

Retinal Capillary Hemangiomas: Clinical Manifestations and Visual Prognosis

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Background: To describe the clinical features, visual outcomes, and therapeutic complications of patients with retinal capillary hemangiomas.

Methods: A retrospective, non-comparative, observational case study of patients diagnosed with retinal capillary hemangiomas was conducted. Twelve patients (13 eyes) at Chang Gung Memorial Hospital of Kaohsiung from July 1987 to June 2001 were reviewed. Pre- and post-treatment visual acuity and ocular complications are described.

Results: One patient had bilateral and another had unilateral juxtapapillary hemangiomas. All of the other 10 patients were diagnosed with peripheral retinal capillary hemangiomas. More patients had retinal capillary hemangiomas located in the temporal peripheral retina and all had endophytic growth patterns. No patient met the diagnostic criteria of von Hippel-Lindau disease. Visual acuity levels of peripheral retinal hemangiomas without exudative retinal detachment often remained the same after focal laser treatment. Two patients received vitreoretinal surgery. Patients with juxtapapillary hemangiomas had variable visual outcomes and visual field defects during follow-up.

Conclusion: Early diagnosis of capillary hemangiomas in the retinal periphery and treatment by focal laser produced good visual outcomes. If untreated, the tumors may eventually be complicated with exudative retinal detachment and have a worse visual prognosis even with vitreoretinal surgery.
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Key words: retinal capillary hemangioma, von Hippel-Lindau (VHL) disease, exudative retinal detachment.

Retinal capillary hemangiomas are benign vascular tumors in the retina or optic nerve head. They are orange-red spherical tumors fed by a dilated, tortuous retinal artery and drained by an engorged vein.⁽¹⁾ The tumor can present as being either endophytic or exophytic.⁽²⁾ Retinal capillary hemangiomas occurring as isolated tumors have also

been called angiomatosis retinae, retinal angiomatosis, retinal hemangioblastoma, von Hippel's disease, and von Hippel tumor. Those occurring with tumors in other systems, especially central nervous system hemangioblastomas and renal cell carcinomas, were named von Hippel-Lindau (VHL) disease.^(3,4) VHL disease is a hereditary familial multiple-system can-

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cer syndrome. The cardinal features include retinal capillary hemangiomas, central nervous system hemangioblastomas, renal cell carcinomas, pheochromocytomas, and pancreatic, renal, and epididymal cysts.⁽⁵⁾ Retinal capillary hemangiomas are the most common presenting feature and often the first manifestation of von Hippel-Lindau disease.⁽⁶⁾ Although retinal hemangiomas are benign, they can enlarge and produce visual loss by complicated retinal exudates, exudative retinal detachment, an epiretinal membrane, and vitreous hemorrhage.⁽⁷⁻¹⁰⁾ Therefore, ophthalmologists have a critical role in the early detection and management of retinal hemangiomas in order to improve visual outcomes. In addition, early detection of a retinal hemangioma is important for genetic counseling and detection of tumors in other systems at an early pre-symptomatic stage by screening surveys. In this study, we observed patients with retinal capillary hemangiomas in our hospital and reviewed the related literature. This paper describes the clinical feature, visual outcomes, and ocular complications of retinal capillary hemangiomas observed in our study, and discusses its possible pathogenesis based on research over the past few years.

METHODS

In our study, twelve patients (13 eyes) at Chang Gung Memorial Hospital, Kaohsiung from July 1987 to June 2001 were included. Data were collected retrospectively from chart records. General clinical features, including age at diagnosis, gender, physical examination, neurological examination, computed tomography of the central nervous system, and renal ultrasound scan were reviewed. Any pedigree associated with von Hippel-Lindau disease was also recorded, and telephone interviews were carried out if the pedigree record was found to be incomplete. The ophthalmic examinations recorded initial visual acuity, visual acuity at the final visit, the eye involved, tumor growth pattern, tumor location, treatment modality, ocular complications, and follow-up period. Initial fundus photographs and fluorescein angiographs as well as those taken during follow-up were reviewed. Diagnostic criteria for von Hippel-Lindau disease are adopted from the observations of Melmon and Rosen (Table 1).⁽³⁾

Table 1. Clinical Diagnostic Criteria for Von Hippel-Lindau Disease⁽³⁾

<i>With VHL family history*</i>
One or more diagnostic lesions required:
Retinal capillary hemangioma
CNS hemangioblastoma
Visceral lesion †
<i>Without VHL family history</i>
Retinal capillary hemangioma and/or CNS hemangioblastoma
If just one of the above, then a visceral lesion † required

*: VHL family history indicates a family history of retinal capillary hemangioma, CNS hemangioblastoma, or visceral lesion.

