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Classification and management of hereditary retinal angiomas

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Abstract

Two distinct types of retinal angiomas are currently recognized. Capillary hemangiomas occur most characteristically as part of the von Hippel-Lindau syndrome. The retinal capillary hemangiomas typically appear as globular red-orange tumors with dilated and tortuous afferent arterioles and efferent venules. Cavernous hemangiomas typically appear as grape-like clusters of dilated vascular sacs without pronounced alteration in the adjacent arterioles and venules. The spectrum of clinical features of these two types of hemangiomatosis and current approaches to management of patients with these disorders is reviewed.

Introduction

Hemangioma is a term used to denote a hamartoma composed principally of blood vessels. Two types of hemangioma are encountered in the retina, the capillary hemangioma (*angiomatosis retinae*) and the less common cavernous hemangioma. Capillary hemangiomas of the retina are well known ophthalmic features of the oculo-neuro-cutaneous syndrome (phakomatosis) of von Hippel and Lindau. Evidence that cavernous hemangiomas of the retina can occur as part of an oculo-neuro-cutaneous phakomatosis has been presented in recent years but remains controversial.

The fundus condition known as racemose angioma of the retina (35) is not a true hemangiomatosis. This condition is probably more appropriately designated congenital retinal arteriovenous malformation (3). The anomalous retinal arteriovenous communications in this condition are generally considered to be retinal vascular hamartias. Since this review addresses the subject of true retinal hemangiomas, further comments on congenital retinal arteriovenous malformation are omitted.

This article will discuss the clinical features, associated systemic findings, genetics, and management of persons with capillary and cavernous hemangiomas of the retina and optic disc.

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Capillary hemangiomatosis

Angiomatosis retinae, von Hippel's disease, von Hippel-Lindau syndrome

Capillary hemangiomatosis of the retina and optic disc is an unusual ophthalmic disorder characterized by the presence of one or more benign

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capillary hamartomas involving the retina and/or optic papilla. Although examples of this condition were reported prior to 1900 (9), von Hippel (30) is commonly credited with establishing *angiomatosis retinae* as a distinct ophthalmic entity. Lindau (21) is generally credited with pointing out the pertinent association between *angiomatosis retinae* and central nervous system hemangiomatosis. He also recognized the common occurrence of visceral cysts and tumors in persons with this neuro-ocular hemangiomatosis. This oculo-neuro-visceral syndrome of von Hippel and Lindau was included among the phakomatoses by van der Hoeve (28) in his Doyne Memorial Lecture of 1932. For a more extensive historical review, the reader is referred to the comments of Duke-Elder (9).

Clinical features

Capillary hemangiomatosis of the retina and optic disc has a wide range of clinical expression depending upon the age of the affected individual, the location and number of vascular tumors in the fundus, the stage of development of the tumor(s), and the extent of accompanying abnormalities in the surrounding tissues.

Individual capillary hemangiomas

Hemangiomas of the retina

The characteristic lesion of capillary hemangiomatosis is a well-defined, spherical, reddish vascular tumor arising within the retina (Fig. 1). Such tumors range in size from approximately 0.5 mm to 10.0 mm or more. The smaller tumors can be entirely intraretinal, but the larger lesions project either into the vitreous (endophytic capillary hemangioma) or into the subretinal space (exophytic capillary hemangioma). These hemangiomas can arise from any portion of the retina, but most of them appear to occur in the temporal equatorial and pre-equatorial fundus. Well-developed tumors typically have dilated and tortuous feeder (afferent arteriole) and drainer (efferent venule) vessels (Fig. 1) or as an exudative mound (exaggerated macular exudative response) (34) with an exudate free interval between the hemangioma and the macula (Fig. 3).

Incipient lesions of capillary hemangiomatosis do not exhibit all the classic features just described for well developed hemangiomas. The earliest lesions appear to be small aneurysmal dilations of retinal capillaries (18, 26). A slight, generalized increase in caliber of capillaries proximal and distal to the aneurysmal lesion(s) can be noted as an early feature in some cases, although the afferent arteriole and efferent venule are not commonly affected at this stage. Even small hemangiomas such as this can leak enough plasma components to result in accumulation of surrounding intraretinal and/or subretinal exudates. A high index of suspicion is usually required to permit identification of such incipient lesions. Fluorescein angiography (see below) may reveal lesions which would elude conventional examination techniques.

Large retinal capillary hemangiomas are also difficult to identify in some cases. The difficulty stems from the marked abnormalities in the tissues surrounding and overlying many large retinal capillary hemangiomas which can partially or totally obscure one's view of the tumor. Accumulation of exudates on the surface of the hemangioma and around it and gliosis of the involved retina can make the vascular tumor appear white or light gray in color and less well-defined in contour. Exophytic hemangiomas can be completely obscured by exudative subretinal fluid. Some endophytic retinal

capillary hemangiomas bleed spontaneously, and the overlying blood can partially obscure the tumor (Fig. 4). In such cases observation of the dilated and tortuous afferent and efferent vessels, which can exhibit fusiform aneurysmal beading, should alert one to the possibility of this condition. Demonstration of a more recognizable hemangioma in another region of an eye with this sort of advanced lesion, observation of a capillary hemangioma in the fellow eye of such a patient, or detection of von Hippel's disease or the von Hippel-Lindau syndrome in other family members should help to establish the diagnosis. Unfortunately, these indicators are not available in many advanced cases, in which the profuse exudative response can lead to total exudative retinal detachment, secondary neovascular glaucoma, blindness, and ultimately phthisis bulbi (2, 4).

Hemangiomas of the optic disc

Three clinical types of capillary hemangioma of the optic disc have been described in persons with von Hippel's disease (13). The most easily recognized type is the endophytic hemangioma. Papillary tumors of this type appear as reddish, spherical, well-defined vascular lesions projecting into the prepapillary vitreous. Circumpapillary subretinal fluid and exudates can accumulate, but prominent feeder and drainer vessels are either not present or not recognized in these cases.

