Retinal Vascular Tumors

3

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Contents

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Retinal vascular tumors represent at least four distinct clinical entities which include retinal capillary hemangiomas, retinal cavernous hemangiomas, retinal arteriovenous communications (Wyburn-Mason syndrome), and retinal vasoproliferative tumor. Retinal vascular tumors can also be considered as congenital or prenatal in origin, maintaining retinal tight junctions and hence not manifesting retinal leakage, such as subretinal fluid or hard exudates (retinal cavernous hemangioma and retinal arteriovenous communications [Wyburn-Mason syndrome]), or acquired/postnatal in origin without retinal tight junctions and hence manifesting retinal leakage, such as subretinal fluid or hard exudates (retinal capillary hemangioma and retinal vasoproliferative tumor). Each of the subtypes has characteristic

A.D. Singh, B. Damato (eds.), *Clinical Ophthalmic Oncology*,
DOI 10.1007/978-3-642-39489-8_3, © Springer-Verlag Berlin Heidelberg 2014

Table 3.1 Diagnostic features of various retinal vascular tumors

Type	Appearance	Location	Feeder vessels	Exudation	Systemic association
Capillary hemangioma	Round red mass	Juxtapapillary/ peripheral	Prominent	Present	VHL disease
Cavernous hemangioma	Grapelike clusters	Nonspecific	Absent	Absent	CNS hemangioma
Arteriovenous malformations	Dilated/tortuousretinal vessels	Near the disc	Absent	Absent	Wyburn-Mason syndrome
Vasoproliferative tumor	Globular pale mass	Periphery	Absent	Present	Absent

VHL von Hippel-Lindau disease

clinical features and an attempt should be made to differentiate them because of specific systemic associations, treatment, and prognosis associated with them. The clinical features and systemic associations of retinal vascular tumors are summarized in Table 3.1. Only a brief description of retinal capillary hemangioma and retinal arteriovenous communications (Wyburn-Mason syndrome) is included in this chapter as these topics are further discussed under neuro-oculocutaneous syndromes (phakomatoses) (Chap. 9).

3.1 Retinal Capillary Hemangioma

3.1.1 Introduction

Although these retinal vascular tumors have been characterized as hemangioblastomas, various authors have recommended that the term capillary hemangioma rather than hemangioblastoma or hemangioendothelioma be used to describe these vascular tumors [1]. Retinal capillary hemangiomas can be further classified on the basis of their location within the retina (peripheral and juxtapapillary), morphology (endophytic, exophytic, and sessile), effects on the retina (exudative form and tractional form), and their relationship to von Hippel-Lindau (VHL) disease (with or without VHL disease).

3.1.2 Clinical Features

Retinal capillary hemangiomas are multiple in about one-third of patients, and up to half of the cases have bilateral involvement. The mean age at diagnosis of retinal capillary hemangioma in VHL disease is approximately 25 years [2].

3.1.2.1 Symptoms

Patients typically notice progressive worsening of vision which may be associated with photopsia. Many patients are asymptomatic and are detected on a routine examination or on screening evaluation because of the family history of VHL disease [3].

3.1.2.2 Signs

Ophthalmoscopically, a retinal capillary hemangioma appears as a circumscribed, round retinal lesion with an orange-red color with prominent feeder vessels (Fig. 3.1). Intraretinal and subretinal exudates are often seen around the tumor or in the macula. The majority of retinal capillary hemangiomas are located in the superotemporal and inferotemporal peripheral retina [4]. Prominent retinal vessels emerging from the optic disc are highly suggestive of a peripherally located retinal capillary hemangioma. In contrast, juxtapapillary retinal capillary hemangiomas are not associated with visible prominent feeder vessels.

3.1.3 Diagnostic Evaluation

The fundus findings of retinal capillary hemangiomas are characteristic and the diagnosis can usually be made based solely on ophthalmoscopic examination. Fluorescein angiography is the most informative diagnostic tool because of the vascular nature of the tumor (Fig. 3.1) [5]. Fluorescein angiography also helps in differentiating the