†: Visceral lesions include renal cell carcinomas, pheochromocytomas, pancreatic and/or renal cysts, islet cell tumors, paragangliomas, epididymal cystadenomas, and endolymphatic sac tumors.

RESULTS

In the 12 subjects, 13 eyes were identified with retinal capillary hemangiomas. The mean follow-up time was 1.82 years, and ranged from 2 months to 5.48 years. There were 7 male patients (7 eyes) and 5 female patients (6 eyes). Four patients had right eye involvement, 7 patients had left eye involvement, and 1 patient had both eyes involved. The mean age of diagnosis for all patients was 37.46 (range, 18 to 51) years. The mean age of diagnosis was 39.5 years for men, and 34.7 for women. The growth pattern of the tumors was endophytic in all patients. The locations of the tumors included 4 in the superior temporal retina, 1 in the temporal retina, 3 in the inferior temporal retina, 2 in the inferior retina, and 3 in the juxtapapillary area (Table 2). Initial visual acuity was from 1.0 to counting finger at 5 cm, while visual acuity at the final visit was from 1.0 to only light perception (Fig. 1). Most patients with management maintained their visual acuity before treatment, except those with complicated exudative retinal detachment and those with juxtapapillary retinal capillary hemangiomas. Eight patients responded well to focal laser treatment. One patient received cryotherapy after focal laser treatment due to persistent symptoms, and responded well to the adjunctive cryotherapy. Two patients with peripheral retinal hemangiomas had exudative retinal detachment at their first visit, and both ultimately received vitreoretinal surgery due to failure of laser treatment and

Table 2. Clinical Features of Patients with Retinal Capillary Hemangiomas

Patient no.	Gender	Age when diagnosed (years)	Symptoms when diagnosed	Position	Quadrant (affected eye)	VA when	VA at diagnosed	Follow-up final visit	Complications time (years)	Treatment	Comments methods
1	female	36	floaters sensation	peripheral retina	ST*(OS)	1.00	1.00	2.02	retinal exudate	laser	
2	male	41	visual field defect	juxta-papillary	nasal (OD)	0.40	0.10	2.26	retinal exudate, exudative RD ^{II}	laser	mother with adrenal tumor
3	female	19	blurred vision	juxta-papillary	temporal (OD)	CF 60-70 cm	LS (+)	5.48	retinal exudate, exudative RD ^{II} , exotropia	none	OD eye progressed to total RD ^{II} and only LP**
					nasal (OS)	1.00	0.90		retinal exudate		
4	male	46	blurred vision	peripheral retina	ST* (OD)	CF 5 cm	0.20	2.31	increased IOP [±] , retinal exudate and exudative RD ^{II}	laser, cryo [‡] , and surgery ^{††}	
5	male	38	blurred vision	one in the peripheral retina, the other one posterior to the equator	inferior (OS)	0.03	0.01	0.27	disc neovascularization, epiretinal membrane, retinal exudate	laser	2 hemangiomas shared the same feeder and drainage system
6	male	37	visual field defect	peripheral retina	IT ⁺ (OS)	1.00	CF 25cm	2.73	retinal exudate, exudative RD ^{II}	laser, cryo [‡] , surgery ^{††}	
7	male	43	blurred vision	peripheral retina	inferior (OS)	1.00	1.00	0.62	retinal exudate	laser	
8	female	52	photopsia	peripheral retina	temporal (OS)	0.70	0.70	2.58	increased IOP [±] , preretinal hemorrhage, retinal exudate	laser, cryo [‡]	
9	male	38	visual field defect	peripheral retina	IT ⁺ (OS)	1.00	1.00	3.04	retinal exudate	laser	
10	female	21	floaters sensation	peripheral retina	ST*(OD)	1.00	1.00	0.19	retinal exudate	laser	
11	male	34	floaters sensation	peripheral retina	ST*(OD)	0.60	0.60	0.26	retinal exudate	laser	
12	female	46	floaters sensation	peripheral retina	IT ⁺ (OS)	1.00	1.00	0.14	vitreous hemorrhage, retinal exudate	laser	

*ST: superotemporal; †IT: inferotemporal; ‡Cryo: cryotherapy; ^{II}RD: retinal detachment; [±]IOP: intraocular pressure; **LP: light perception; ††surgery: in case no. 4, the first surgical methods included segmental scleral buckling, cryopexy, external subretinal drainage, and focal laser. The second surgical methods for recurrent retinal detachment included pars plana vitrectomy, air-fluid exchange, endolaser photocoagulation, and gas tamponade. In case no. 6, segmental scleral buckling and other similar vitreoretinal procedures were performed at another teaching hospital.