Less commonly recognized are the sessile and exophytic types of capillary hemangioma of the optic disc. The exophytic type appears as an indistinct, nodular, yellow-orange tumor that extends from the disc margin into the juxtapapillary subretinal space. The detached retina overlying such tumors appears gray and thickened, and it typically contains some dilated blood vessels which dip downward into the lesion. The sessile type appears as an ill-defined thickening and slight orange discoloration of the disc and juxrapapillary retina without a distinct mass. Both types can produce circumpapillary retinal edema, subretinal exudates and retinal detachment.

Multiple capillary hemangiomas

More than one capillary hemangioma can be detected in the fundus of approximately one-third of affected persons (2, 21, 26). The individual lesions are typically at different stages of maturation. Disc and retinal capillary hemangiomas occur together in the same eye in some affected persons. Eyes with a capillary hemangioma of the disc appear to have at least one associated retinal capillary hemangioma in from 43% (27) to 50% (13) of cases.

Bilateral capillary hemangiomas

Approximately one-third (26) to one-half (6) of persons with capillary hemangiomatosis of the optic disc and retina have bilateral ocular involvement. The individual lesions in the two eyes are commonly at different stages of development, and the extent of the abnormalities in the two eyes can be markedly asymmetric. Aa affected person can have a papillary hemangioma in one eye and a retinal hemangioma in the other (13).

Patient characteristics

Persons with capillary hemangiomatosis of the retina and/or optic disc are generally detected to have this condition between the ages of 15 and 40 years (2). Males and females appear to be affected in equal proportions. Prospective evaluation of relatives of persons with von Hippel's disease generally permits identification of individuals with capillary hemangiomas of the retina and/or optic disc at an earlier age than the range cited above (26), but the diagnosis of this condition in newborns and small children is unusual.

Symptoms

The majority of older children and adults with capillary hemangiomatosis of the retina and/or optic disc are diagnosed to have this condition when they seek ophthalmic advice because of blur-

red vision. Young children are commonly diagnosed following a failed school vision test. Affected persons typically have painless, progressive visual loss in the involved eye due to accumulation of exudates in the macula or development of an exudative retinal detachment (4). Leukocoria or strabismus can be presenting features in an occasional child with an extensive, exudative retinal detachment. Persons with small and/or peripheral retinal capillary hemangiomas with little or no exudative reaction are generally asymptomatic.

Fluorescein angiography

Fundus fluorescein angiography of an eye with capillary hemangiomatosis of the retina (Fig. 1 and 4) typically demonstrates rapid arteriovenous transit of blood through the vascular tumor (11). One can usually identify one or more afferent arterioles and one or more efferent venules associated with each capillary hemangioma of the retina. The hemangioma itself characteristically fills promptly in the arterial phase and then leaks profusely into the surrounding tissues in the venous and recirculation phases of the study. Some small lesions and some well-encapsulated larger tumors, however, do not exhibit this characteristic pattern of leakage.

Fluorescein angiography of a capillary hemangioma of the optic disc (13) typically shows prompt filling of the capillary channels that comprise the tumor. However, afferent and efferent large vessels are not commonly apparent. The typical hemangioma of the disc also exhibits characteristic marked hyperfluorescence due to leakage into the surrounding tissues by the venous and recirculation phases of the angiogram.

Natural history of capillary hemangiomas of retina and optic disc

The natural history of untreated capillary hemangiomas has never been determined in a long-term, prospective study. There is some evidence, however, that untreated capillary hemangiomas of the retina and optic disc show progressive growth with exudative and hemorrhagic complications (2, 4, 6, 11). First, detection of well-developed capillary hemangiomas is unusual in young children (26). Although typical vascular hamartomas have been demonstrated in the eyes of full term and even prematurely born neonates (4), most hemangiomas are not detected until the juvenile or young adult years (2, 26). Second, many capillary hemangiomas have been documented to grow during periods of follow-up by various individuals (18). Third, most eyes with massive exudative retinal detachment and intravitreal and/or subretinal hemorrhage due to capillary hemangiomatosis of the retina and/or optic disc have one or more rather large vascular tumors (31).

Although we believe that most capillary hemangiomas progress, we also recognize that some small lesions do not change during several years of follow-up (Fig. 5). The ultimate prognosis for eyes with stable, small capillary hemangiomas is uncertain with regard to long-term follow-up.

Development of new capillary hemangiomas from previously normal appearing portions of the retinal capillary network has been noted by a number of individuals (4, 31). The implications of these observations with regard to current concepts of etiology of these tumors is uncertain. Certainly, many capillary hemangiomas of the retina and optic disc do not appear to be congenital. The presence of a congenital vascular endothelial cell rests at the site of subsequent development of a capillary hemangioma is speculative in such cases.

Table. Relatively common lesions occurring in persons with capillary hemangiomatosis of retina and optic disc.

Eye (Retina and Optic Disc)	capillary hemangiomas
Central Nervous System (Cerebellum and Spinal Cord)	
Visceral Organs	hemangioblastoma
Kidney	cysts
	pheochromocytoma
	renal cell carcinoma
Pancreas	cysts
Liver	cysts
Epididymis	cysts
Lung	cysts
Skin	nevi
	café au lait spots

Management of capillary hemangiomas of optic disc and retina general considerations

Because most capillary hemangiomas grow progressively and eventuate in exudative and/or hemorrhagic complications, most authorities recommend obliterative therapy for all retinal capillary hemangiomas, except for those that occur in or near the macula (2, 6). In contrast, because of the inherent risks of visual impairment associated with treatment of optic disc lesions, most experts currently recommend obliterative therapy to only those disc tumors associated with visual impairment. The actual indications for obliterative therapy of asymptomatic capillary hemangiomas of the retina, and optic disc cannot be stated with certainty, since no large, prospective, long-term study of untreated capillary hemangiomas has been performed. Individual bias based on anecdotal or limited experience with this condition precludes uniformity of opinion regarding management at the present time.