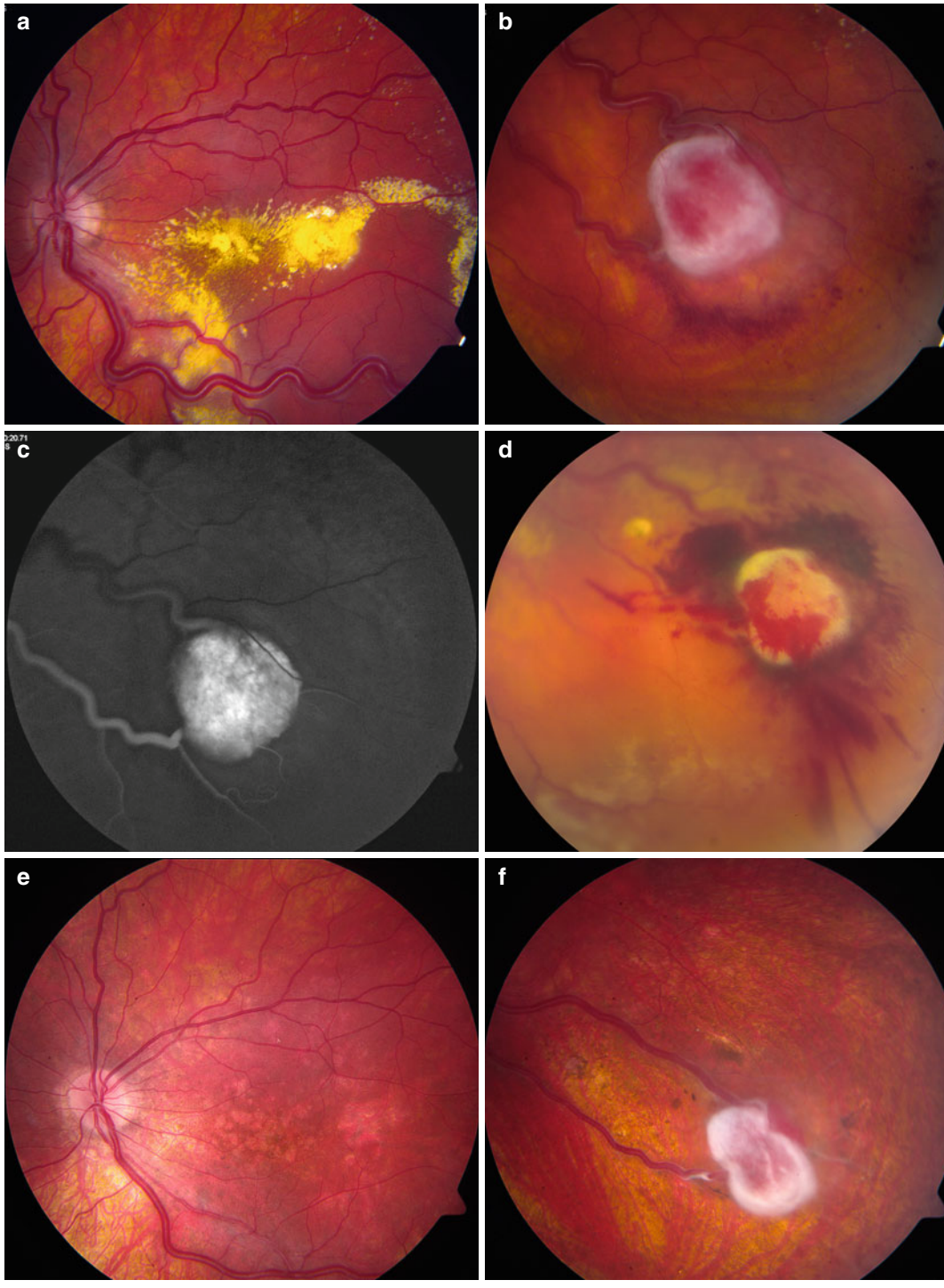

Fig. 3.1 Fundus photograph of a retinal capillary hemangioma. Note prominent feeder vessels and retinal exudation (**a**). The hemangioma has a rim of gliosis and surrounding and subretinal fluid and hemorrhage (**b**). Fluorescein angiography identifies the feeder artery (**c**). Marked hyperfluorescence and leakage are characteristic findings. One week after treatment with standard-fluence photodynamic therapy, increased gliosis hemorrhage (**d**). Six months after the treatment, there is complete resolution of macular exudates and reduction in size of the feeder vessels (**e**). The lesion has regressed with increased gliosis and total resolution of surrounding and subretinal fluid and hemorrhage

feeder arteriole from the draining vein and is therefore important for treatment planning.

3.1.4 Salient Diagnostic Findings (Box 3.1)

- Single or multiple, circumscribed, orange-red colored, round retinal lesion.
- Retinal exudation and or subretinal fluid surrounding the lesion which may extend into the macular region.
- Prominent feeder vessels extending from the optic disc (absent in juxtapapillary variant).
- Prominent and early filling on fluorescein angiography with late leakage.

3.1.5 Differential Diagnosis

Some of the conditions that should be considered in the differential diagnosis include Coats' disease, macroaneurysm, and other forms of retinal vascular tumor [6]. Coats' disease is an idiopathic unilateral retinal vascular disease of young males which is characterized by retinal telangiectasia and retinal exudation [7]. The younger age of onset, unilateral involvement, predilection for males, and lack of systemic features are helpful differentiating features. Moreover, Coats' disease has prominent areas of retinal telangiectasia rather than distinct retinal vascular tumors.

Retinal macroaneurysm has many features that differentiate it from retinal capillary hemangioma [8]. In general, macroaneurysm is seen as a single lesion in the posterior pole in older individuals and is more likely to present with subretinal, intraretinal, or vitreous hemorrhage rather than retinal exudation. Most importantly, the feeder vessels are absent and careful fundus examination reveals that the macroaneurysm is centered on the retinal arteriole.

Important findings that differentiate a retinal capillary hemangioma from a vasoproliferative tumor are the absence of prominent feeder vessels in a vasoproliferative tumor and its extreme peripheral location in the inferior retina [9]. Retinal capillary hemangioma is more commonly seen in the temporal quadrants of the mid-peripheral retina [6]. Unlike retinal capillary hemangioma, vasoproliferative tumors are nonfamilial and lack significant systemic association [9].

3.1.6 Treatment of Retinal Capillary Hemangioma

There are several methods of treating a retinal capillary hemangioma and the choice of treatment is determined by the size, location, and associated findings of subretinal fluid, retinal traction, and the visual potential of the eye [10]. The treatment can be challenging due to the presence of multiple tumors in both eyes and the potential for the onset of new tumors.

3.1.6.1 Observation

Careful observation in a reliable patient can be recommended if the retinal capillary hemangioma is very small (up to 500 μm), is not associated with exudation or subretinal fluid, and is not visually threatening [10]. Initial observation should always be considered in juxtapapillary retinal capillary hemangioma as they tend to remain stable [11].

3.1.6.2 Laser Photocoagulation

Laser photocoagulation, applied over many sessions, is effective (91–100 %) in treating retinal capillary hemangiomas that are up to 4.5 mm in size, but is most effective in tumors that are 1.5 mm or smaller in size (Fig. 3.2) [12]. Photocoagulation can be applied directly to the tumor, to the feeder artery, or a combination of both techniques can be used [13].