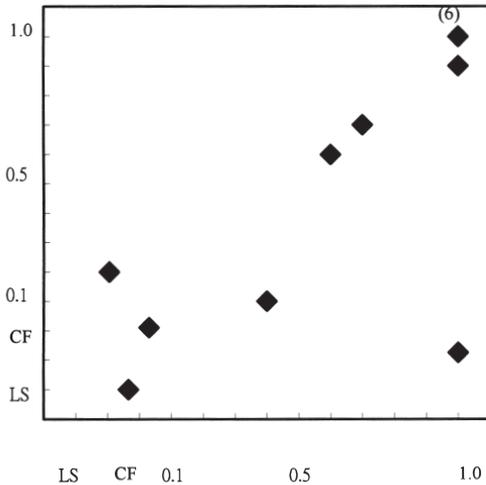


Fig. 1 Visual acuity at diagnosis compared with visual acuity at the final visit. The transverse axis represents the visual acuity at onset, and the longitudinal axis represents the visual acuity at the final visit after management. The number in parentheses (6) represents the number of patients at the same point, i.e., there are 6 patients who maintained a visual acuity of 1.0 after treatment. Most of the patients retained good visual acuity after management.

cryotherapy. One patient (no. 4) received segmental scleral buckling, cryotherapy, external subretinal drainage, and focal laser at the first operation. Due to recurrent retinal detachment, a second operation consisting of pars plana vitrectomy, air-fluid exchange, endolaser photocoagulation, and gas tamponade was performed after 1 month. The other patient (no. 6) received laser treatment and cryotherapy, but these failed in our hospital, and that patient received segmental scleral buckling and other similar vitreoretinal procedures at another teaching hospital. Two patients with juxtapapillary hemangiomas had exudative retinal detachment at their first visit. One patient (patient no. 3) received close observation without laser or any other treatment, and her visual acuity at the final visit was light perception only. The other patient (no. 2) received repeated focal laser, and his visual acuity at the final visit was 0.1. In the 12 patients, the major ocular complications included retinal exudation and exudative retinal detachment. All patients suffered from retinal exudation, and 4 patients suffered from exudative retinal detachment. Other ocular complications included 2 patients with increased intraocular pressure, 1 patient

with an epiretinal membrane, 1 patient with preretinal hemorrhage, 1 patient with vitreous hemorrhage, 1 patient with neovascularization of the disc, and 1 patient with exotropia (Table 2). The pedigree focusing on ocular problems, central nervous system tumors, renal tumors, and other visceral lesions was taken by chart review and was followed up with telephone interviews if the records were incomplete. Seven patients received computed tomography of the brain, and 2 patients received renal ultrasound scans. According to the pedigree and systemic surveys, no patient met the diagnostic criteria of von Hippel-Lindau disease.

Representative cases from the study are described below.

Patient no. 10

A 21-year-old woman complained of a floater sensation in the right eye for about 2 months. Initial visual acuity was 1.0 in the right eye. Dilated fundus examination revealed an endophytic tumor with a dilated tortuous artery and vein in the superotemporal peripheral retina. Retinal exudates surrounded the tumor (Fig. 2A). Fluorescein angiography showed an early filling of the fine tumor capillaries, hyperfluorescence of the retinal hemangioma with dilated feeder arteries and drainage veins, and intense late staining (Fig. 2B). After repeated focal laser treatment, the tumor shrank, and the diameter of the feeder arteries and drainage veins decreased (Fig. 2C). Her visual acuity remained at 1.0 at the final visit.

Patient no. 6

A 37-year-old man suffered from superior visual field defect in the left eye for about 3 weeks. Initial visual acuity was 1.0 in the left eye. Dilated fundus examination showed severe lipid exudation over the inferior retina, and an endophytic red tumor with localized exudative retinal detachment in the inferotemporal retina (Fig. 3A). Fluorescein angiography confirmed the diagnosis of retinal capillary hemangioma (Fig. 3B). After repeated laser treatment, retinal exudation and exudative retinal detachment were still progressing. Therefore, the patient received vitreoretinal surgery at another teaching hospital. Ultimately, the retina of the patient became dry, and his visual acuity was counting fingers at about 25 cm at the final visit.

