photodynamic therapy in age-related macular degeneration and polypoidal choroidal vasculopathy in Japanese patients. Ophthalmology 2008;115:141–146.
113 Chan WM, Lam DS, Lai TY, Liu DT, Li KK, Yao Y, et al: Photodynamic therapy with verteporfin for symptomatic polypoidal choroidal vasculopathy. Ophthalmology 2004;111:1576–1584.
114 Akaza E, Yuzawa M, Matsumoto Y, Kashiwakura S, Fujita K, Mori R: Role of photodynamic therapy in polypoidal choroidal vasculopathy. Jpn J Ophthalmol 2007;51:270–277.
115 Lee WK, Kim KS, Kim W, Lee SB, Jeon S: Responses to photodynamic therapy in patients with polypoidal choroidal vasculopathy consisting of polyps resembling grape clusters. Am J Ophthalmol 2012;154:355–365.