3.1.6.3 Cryotherapy

Cryotherapy is preferable to photocoagulation when the retinal capillary hemangioma is located anteriorly and the retinal capillary hemangioma is more than 3.0 mm in diameter (Fig. 3.3) [14]. Cryotherapy may also be preferred when there is

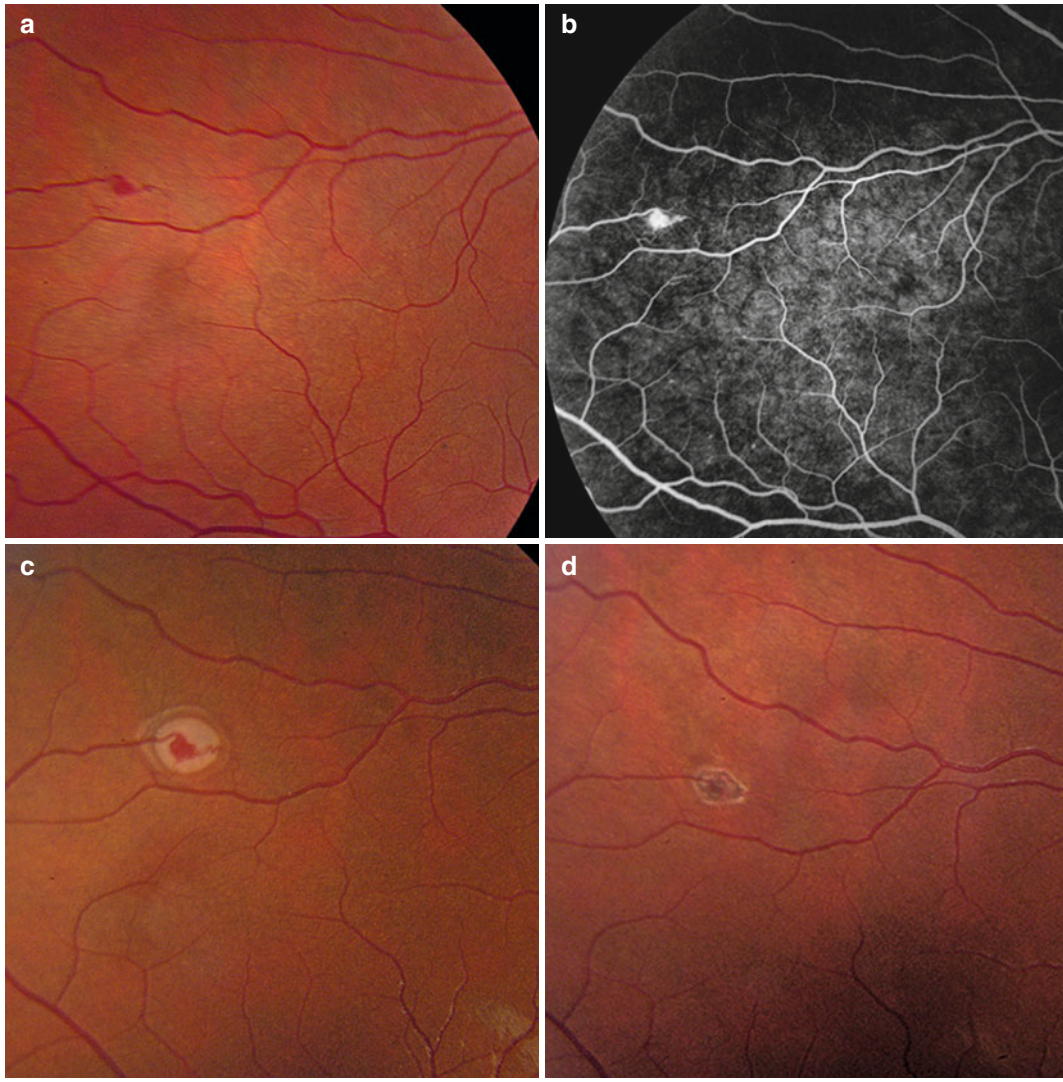

Fig. 3.2 Small retinal capillary hemangioma observed on surveillance examination in a patient with VHL disease (**a**). The hemangioma could be visualized with fluorescein angiography (**b**). Appearance immediately after laser photocoagulation (**c**). Four weeks later, the hemangioma is partially regressed and surrounded by a chorioretinal scar (**d**) (Reproduced with permission from Singh and Schachat [53])

moderate amount of subretinal fluid. The efficacy of cryotherapy is greater with smaller tumors (less than 1.5 mm) [10].

3.1.6.4 Photodynamic Therapy

More recently, photodynamic therapy has been reported to induce occlusion of peripheral (Fig. 3.1) and juxtapapillary retinal capillary hemangioma (Fig. 3.4) [11, 15–17].

3.1.6.5 Radiotherapy

Retinal capillary hemangiomas that are greater than 4 mm show a poor response to cryotherapy and laser photocoagulation and such tumors can be treated successfully with plaque radiotherapy [18]. Low-dose external beam radiotherapy is also an option in cases that do not respond to the usual methods of treatment listed above [19].