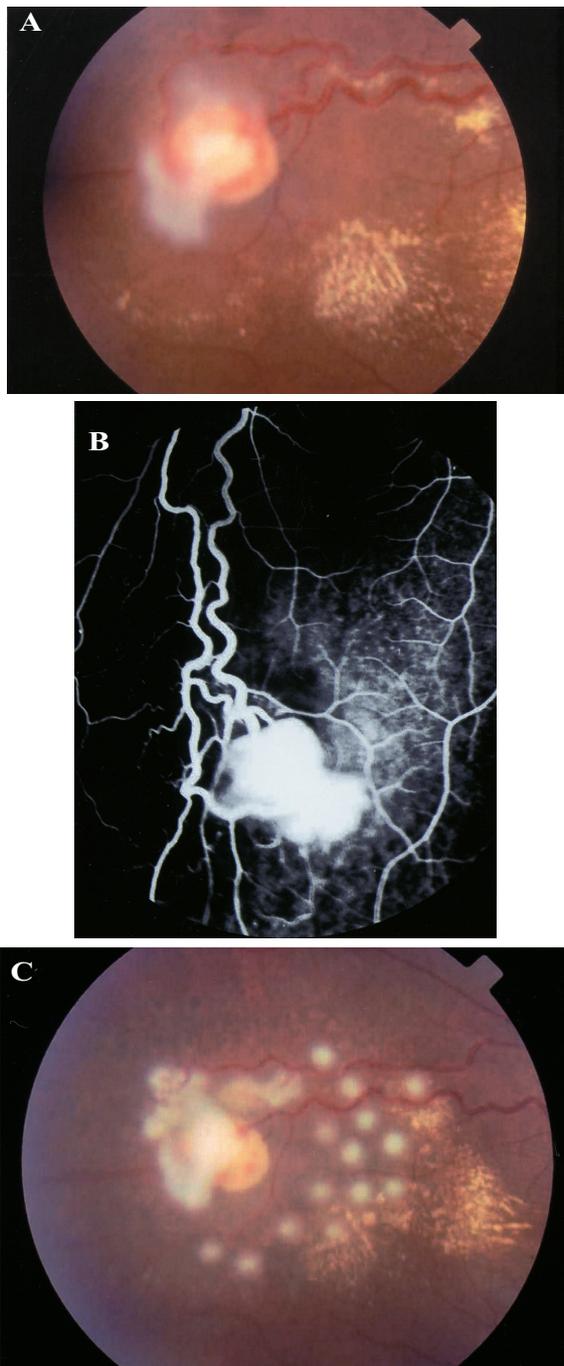


Fig. 2 (A). Fundus photograph revealing an endophytic tumor with dilated tortuous artery and vein with surrounding retinal exudates. (B). Fluorescein angiograph showing hyperfluorescence of the retinal hemangioma with dilated feeder arteries and drainage veins, and intense staining. (C). After treatment. The tumor had shrunk and the diameters of the feeder arteries and drainage veins had decreased after repeated focal laser treatment.