Methods of treatment

The methods of treatment currently advocated for capillary hemangiomas of the retina include photocoagulation, cryotherapy, and diathermy, with or without scleral buckling. The method most appropriate for an individual case depends on several factors, including size of the hemangioma(s), location of the hemangioma(s), clarity of ocular media, presence of retinal detachment, number of hemangiomas in the eye, age of patient and the patient's ability to cooperate.

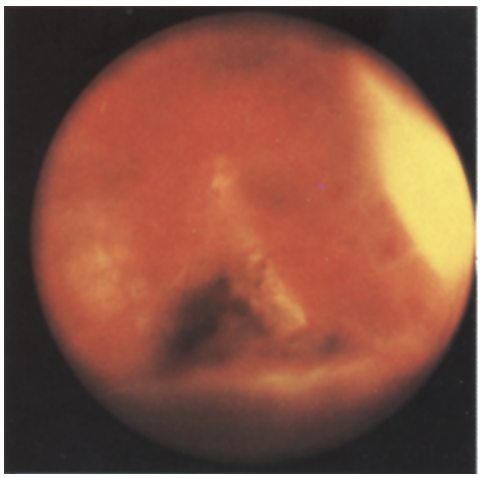
Photocoagulation

Small retinal capillary hemangiomas can be effectively treated with photocoagulation using either the xenon arc photocoagulator or the argon laser (2, 15, 23). Most hemangiomas up to 2.5 disc diameters in size can be treated effectively by photocoagulation (2). Photocoagulation is applicable to small hemangiomas in the posterior or midzones of the fundus and to those far pheripheral tumors that can be brought into view by simultaneous scleral depression (applicable to the xenon arc photocoagulator delivery systems) or that can be clearly viewed with a wide angle or mirrored contact lens at the slit lamp biomicroscope (applicable to the argon laser delivery system).

Photocoagulation burns are generally applied around the margins and to the entire surface of each and every retinal capillary hemangioma. Rather large spot sizes and long durations of exposure are commonly recommended. Energy sufficient to fully whiten the retina with each exposure is generally advised. Such treatment typically causes a temporary increase in trans-endothelial leakage of fluid components of plasma leading to an increase in subretinal exudative fluid. Such an exudative response to photocoagulation can lead to total, bullous, non-rhegmatogenous retinal detachment (*ablatio fugax*), which is typically self-limited over several weeks. Several sessions of photocoagulation of the type described above at two to six week intervals are generally advocated instead of a single session of extremely intense photocoagulation because of the increased risks of bleeding from the treated site(s), stimulation of surface wrinkling retinopathy, and development of a massive exudative reaction following the latter type of treatment.

Effective photocoagulation appears clinically to destroy the capillary hemangioma and leave in its place an irregularly depigmented and pigmented flat scar. Such a scar commonly remains following resolution of the exudative subretinal fluid and can be responsible for persistent visual impairment.

Photocoagulation is not applicable in eyes with capillary hemangiomatosis of the retina that have hazy or opaque media or that have bullous retinal detachment involving the portion of the retina containing the hemangioma(s). Vitrectomy combined with scleral buckling and photocoagulation may be considered in selected eyes with extensive vitreous hemorrhage and retinal detachment due to capillary hemangiomatosis.



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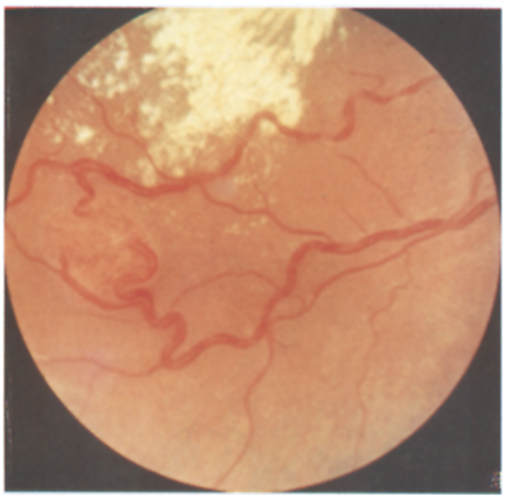

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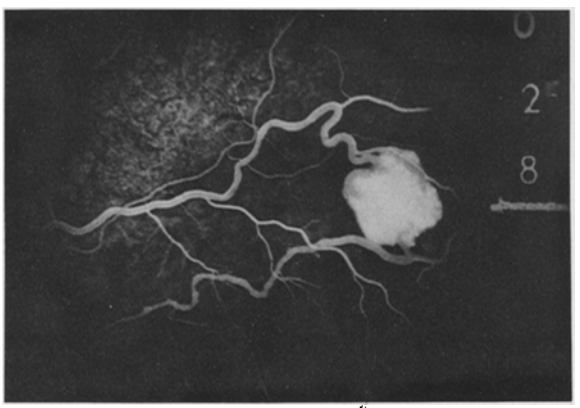
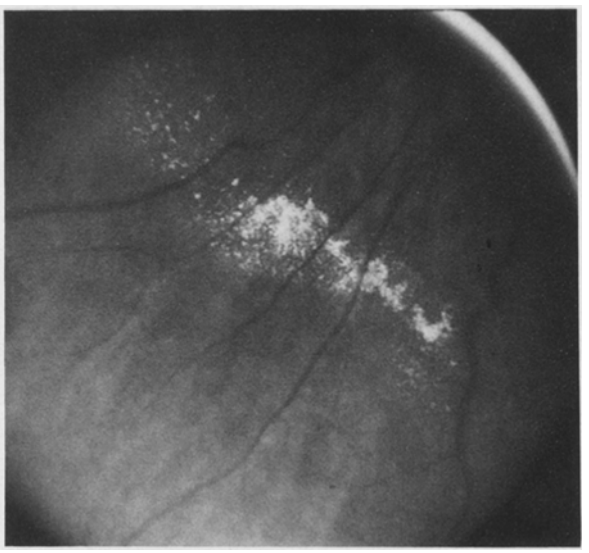