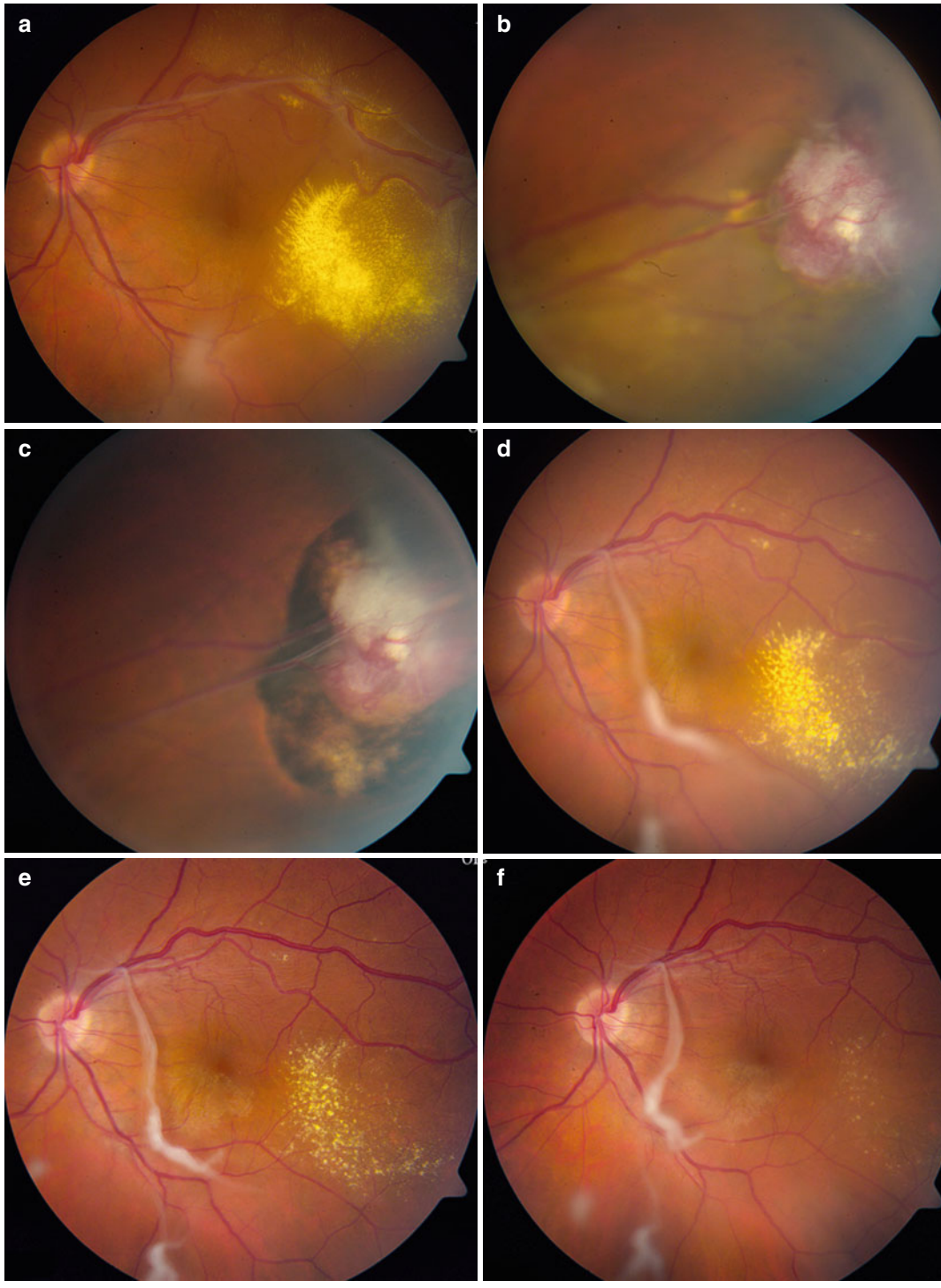

Fig. 3.3 Cryotherapy for retinal capillary hemangioma. Macular exudation (**a**) and peripheral solitary retinal capillary hemangioma (**b**). Note reduction in tumor vascularity and surrounding reactive pigment proliferation 3 months after double freeze-thaw cryotherapy (**c**) and reduction in macular exudation (**d**). The macular appearance continues to improve with slow resolution of exudation (**e**, 6 months) without additional intervention (**f**, 12 months). Cryotherapy also led to partial peeling of the epiretinal membrane (final visual acuity 20/20)