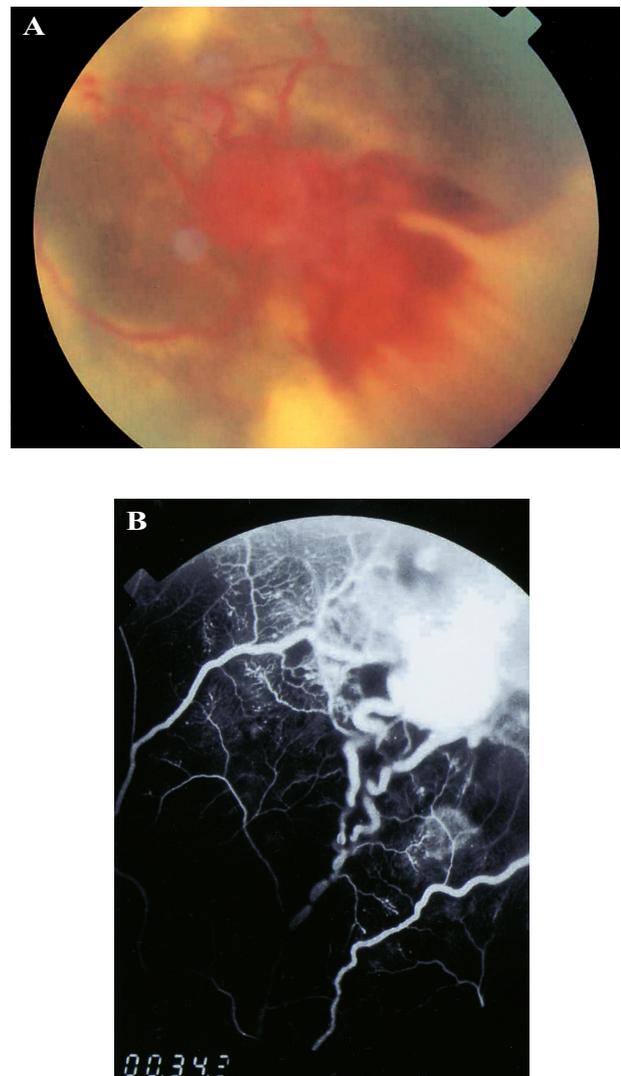


Fig. 3 (A). Severe lipid exudation over the inferior retina, and an endophytic red tumor with localized exudative retinal detachment at the inferotemporal retina. (B). Fluorescein angiograph of this case.

Patient no. 2

A 41-year-old man complained of superior visual field defect in his right eye for about 2 weeks. Initial visual acuity was 0.4 in the right eye. Dilated fundus examination revealed an endophytic juxta-papillary retinal capillary hemangioma in the inferonasal disc with surrounding serous retinal detachment involving the macula (Fig. 4A). The patient received repeated laser treatment over and surround-

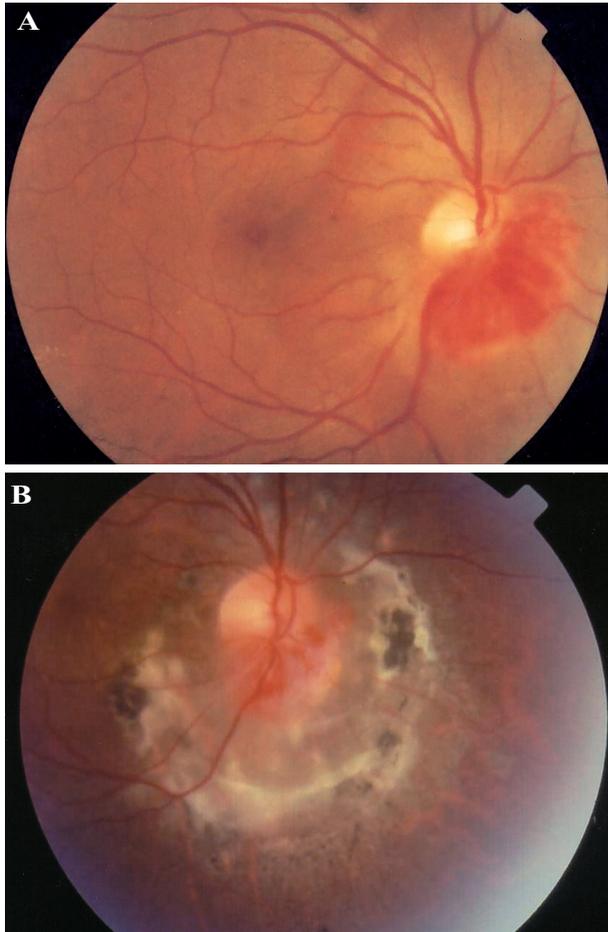


Fig. 4 An endophytic juxtapapillary retinal capillary hemangioma in the inferonasal disc with surrounding serous retinal detachment involving the macula. B. After treatment. The tumor had shrunk and the serous retinal detachment had subsided after repeated laser treatment.

ing the tumor. The tumor shrank, and serous retinal detachment subsided after laser treatment (Fig. 4B). His visual acuity was 0.1 at the final visit.

DISCUSSION

Thanks to advances in molecular biology, we know that VHL disease is induced by a VHL gene defect. The VHL gene was mapped to chromosome 3q25-26 by DNA linkage analysis in 1988,⁽¹¹⁾ and it was identified as a tumor suppressor gene by positional cloning in 1993.⁽¹²⁾ The VHL gene encodes a