Fig. 1. a. Wide angle fundus photograph shows solitary retinal capillary hemangioma superotemporal from left macula. b. Higher power fundus photograph shows red-orange tumor, dilated and tortuous afferent and efferent vessels and exudates extending into macula. c. Fluorescein angiogram frame demonstrates hyperfluorescent tumor. Reprinted with permission from Augsburger, J.J., Goldberg, R.E., Magargal, L.E.: Retinal and choroidal vascular abnormalities and fluorescein angiography. I. In Harley, R.E. (ed): Pediatric Ophthalmology, (Ed II) W.B. Saunders Co., Philadelphia (in press). Photograph courtesy of Dr. William E. Benson.



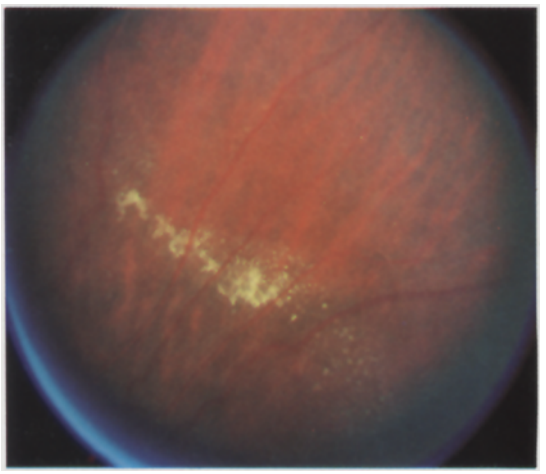


Fig. 2. Arcuate line of exudates between peripheral retinal capillary hemangioma (not demonstrated) and optic disc in 14 year old girl.

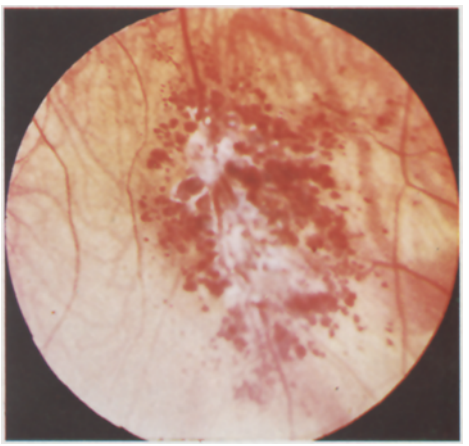


Fig. 3. Macular exudates associated with peripheral retinal capillary hemangioma (not demonstrated).