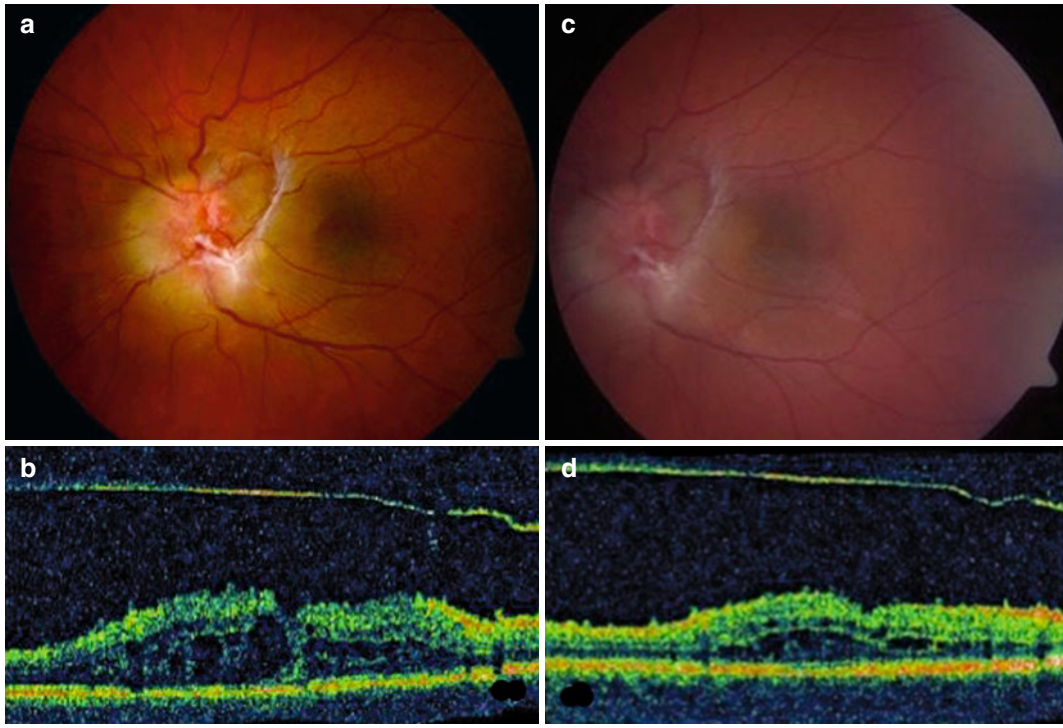

Fig. 3.4 Initial fundoscopic photograph (**a**) and OCT (**b**, fovea) of left eye of 27-year-old female (patient 1) with juxtapapillary retinal capillary hemangioma and associated cystoid macular edema. Fundoscopic photograph (**c**) and OCT (**d**) approximately 2 years following photodynamic therapy in same patient, which reveals stabilization of tumor with decreased edema (Reproduced with permission from Sachdeva et al. [15])

3.1.6.6 Anti-VEGF Therapy

Although anti-VEGF therapy is extensively used in a variety of retinal vascular conditions, its use in the treatment of retinal capillary hemangioma remains unproven with variable response in lesion size and exudation [20, 21].

3.1.6.7 Vitreoretinal Procedures

Pars plana vitrectomy, retinal detachment repair, and other related procedures are usually required for larger retinal capillary hemangiomas that are complicated by rhegmatogenous or tractional retinal detachments.

3.1.7 Association with Von Hippel-Lindau Disease

Retinal capillary hemangiomas can occur sporadically or in association with VHL disease [6, 22]. The association of retinal capillary hemangioma with VHL disease is discussed in detail under neuro-oculo-cutaneous syndromes (phakomatoses) (Chap. 9).

3.1.8 Prognosis

The visual prognosis, even in adequately treated cases, is guarded [6]. Overall, more than 25 % of affected patients show permanent visual loss, and about 20 % have vision of less than 20/100 in at least one eye [4]. However, the visual outcome is greatly dependent on the size, location, and number of retinal capillary hemangiomas and the presence of exudative or tractional retinal detachment. As retinal capillary hemangiomas progressively enlarge, the visual outcome is much better in cases that are diagnosed and treated before the onset of symptoms [4].

3.2 Cavernous Hemangioma of the Retina

3.2.1 Introduction

Cavernous hemangiomas of the retina are composed of multiple, thin-walled dilated vascular channels with surface gliosis [23]. The walls are lined by non-fenestrated endothelium, explaining the lack of exudation [24]. Two forms of cavernous hemangioma of the retina are recognized: sporadic and syndromic [23]. It has been suggested that the cerebral cavernous malformation syndromes should be included with the neuro-oculo-cutaneous (phakomatoses) syndromes, but the association of cerebral and cutaneous hemangiomas is inconsistent [23].

3.2.2 Clinical Features

Cavernous hemangiomas of the retina are believed to be a rare form of congenital hamartoma. The age of presentation in a series of nine patients ranged from 1 to 55 years [25].

3.2.2.1 Symptoms

Patients with cavernous hemangioma of the retina may be asymptomatic or may present with reduced vision from a macular location of the hemangioma, macular fibrosis, or vitreous hemorrhage. Recent OCT studies have revealed OCT an overlying epiretinal membrane forming bridges between the saccules, contraction of which could exert traction and cause vitreous hemorrhage (Fig. 3.5) [26].

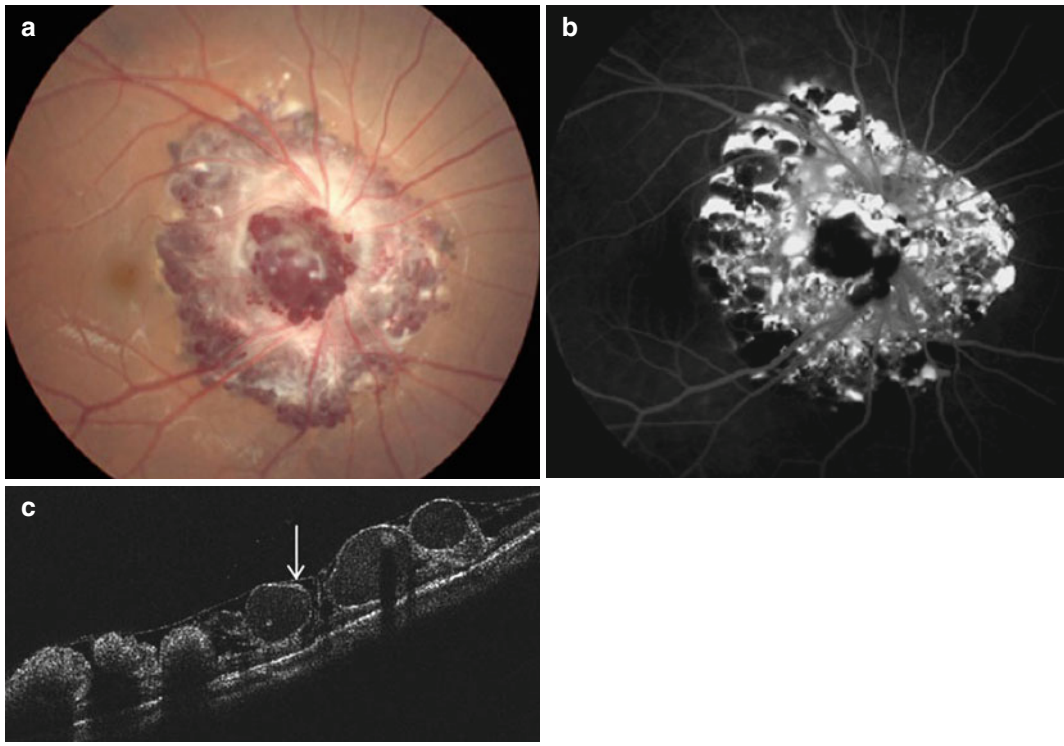

Fig. 3.5 Fundus photograph of a papillary cavernous hemangioma of the retina (**a**). Note the absence of retinal exudation. On fluorescein angiogram, characteristic hyperfluorescent saccular dilatations are evident (**b**) (Reproduced with permission from Patikulsila et al. [54]). Optical coherence tomography of the retinal cavernous hemangioma. An overlying epiretinal membrane is imaged as a continuous hyper-reflective signal attached to the saccules and forming bridges between them (**c**, *arrow*) (Reproduced with permission from Pringle et al. [26])