protein with 213 amino acid residues and a molecular weight of between 24 and 30 kDa. A secondary isoform, which exhibits similar behavior, arising from internal translation initiation, and with a molecular weight of between 18 and 20 kDa was subsequently identified.⁽¹³⁾ The VHL gene product, the VHL protein, is a component of an E3 ubiquitin ligase that can destroy the (subunits of the hypoxia-inducible factor (HIF) transcription factor in the presence of oxygen. If cells lack the VHL protein, the products of HIF target genes, such as vascular endothelial growth factor and transforming growth factor α , will be overproduced.^(14,15) In consequence, VHL-associated tumors with angiogenic character may develop. In VHL disease, the identified types of mutations include missense mutations, nonsense mutations, insertions, microdeletions, deletions, and splice sites.^(16,17) The tumorigenesis of retinal capillary hemangiomas, like other VHL-associated tumors, such as cerebellar hemangioblastomas and renal cell carcinomas,⁽¹⁸⁾ is consistent with the Knudson 2-hit model.⁽¹⁹⁾ In patients with VHL disease who already carry a germline mutation, only a single somatic mutation is needed for tumor development. Therefore, the onset of tumor formation occurs earlier, as well as there being multiple tumors in single or bilateral eyes, and a secondary VHL-associated tumor in other susceptible tissues can occur more easily. On the contrary, in sporadic cases, mutation of both alleles of the VHL gene is necessary for tumor development. Regarding the genotype-phenotype correlation in VHL disease, although the type of mutations responsible for VHL without pheochromocytomas differ from those responsible for VHL with pheochromocytomas,⁽²⁰⁾ there was no association between the type or position of the mutation and the severity of retinal capillary hemangiomas.⁽¹⁰⁾ The prevalence of VHL disease was estimated to be about 19 per million,⁽²¹⁾ and the prevalence of solitary retinal capillary hemangiomas is reported to be 9 per million.⁽²²⁾ The prevalence of solitary retinal capillary hemangiomas in patients with VHL disease is about 22% to 58%.^(10,23,24) The probability of VHL disease in patients with solitary retinal capillary hemangiomas was estimated to be 46%.⁽²⁵⁾ The mean age of diagnosis was about 17 to 27 (range, 1-67) years for retinal capillary hemangioma patients with VHL disease.^(9,19,24,26) The mean age of diagnosis was about 30

to 40 (range, 3-74) years for retinal capillary hemangioma patients without VHL disease.^(19,24,26) In our study, none of the 12 patients with retinal capillary hemangiomas met the diagnostic criteria of VHL disease by systemic survey and pedigree investigation. One patient (no. 3) had bilateral juxtapapillary hemangiomas, but a systemic survey revealed that she had no VHL family history or other VHL-associated tumor herself. Another patient (no. 5) had 2 retinal capillary hemangiomas in 1 eye, but a systemic survey also indicated that he had neither VHL family history nor other VHL-associated tumors himself. The mother of Patient no. 2 had died of an adrenal tumor, but his mother had no hypertension history, and pheochromocytoma was therefore not favored. The average diagnosis age of all 12 patients was 37.46 (range, 18-51) years, much later than that of previous studies. The difference can be explained by the Knudson 2-hit theory, because none of the patients seemed to have a VHL gene germline mutation. Although our cases had not received VHL gene mutation analysis due to the instrumentation and technique being unavailable, we speculate that most of them should have no VHL gene germline mutation according to the diagnostic criteria and age-dependent penetration character of VHL disease. The mean diagnostic age of VHL disease by retinal capillary hemangioma is mentioned above, while by cerebellar hemangioma it is 30 (range, 1-67) years, and by renal cell carcinoma it is 37 (range, 16-67) years.^(6,18) The cumulative risks of a VHL disease patient developing a retinal capillary hemangioma, cerebellar hemangioblastoma, and renal cell carcinoma at age 30 years are 44%, 38%, and 5%, respectively, rising to 84%, 70%, and 69%, respectively, at age 60 years.⁽⁹⁾ The age-dependent penetration of VHL disease reaches over 52% for 30-year-old patients and over 96% for 60-year-old patients.⁽²¹⁾ Therefore, according to their family and personal histories, and systemic screening, the probability of patients in this study having VHL germline mutations is very small. Second, the study is a retrospective review from a single medical center, and the number of cases is small. In addition, no VHL family occurring in our series is another cause leading to fewer cases and older diagnostic ages.

Clinical features of retinal capillary hemangiomas are a red vascular mass with a dilated feeder