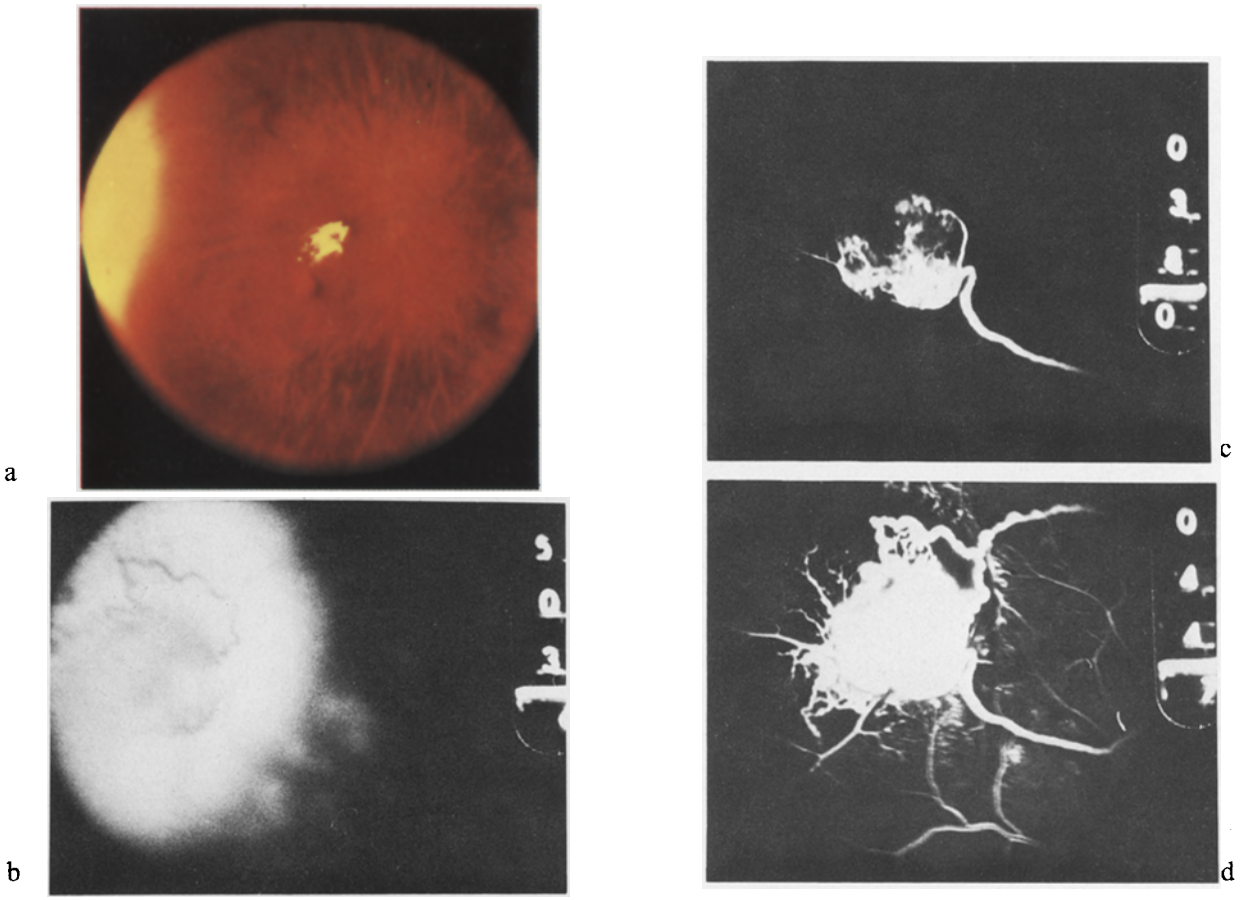


Fig. 4. a. Peripheral yellow-orange retinal capillary hemangioma with associated hemorrhage, exudates and gliosis. b. Arterial phase frame of fluorescein angiogram shows early filling of tumor. c. Venous phase frame shows marked hyperfluorescence of tumor, loss of tumor vessel details, and surrounding retinal vascular abnormalities. d. Late recirculation phase frame shows hyperfluorescence of subretinal fluid due to profuse leakage from tumor vessels.

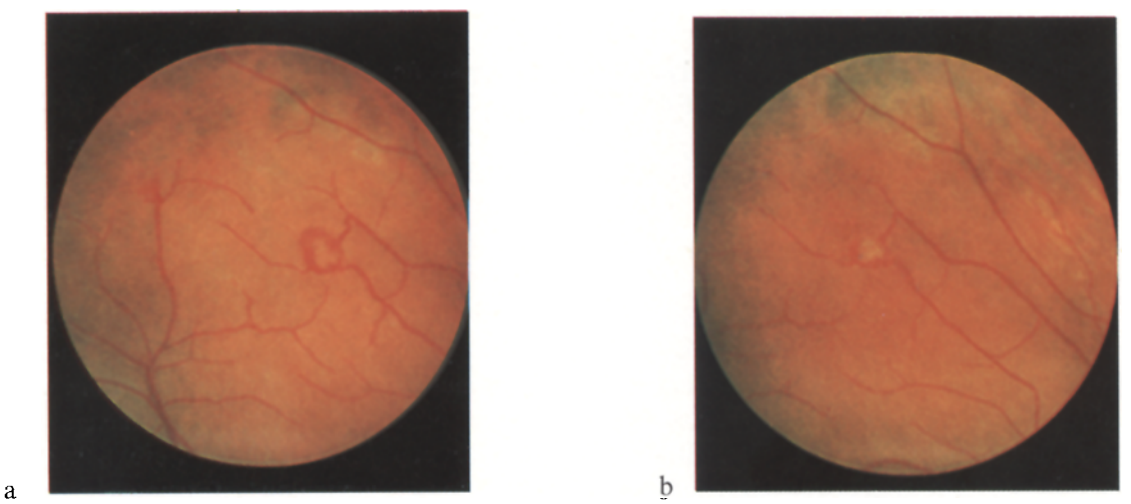


Fig. 5. Retinal capillary hemangioma as it appeared in 1977 (a) and in 1980 (b). No definite change in the lesion is evident.

Cryotherapy

Cryotherapy is an effective modality for treating most capillary hemangiomas of the retina (1, 5, 33). The technique currently advocated involves placement of the tip of a retinal cryoprobe on the conjunctiva or bare sclera directly exterior to the site of the retinal hemangioma. Activation of the probe freezes the underlying tissues, including the hemangioma, to a temperature of approximately −70° to −80° C. The ice ball is allowed to thaw slowly without the assistance of probe warmers or irrigation of the probe tip. This freeze-thaw cycle is immediately repeated twice. This triple freeze-thaw technique typically produces an irregularly pigmented and depigmented chorioretinal scar incorporating the hemangioma within two to four weeks, but it commonly must be repeated on several occasions at intervals of several weeks to a few months to effectively eliminate the tumor (31). Even after development of a satisfactory scar, some of the vessels comprising a treated capillary hemangioma typically persist. In such cases, the afferent and efferent vessels associated with the treated tumor commonly continue to exhibit dilation and tortuosity (31), but the exudative reaction generally resolves completely if treatment has been adequate.

The complications associated with cryotherapy of retinal capillary hemangiomas include an initial increase in the amount of exudative subretinal fluid and stimulation of vitreoretinal membranes and surface wrinkling retinopathy. Hemorrhage from the tumor into the vitreous and/or subretinal space appears to be rather uncommon following cryotherapy.

Cryotherapy is most applicable to retinal capillary hemangiomas in the peripheral retina, where they can be visualized readily by indirect ophthalmoscopy with scleral depression. It is certainly an effective modality for treatment of small hemangiomas, but it produces a rather large chorioretinal scar relative to the size of a small tumor. As long as the media are clear, the hemangioma is accessible for photocoagulation, and the retina at the site of the lesion is not greatly elevated by exudative subretinal fluid, photocoagulation is probably the method of choice rather than cryotherapy for small tumors because of the more limited amount of scarring it produces. For most hemangiomas larger than 2.5 DD, for those occurring in eyes with hazy media and for those inaccessible to photocoagulation, cryotherapy appears to be the currently recommended treatment of choice. Some eyes with bullous retinal detachment require drainage of subretinal fluid just prior to cryotherapy.

Diathermy

Diathermy is an effective form of therapy applicable to the treatment of some large retinal capillary hemangiomas (5). The technique advocated is surgical development of a lamellar scleral bed external to the hemangioma, placement of the penetrating diathermy tip directly into the hemangioma under indirect ophthalmoscopic monitoring by passing it through the lamellar sclera, choroid, Bruch's membrane, retinal pigment epithelium and any subretinal fluid that is present, and activation of the probe to cauterize the tumor. This technique is generally performed as part of a scleral buckling procedure. A number of potential complications can be anticipated with this procedure, including retinal incarceration, retinal hole formation, and subretinal hemorrhage. As a result, penetrating diathermy is rarely advocated except for very large tumors unresponsive to cryotherapy.