3.2.2.2 Signs

Retinal lesions appear as grapelike clusters of blood-filled saccular spaces in the inner layers of the retina or on the surface of the optic disc (Fig. 3.5) [23]. The size and location of the hemangioma are variable but most are solitary small (1–2 disc diameters) lesions involving the mid-peripheral or peripheral retina [22]. Epiretinal membranes are usually present. There are no prominent feeder vessels, and there is a lack of subretinal or intraretinal exudation. Rarely, cavernous hemangiomas may be multiple and extensive involving 360° of the mid-peripheral retina [27].

3.2.3 Diagnostic Evaluation

The ophthalmoscopic findings of cavernous hemangiomas of the retina are characteristic. Fluorescein angiography is the most helpful diagnostic test in establishing the correct diagnosis. It demonstrates the retinal origin of the hemangioma with a low flow system and hence delayed filling in the venous phase (Fig. 3.5). The saccular dilatations in the hemangioma appear as fluorescent caps due to staining of supernatant plasma overlying collections of sedimented erythrocytes. Although cavernous hemangiomas are distributed randomly in the fundus, they tend to follow the course of a major vein; however, feeder vessels are not prominent. There is characteristic absence of leakage.

3.2.4 Salient Diagnostic Findings (Box 3.2)

- Retinal lesions appear as grapelike clusters of blood-filled saccular spaces in the inner layers of the retina or on the surface of the optic disc.
- Overlying epiretinal membranes are usually present.
- Absence of prominent feeder vessels.
- Lack of subretinal fluid and intraretinal exudation.
- May be associated with CNS hemangioma.

3.2.5 Differential Diagnosis

Cavernous hemangiomas of the retina should be differentiated from other vascular disorders such as Coats' disease, retinal capillary hemangiomas, retinal arteriovenous communications, and retinal vasoproliferative tumors. Presence of dilated feeder vessels and retinal exudation do not support the diagnosis of retinal cavernous hemangioma.

3.2.6 Treatment of Retinal Cavernous Hemangioma

In general, cavernous hemangiomas of the retina are nonprogressive, may undergo spontaneous thrombosis, and rarely cause vitreous hemorrhage. No effective treatment is known or indeed required, although laser photocoagulation has been attempted in a few cases [23].

3.2.7 Association with CNS Hemangioma

Cavernous hemangiomas of the retina may be associated with cerebral cavernous malformations in the context of an autosomal dominant syndrome with high penetrance and variable expressivity [28–30]. The association between retinal and CNS hemangiomas is discussed in detail under neuro-oculo-cutaneous syndromes (phakomatoses) (Chap. 9).

3.2.8 Prognosis

The vast majority of cases of cavernous hemangioma of the retina remain asymptomatic, do not progress, and require no treatment. A small number of cases of may have an associated self-limiting vitreous hemorrhage. With time, cavernous hemangiomas of the retina undergo progressive thrombosis and often demonstrate an increase in surface gliosis. In contrast, cerebral cavernous hemangiomas may have serious consequences such as seizures, intracranial hemorrhages, and even death [28].

3.3 Wyburn-Mason Syndrome

3.3.1 Introduction

Wyburn-Mason syndrome is a rare sporadic disorder characterized by congenital arteriovenous malformations principally of the retina and brain. Other involved tissues may include the skin, bones, kidneys, muscles, and gastrointestinal tract [31, 32].

3.3.2 Clinical Features

Although usually congenital in origin, the diagnosis of retinal arteriovenous malformations is most commonly made later in childhood.

3.3.2.1 Symptoms

Patients with retinal arteriovenous malformations may be asymptomatic. These lesions are often detected as an incidental finding in an asymptomatic patient or as a cause of visual impairment in an "amblyopic" eye.

3.3.2.2 Signs

Arteriovenous malformations are seen readily on ophthalmoscopic evaluation. These malformations have been classified into three groups depending upon the severity of vascular malformation [33]. Those in group I have an abnormal capillary plexus between the major vessels of the arteriovenous malformations. Group II arteriovenous malformations lack any intervening capillary between the artery and vein. Group III arteriovenous malformations are the most extensive with dilated and tortuous vessels and no apparent distinction between the artery and vein (Fig. 3.6).

3.3.3 Diagnostic Evaluation

The ophthalmoscopic findings of arteriovenous malformations of the retina are characteristic. Fluorescein angiography is the most helpful diagnostic test in establishing the correct diagnosis. It demonstrates abnormal arteriovenous connections and presence or absence of intervening capillaries. In the most severe cases (grade III), arteries and veins cannot be differentiated even on angiography (Fig. 3.6). Abnormal retinal vasculature characteristically demonstrates absence of leakage.