artery and drainage vein. They are usually located at the retinal periphery, but also occur on the posterior pole.^(1,22) In our study, the hemangiomas of 9 of the 13 eyes were located at the retinal peripheral. One patient had 2 retinal capillary hemangiomas with the same feeder artery and drainage vein in his left eye, one located at the retinal peripheral and the other located at the posterior pole. The remaining hemangiomas of 3 eyes of 2 patients were located in the juxtapapillary area. Retinal capillary hemangiomas can grow with an endophytic or an exophytic pattern. The endophytic type is more common than the exophytic type. Exophytic growth is more difficult to detect. This may be one of the reasons why there are few cases, and all patients in our study had an endophytic growth pattern. If a retinal capillary hemangioma is located away from the optic disc and retinal exudation is prominent, it must be differentiated from telangiectasia, an arterial macroaneurysm, a cavernous hemangioma,⁽²⁷⁾ familial exudative vitreoretinopathy, and a vasoproliferative tumor.⁽²⁸⁾ If a retinal capillary hemangioma is located away from the optic disc and is obscured by vitreous hemorrhage or retinal detachment, dilated feeder vessels can cause it to be confused with a racemose hemangioma, or anastomoses between tumor vessels and retinal vessels like a retinoblastoma. If it is located in the juxtapapillary area, it must be differentiated from a papilloedema, papillitis, juxtapapillary choroiditis, juxtapapillary subretinal neovascularization, and a choroidal hemangioma.⁽²⁾ Ocular complications due to retinal capillary hemangiomas in VHL carriers include exudative retinal detachment, secondary angiomatosis, intraretinal exudation, an epiretinal membrane, vitreous hemorrhage, a retinal break or rhegmatogenous retinal detachment, and neovascularization of the disc or retinal periphery.^(10,22) In our study, ocular complications had similar proportions, except that there were fewer instances of secondary angiomatosis. This can also be explained by the Knudson 2-hit model, and the evidence is more persuasive that most of our patients should only be sporadic cases of retinal capillary hemangioma without VHL germline mutations.

Although retinal capillary hemangiomas may spontaneously regress,⁽²⁹⁾ it is better to treat them in order to prevent tumor growth and subsequent ocular complications. Peripheral retinal capillary heman-

giomas respond well to treatment especially if they are small, but the outcome of treatment is still disappointing for juxtapapillary capillary hemangiomas. The mainstay of treatment is laser therapy. The krypton laser or argon laser,^(7,30) which can be well absorbed by hemoglobin, is a good choice. Larger lesions (greater than 3 mm in diameter), lesions in the extreme periphery, and those with underlying subretinal fluid are well managed with cryotherapy.^(7,8,31) Patients with juxtapapillary capillary hemangiomas treated by either observation or laser generally have variable visual acuity.^(2,30,32) The treatment of juxtapapillary capillary hemangiomas by diode transpupillary thermophotocoagulation remains controversial.^(33,34) For patients with ocular complications, such as retinal exudates, exudative retinal detachment, epiretinal membrane formation, and vitreous hemorrhage, vitreoretinal surgery is ultimately required, and blindness is common.^(10,22,35) In our study, for those patients with retinal capillary hemangioma away from the disc, initial visual acuity was 1.0 in 6 of 10 eyes, ≥ 0.4 in 8 of 10 eyes, and ≥ 0.1 in 8 of 10 eyes. The visual acuity at the final visit was

1.0 in 5 of 10 eyes, ≥ 0.4 in 7 of 10 eyes, and ≥ 0.1 in 8 of 10 eyes. Most of the patients retained good visual acuity after treatment, except for 2 patients with a severe complicated exudative retinal detachment who ultimately received vitreoretinal surgery. In one of the patients with a juxtapapillary capillary hemangioma who received laser treatment, initial visual acuity was 0.4, while it was 0.1 at the final follow-up. For the other patient with bilateral juxtapapillary capillary hemangiomas who received observation only, initial visual acuity was counting finger at 60-70 cm for her right eye, and 1.0 for her left eye. Visual acuity at the final visit was light perception only for her right eye, and 0.9 for her left eye. The visual outcomes in our study are comparable with those of previous studies.^(7,22)

Although none of our patients with retinal capillary hemangiomas were associated with VHL disease, we should still pay more attention to the high correlation between these entities due to the high morbidity and mortality of VHL disease. Ophthalmologists usually are the earliest detectors of VHL disease. Therefore, once a retinal capillary

Table 3. Screening Protocols for Patients with or at Risk for Von Hippel-Lindau Disease