Prognosis for vision

Because of the tendency for an exaggerated macular exudative reaction and/or macular retinal detachment in capillary hemangiomatosis of the retina and because of the occurrence of complications such as surface wrinkling retinopathy involving the macula following photocoagulation or cryotherapy, the prognosis for visual acuity following treatment must be guarded. For eyes with one or more tumors all less than 2.5 disc diameters in size, Annesley et al. (2) found 14 of 52 eyes (29%) treated by various combinations of xenon arc or argon laser photocoagulation or cryotherapy to have a final visual acuity worse than 6/21. For those eyes

with one or more tumors, the largest of which was greater than 2.5 disc diameters in size, these same authors found 34 of 75 eyes (47%) to have a final post treatment visual acuity worse than 6/21 following photocoagulation, cryotherapy, and/or diathermy. These findings appear to support the contention of some experts (2, 6) that all retinal capillary hemangiomas be treated as soon as they are detected, while they are still small because of the improved visual prognosis in such eyes. As pointed out in the preceding comments on natural history, however, this contention has not been unequivocally established in any randomized, controlled study.

Non ocular abnormalities in patients with capillary hemangiomatosis of the retina and optic disc

As pointed out in the introductory comments, capillary hemangiomatosis of the retina and optic disc is commonly associated with vascular lesions of the central nervous system and cysts and tumors of multiple viscera. The most common associated lesions are the solid and cystic capillary hemangioblastomas of the cerebellum (Fig. 6). Similar vascular lesions occur in the spinal cord in some affected persons. The most characteristic of the visceral lesions are pheochromocytoma, renal cell carcinoma, and pancreatic cysts. The table lists most of the pertinent and relatively common lesions that occur in persons with capillary hemangiomatosis of the retina and optic disc.

Approximately twenty-five per cent of persons with capillary hemangiomatosis of the retina and optic disc develop signs and symptoms attributable to central nervous system lesions (31). Asymptomatic CNS lesions probably occur in many other persons. Renal cysts and tumors have been detected at autopsy in about two-thirds of affected patients in one series (22). Because of the rather high prevalence of some of these associated cysts and tumors, most experts advise referral of all patients with capillary hemangiomatosis of the retina and optic disc for neurologic and complete medical evaluation and subsequent follow-up. The decision to perform CNS studies such as CT scanning and carotid arteriography is probably most appropriately left to the discretion of the neurologist, and the decision to perform studies such as intravenous pyelography, whole body CT scanning, and pharmacologic testing for pheochromocytoma is probably most appropriately left to the discretion of an internist or pediatrician familiar with the visceral manifestations of the von Hippel-Lindau syndrome.

Heredofamilial considerations

The von Hippel-Lindau syndrome appears to be inherited as an autosomal dominant condition with relatively high penetrance (26). Expression of the disorder in affected family members, however, is less than one might anticipate because of the asymptomatic nature and difficulty in detection of many of the small lesions that can occur in the retina, central nervous system, and/or viscera. Only a negative autopsy is reliable evidence that a person in a family with the von Hippel-Lindau syndrome does not have the disorder. Approximately one-half of the members of an affected kindred will have one or more of the lesions of the von Hippel-Lindau syndrome (26). However, less than half of affected family members are likely to have capillary hemangiomatosis of the retina and optic disc in a large kindred with von Hippel-Lindau disease (26).

Because of the familial nature of this disorder and because of the potentially serious ocular, neurologic and visceral complications of this disorder, early screening and regular interval follow-up of all family members by ophthalmologists, neurologists, pediatricians and internists is generally recommended. Even in those instances in which the condition appears to be sporadic (50–70% of cases) (4, 6), one should probably advise screening of all family members because of the rather common occurrence of clinically silent lesions in individuals with this syndrome.

Cavernous hemangiomatosis

Cavernous hemangiomatosis of the retina and optic disc is a rare condition characterized by distinctive,

benign, vascular hamartomas. Cavernous hemangiomas can be readily distinguished from capillary hemangiomas of the retina and optic disc in most cases. Although cavernous hemangiomatosis was undoubtedly observed prior to 1970, Gass (10) is generally credited with identification of this condition as a specific entity apart from conditions such as Von Hippel's disease and idiopathic retinal telangiectasia. Gass (10–12) and other authors (7, 14, 17, 24, 32) have pointed out that cavernous hemangiomatosis of the retina and optic disc can coexist with various neurologic and/or cutaneous lesions and have suggested that this condition should be considered a phakomatosis similar to the Von Hippel-Lindau syndrome.

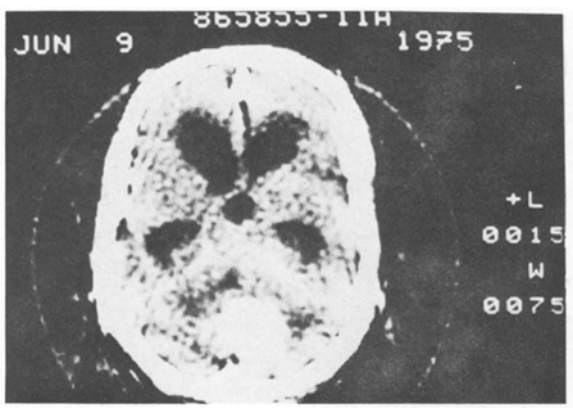
Clinical features

Cavernous hemangiomas of the retina and/or optic disc have a characteristic, readily identifiable appearance (8, 10, 19, 20). Each hamartoma is composed of multiple vascular sacs of various sizes, ranging from tiny lesions that resemble microaneurysms to larger sacs that are generally not greater than one disc diameter in size. An individual cavernous hemangioma (Fig. 7) typically consists of a grape-like cluster of these vascular sacs, the smaller sacs generally surrounding the larger central sacs. The entire hamartoma can involve an area several disc diameters in size. The blood within the saccular compartments of a cavernous hemangioma characteristically appears dark and venous in nature. Some of the larger sacs exhibit characteristic plasma-erythrocyte separation. Glial and fibrous proliferation on the surface of a cavernous hemangioma (Fig. 8) is not uncommon. When it is pronounced, the glial and fibrous tissue can partially obscure the component sacs of the hemangioma.