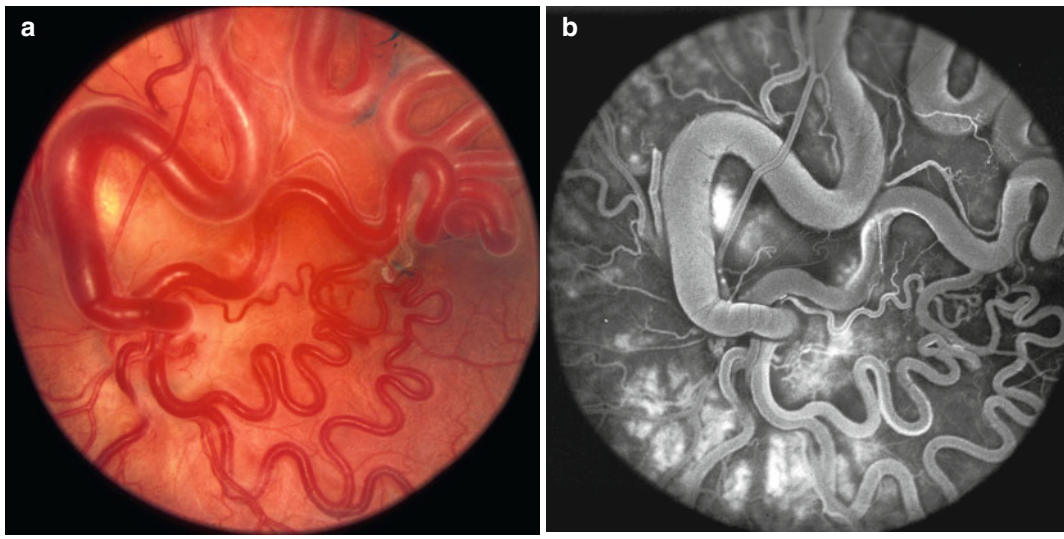

Fig. 3.6 Fundus appearance of a typical retinal arteriovenous malformation (**a**). On fluorescein angiography, arteries and veins appear undistinguishable (**b**)

3.3.4 Salient Diagnostic Findings (Box 3.3)

- Retinal arteriovenous malformations appear as abnormally dilated and tortuous retinal vessels.
- Absence of prominent feeder vessels.
- Lack of subretinal fluid and intraretinal exudation.
- May be associated with intracranial arteriovenous malformations.

3.3.5 Differential Diagnosis

Retinal arteriovenous communications should be differentiated from other vascular disorders listed above. Presence of dilated feeder vessels and retinal exudation goes against the diagnosis of retinal arteriovenous communications.

3.3.6 Treatment of Retinal Arteriovenous Communications

The retinal vascular malformations are usually not amenable to any therapy.

3.3.7 Association with Intracranial Arteriovenous Malformations

The exact incidence of intracranial arteriovenous malformations in patients with retinal arteriovenous malformations is not known. This topic is discussed in detail elsewhere.

3.3.8 Prognosis

The retinal vascular anomalies may alter in configuration over many years exhibiting increasing tortuosity [34] and sometimes leading to vascular occlusions [35] and retinal ischemia with the development of neovascular glaucoma. Patients with group III retinal arteriovenous malformations have a high risk of visual loss either as a result of retinal decompensation or via direct compression of retinal nerve fibers or optic nerve [36, 37].

3.4 Retinal Vasoproliferative Tumor

3.4.1 Introduction

Retinal vasoproliferative tumors are uncommon retinal lesions which have only been recognized as a distinct clinical entity since 1982 when Baines reported the combination of a peripheral telangiectatic nodules and posterior fibrocellular membranes in five patients [38]. These lesions were initially termed as "presumed acquired retinal hemangiomas" to differentiate them from capillary hemangiomas [39]. The nomenclature has varied in the literature, but at present, vasoproliferative retinal tumors are the widely accepted terminology [9]. Histologically, these lesions are composed of a mixture of glial cells, retinal pigment epithelial cells, and a network of fine capillaries with some larger dilated blood vessels [40, 41]. The histological appearances of vasoproliferative tumors have led to the speculation that these lesions are not true tumors but rather reactive proliferations [38]. Vasoproliferative retinal tumors may be primary (74 %) or secondary to a preexisting ocular disease (26 %) [9].

3.4.2 Clinical Features

Vasoproliferative retinal tumor usually presents in the third or fourth decade and both sexes are equally affected [9]. The majority of patients with primary tumors are solitary (87 %) in contrast to those with secondary tumors where multiple lesions were found in 42 % of cases.

3.4.2.1 Symptoms

Reduced vision, photopsia, and metamorphopsia are common presenting symptoms. Some asymptomatic cases are diagnosed incidentally on an ophthalmoscopic evaluation.

3.4.2.2 Signs

Vasoproliferative tumor appears as a globular yellowish-pink vascular mass in the peripheral retina (Fig. 3.7). These lesions lack the dilated, tortuous, feeder vessels typically seen in retinal capillary hemangioma, but retinal vessels of normal or near-normal caliber may be seen entering the lesion posteriorly. Vasoproliferative retinal tumors have a predilection for the inferior retina. Subretinal exudation, which may be extensive, is common occurring in over 80 % of cases [9]. Exudative retinal detachment, retinal and vitreous hemorrhage, vitreous, and epiretinal membrane cells are frequent associated findings (Fig. 3.8). Retinal pigment epithelial hyperplasia adjacent to the vasoproliferative retinal tumors may be evident especially in secondary tumors [9]. Macular fibrosis (31 %) and edema (18 %) may lead to visual loss (Fig. 3.7).

3.4.3 Diagnostic Evaluation

Ancillary investigations such as fluorescein angiography are of limited value because of the peripheral nature of most lesions. In cases where angiography is possible, the lesions typically fill rapidly in the early phase with increasingly hyperfluorescence and diffuse leakage in the late phases (Fig. 3.7). Telangiectatic and dilated vessels are frequently observed within the tumor mass. Ultrasonography confirms a raised solid lesion with high internal reflectivity on both A and B scans. Intraocular biopsy may be necessary to establish a diagnosis in difficult cases [42].