Examination	Hawaii ⁽⁵⁾	Newfoundland ⁽⁸⁾	Cambridge ⁽⁹⁾
Ophthalmoscopy	from age 6, every 1-5 years for those at risk, every 6-12 months for affected members	every year for those at risk, at least 6 months for affected members	from age 5 to 60, every year
Flourescein angiography	not routine	not routine	from age 10, every year
Physical examination and 24-h urine collection for catecholamines	from age 10, every 1-5 years for those at risk, every year for affected members	every year, plasma catecholamines testing if urine catecholamines are normal but blood pressure is elevated or postural hypotension is present	every year
Enhanced MRI* or CT ⁺ of the brain and spine	from age 20, MRI* of posterior fossa at least every 10 years for those at risk. From age 15-20, every 1-5 years and whenever suggestive symptoms occur for affected members	baseline CT ⁺ in late teens or early twenties; CT ⁺ scan repeated if any suspicious neurological finding	from age 15 to 40, every 3 years, from age 40-60, every 5 years for those at risk. Every 3 years to age 50 and every 5 years thereafter for affected members
Abdominal sonography or CT ⁺	from age 15-20, pancreatic and renal sonography and/or CT ⁺ every 1-5 years.	annual abdominal sonography. CT ⁺ scan if urine or serum abnormal biochemical values found	From age 20 to 60, every 3 years for renal sonography with abdominal CT ⁺ (more frequently if multiple renal cysts present)

*MRI: magnetic resonance imaging; ⁺CT: computed tomography.

hemangioma is identified, a detailed family history should be obtained, and a subsequent systemic screening protocol should be arranged to exclude a fatal central nervous system (CNS) hemangioblastoma and visceral lesions of VHL disease. There are different screening protocols for VHL disease, but they have similar items of examination including ophthalmoscopy, fluorescein angiography, brain and spine magnetic resonance imaging (MRI) or computed tomography (CT), abdominal ultrasound or CT, and urinary catecholamine testing (Table 3).^(5,8,9) Screening regimens can be used for patients with known VHL disease or for patients at risk for this disease to decrease their morbidity and mortality by presymptomatic diagnosis and management. Genetic testing methods that combine quantitative Southern blot analysis for detecting deletions of the entire VHL gene, Southern blotting for detecting gene rearrangement, fluorescence in situ hybridization for conforming deletions, and complete sequencing of the gene have all contributed to high detection rates.⁽³⁶⁾ If molecular biological techniques and equipment are available, DNA testing can be performed to exclude the diagnosis of VHL disease with solitary retinal capillary hemangiomas, to assess the risk of specific mutations in patients with known VHL disease, to screen at-risk relatives, and to do prenatal screening after detailed genetic counseling.^(37,38) None of the 12 patients in the study met the clinical diagnostic criteria of VHL disease, and we hope that the availability of genetic testing in the future can further confirm the diagnosis without the germline mutation of the VHL gene.

In summary, early diagnosis of capillary hemangiomas in the retinal periphery and treatment by focal laser produced good visual outcomes. Cryotherapy is an alternative or adjunctive management for specific situations like larger tumors or those on the extreme peripheral retina. Without treatment or with delayed treatment, capillary hemangiomas in the retinal periphery may be complicated with severe exudation and exudative retinal detachment, and produce a worse visual prognosis even with vitreoretinal surgery. For patients with juxtapapillary retinal capillary hemangiomas, laser treatment should be more prudent due to the variable visual outcomes. Transpupillary thermophotocoagulation is still controversial for the treatment of juxta-

papillary retinal capillary hemangiomas. Better management of juxtapapillary hemangiomas is mandatory, and needs to be determined with further study.

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視網膜微血管瘤之臨床表現及其預後

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- 背景：** 爲了進一步描述視網膜微血管瘤病患之臨床特徵，視力之預後，治療的效果及其併發症。
- 方法：** 迴顧及分析於1987到2001年在高雄長庚醫院的視網膜微血管瘤之病患，共有12位病患(13隻眼睛)，特別針對這些病患治療前後的視力，臨床表現及眼球之併發症加以探討。
- 結果：** 12位病人之中，有一位是雙眼視神經旁各有一個視網膜微血管瘤，另一位是單眼視神經旁有一個視網膜微血管瘤，其餘10位病患皆爲單眼週邊視網膜的視網膜微血管瘤。大部分的視網膜微血管瘤病患其微血管瘤是位於視網膜顛側且這12位病人皆爲內生型。這12位病人皆不符合von Hippel-Lindau disease 之診斷要件。大部分早期診斷的周邊視網膜微血管瘤病患接受局部雷射治療皆能維持原有之視力，有2位病患併發滲出性視網膜剝離而必須接受玻璃體視網膜手術治療。視神經旁視網膜微血管瘤病患不論治療與否，預後變異性大。
- 結論：** 早期診斷及以雷射治療周邊視網膜微血管瘤通常有不錯的預後。如果不加以治療，則可能會併發滲出性視網膜剝離而必須接受玻璃體視網膜手術治療而有較差之預後。
- (長庚醫誌 2002;25:672-82)

關鍵字： 視網膜微血管瘤，von Hippel-Lindau (VHL) disease，滲出性視網膜剝離。