Small cavernous hemangiomas of the retina and/or optic disc are generally rather flat, but larger lesions typically project into the overlying vitreous (Fig. 9). Dilated, tortuous afferent arterioles and efferent venules are not a feature of this condition, in which the adjacent retinal blood vessels appear to maintain their relatively normal caliber and course. Surrounding exudates and exudative subretinal fluid, which are characteristic of eyes with capillary hemangiomas, are uncommon features in eyes with cavernous hemangiomatosis.

Natural history

Most cavernous hemangiomas of the retina and optic disc appear stable over many years of follow-up (7), although clinically visible alterations in the walls of individual sacs do occur in some cases. Growth of an established cavernous hemangioma of the retina and optic disc must be extremely unusual. We have been unable to document unequivocal growth in any of our cases, and reports on cavernous hemangiomatosis that we have reviewed do not appear to document growth of any of these tumors. Bleeding into the vitreous (Fig. 9) and/or subretinal space can be a major complication of some of these hamartomas.



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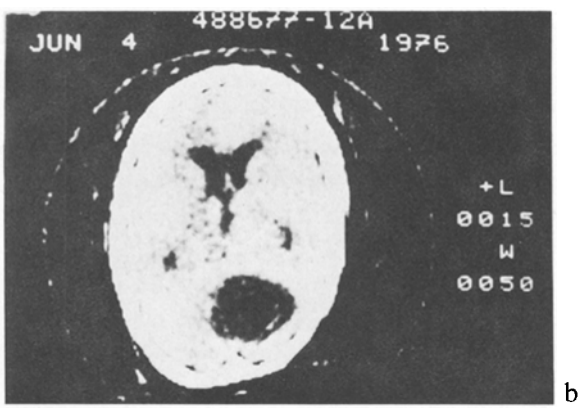

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Fig. 6. CT scans showing typical appearance of solid (a) and cystic (b) cerebellar hemangioblastomas.

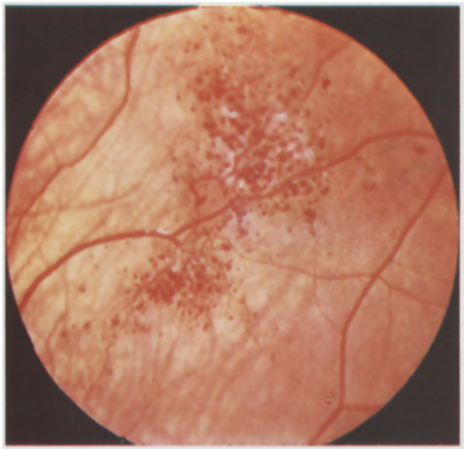

Fig. 7. Retinal cavernous hemangioma composed of multiple small intraretinal vascular sacs. Note absence of associated exudates. Reprinted with permission from Goldberg, R.E., Pheasant, T.R. & Shields, J.A.: Cavernous hemangiomas of the Retina. A four generation pedigree with neurocutaneous manifestations and an example of bilateral retinal involvement. *Arch. Ophthalmol.* 97: *2321–2324*, 1979. Copyright 1979, American Medical Association.

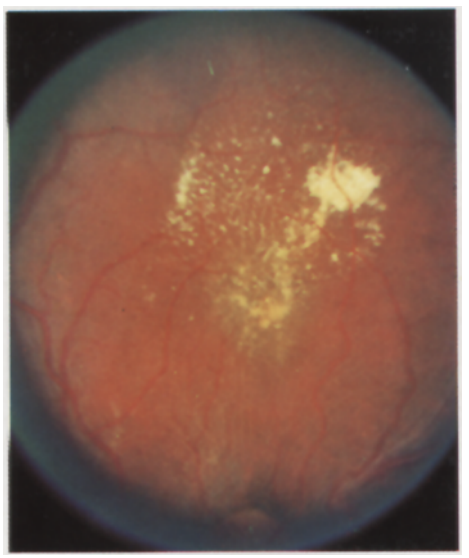

Fig. 8. Retinal cavernous hemangioma with prominent component of white fibro-glial material. Reprinted with permission from Goldberg, R.E., Pheasant, T.R. & Shields, J.A.: Cavernous hemangiomas of the Retina. A four generation pedigree with neurocutaneous manifestations and an example of bilateral retinal involvement. *Arch. Ophthalmol.* 97: *2321–2324*, 1979. Copyright 1979, American Medical Association.

Bilaterality

With few exceptions (17), cavernous hemangiomatosis of the retina and optic disc is a monocular condition. Bilateral involvement has been reported in only four patients to date (17).

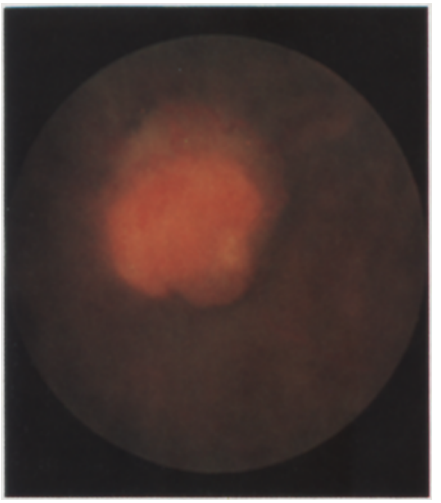

Fig. 9. Wide angle fundus photograph showing large reddish-purple cavernous hemangioma of retina. The tumor is partly obscurred by intravitreal blood which has settled inferiorly.

Multiplicity

Cavernous hemangiomatosis is characteristically and almost exclusively a unifocal condition with regard to the eyes. We have no personal experience with patients having more than one cavernous hemangioma in the same fundus.

Patient characteristics

Most persons with a cavernous hemangioma of the retina and/or optic disc are between 10 and 40 years of age at the time of detection of the tumor. Males and females appear to be affected in nearly equal proportions (7).

Symptoms

Unlike patients with von Hippel's disease, most persons with cavernous hemangiomatosis of the retina and optic disc are asymptomatic. Those persons with a cavernous hemangioma that bleeds into the vitreous, however, are likely to report painless blurred vision with floaters (20).

Fluorescein angiography

Fluorescein angiography of a retinal or papillary cavernous hemangioma (Fig. 10) typically shows hypofluorescence of the saccules of the hamartoma during the arterial phase, slow filling of the saccules during the venous phase, and persistent fluorescence of the lesion in the recirculation phases (11, 12). Individual saccules, especially larger ones with clinically apparent plasma-erythrocyte separation, exhibit characteristic hyperfluorescence of the superior plasma-filled portion and hypofluorescence of the inferior erythrocyte-filled portion in the late phases of the angiograms (Fig. 10). The saccules generally leak little, if any fluorescein, in marked contrast to the vascular channels that comprise capillary hemangiomas.

Management of cavernous hemangiomas of the retina and optic disc

Since most cavernous hemangiomas of the retina are stable lesions that do not impair vision, treatment is rarely indicated. Most hamartomas of this type can be managed appropriately by photographic documentation and regular follow-up. Retinal tumors that bleed into the vitreous can be treated by transconjunctival or transcleral cryotherapy and possibly by photocoagulation, if the media are clear enough (12).

Because of the visual complications associated with their treatment, cavernous hemangiomas of the optic disc should rarely, if ever, be treated.

Non ocular abnormalities in persons with cavernous hemangiomatosis of retina and optic disc

As first shown by Weskamp and Cotlier in Argentina (32), some persons with cavernous hemangiomatosis of the retina and/or optic disc have characteristic neurologic and cutaneous abnormalities. Such persons can present with seizures, cranial nerve palsies, intracranial hemorrhage, paresthesias or multiple neurologic deficits (17, 32). The lesions responsible for these signs and symptoms have generally been found to be cavernous hemangiomas, which typically occur in the pre-Rolandic cerebral cortex, cerebellum, midbrain or pons (29). Unfortunately, many cavernous hemangiomas of the central nervous system are difficult to demonstrate with current techniques of arteriography and computerized tomography (25). A completely negative autopsy is probably the only reliable evidence that a person with a retinal and/or papillary cavernous hemangioma does not have CNS cavernous hemangiomatosis.

Various cutaneous lesions have been noted in some persons with cavernous hemangiomas of the retina and/or optic disc (7, 10, 17). The most commonly associated skinlesion is the capillary hemangioma. However, these lesions are so common in the general population that the significance of their association with cavernous hemangiomatosis of the retina and/or optic disc is difficult to establish. Cavernous hemangiomatosis of the retina has also been associated with angioma serpiginosum (14), an uncommon dermatologic disorder characterized by widespread, progressive dilation of subpapillary venous plexuses of the skin and gradual impairment of peripheral motor and sensory nerve function.

Visceral lesions do not occur with any predictable regularity in persons with cavernous hemangiomatosis of the retina and/or optic disc. One reported patient with this ocular condition was found to have a major congenital malformation involving the heart and great vessels (7). However, this association may be no more than a chance relationship.

Heredo-familial considerations

Most persons with cavernous hemangiomatosis of the retina and/or optic disc have no history of a similarly affected relative, and few of them have any family members with pertinent CNS or dermatologic lesions. In some kindreds, however, an autosomal dominant inheritance pattern with low penetrance and variable expressivity has been postulated (10, 17). Further in-depth family studies on relatives of persons with cavernous hemangiomatosis of the

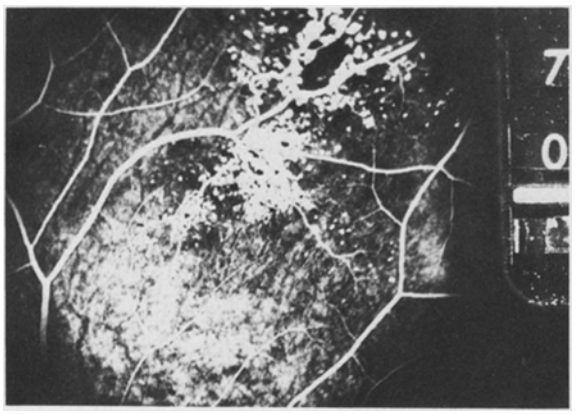

Fig. 10. Fluorescein angiogram frame showing fluorescence of most of component vascular sacs of retinal cavernous hemangioma. Plasma-erythrocyte separation is not well-demonstrated in this angiogram. Reprinted with permission from Goldberg, R.E., Pheasant, T.R. & Shields, J.A.: Cavernous hemangiomas of the Retina. A four generation pedigree with neurocutaneous manifestations and an example of bilateral retinal involvement. *Arch. Ophthalmol.* 97: *2321–2324*, 1979. Copyright 1979, American Medical Association.

retina and/or optic disc will be needed to clarify the heredo-familial nature of this disorder.

Because of the known association with important CNS lesions in some persons with retinal and/or papillary cavernous hemangiomatosis, we recommend referral of all persons with this fundus condition to a neurologist for evaluation and appropriate studies. We also recommend ophthalmic evaluation of all family members.

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