3.4.4 Salient Diagnostic Findings (Box 3.4)

- Vasoproliferative tumor appears as a globular yellowish-pink vascular mass.
- Inferior peripheral retinal location.
- Absence of dilated, tortuous, feeder vessels.
- Associated retinal exudation, subretinal fluid, and macular fibrosis.
- Preexisting ocular disease such as intermediate uveitis, other inflammation, or retinitis pigmentosa.

3.4.5 Differential Diagnosis

Atypical lesions may be confused with retinal capillary hemangioma, eccentric choroidal neovascularization (disciform), or even amelanotic melanoma. The absence of distinct feeder vessels or family history is of value in differentiating a vasoproliferative retinal tumor from a retinal capillary hemangioma. Careful examination of the tumor's vascular supply should confirm their retinal origin in contrast to an eccentric disciform which arises beneath the sensory retina. Similarly, choroidal hemangiomas are subretinal and are rarely surrounded by any significant degree of exudates.

3.4.6 Treatment of Vasoproliferative Tumors

3.4.6.1 Observation

Small peripheral vasoproliferative retinal tumors, lacking significant exudate or maculopathy, can be managed by periodic observation. If the lesion is symptomatic or associated with a significant amount of exudate or detachment, then treatment is warranted.

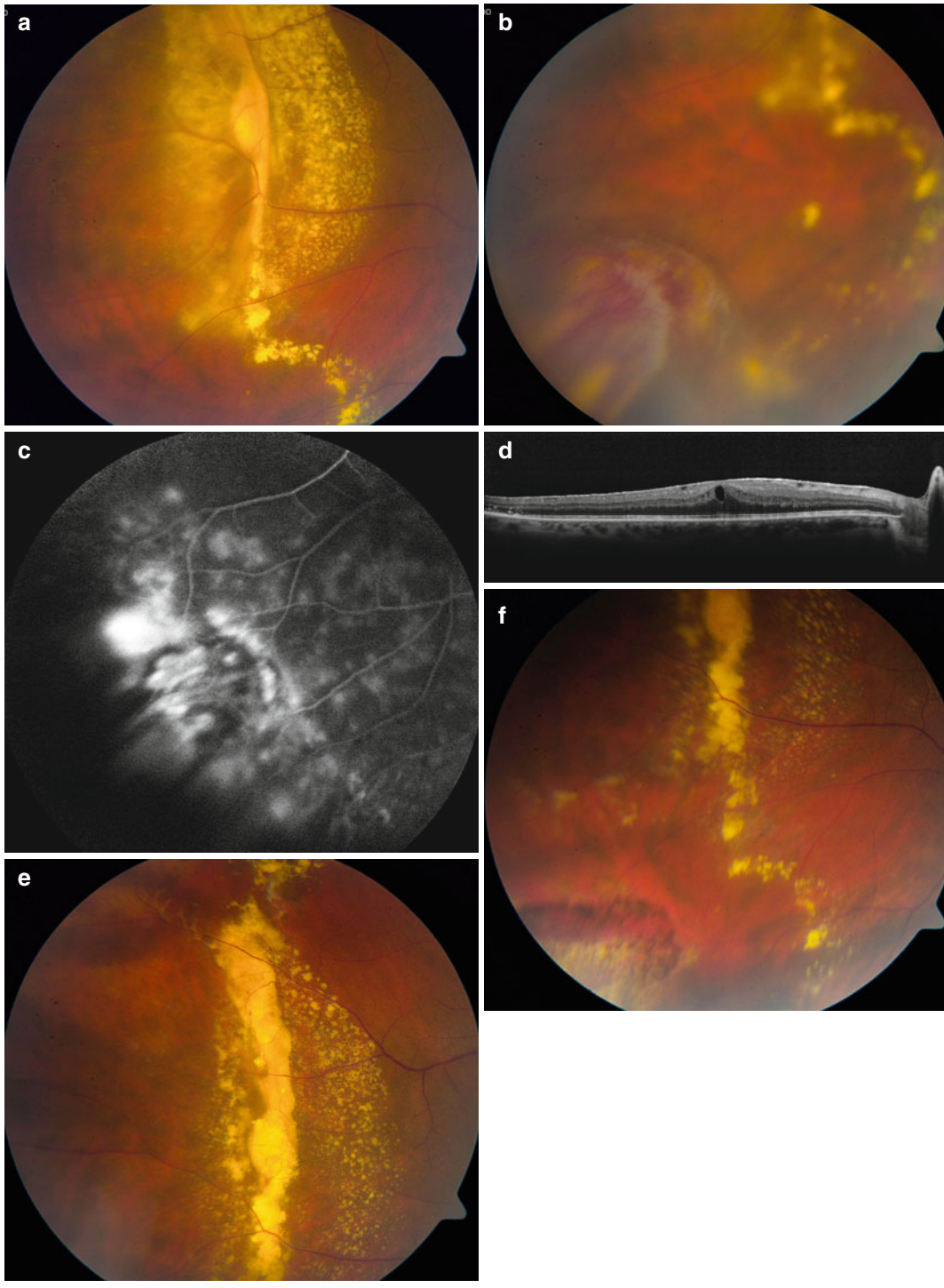

Fig. 3.7 Fundus appearance of a retinal vasoproliferative tumor. Note prominent retinal lipid exudation and bullous exudative retinal detachment (**a**). The vasoproliferative tumor appears as a globular yellowish-pink vascular mass in the peripheral retina (**b**). Diffuse hyperfluorescence in the late phase of the fluorescein angiogram (**c**) and secondary epiretinal membrane (**d**). Six weeks after cryotherapy, there is resolution of lipid exudation, bullous exudative retinal detachment, (**e**) and resolution of the peripheral tumor (**f**)

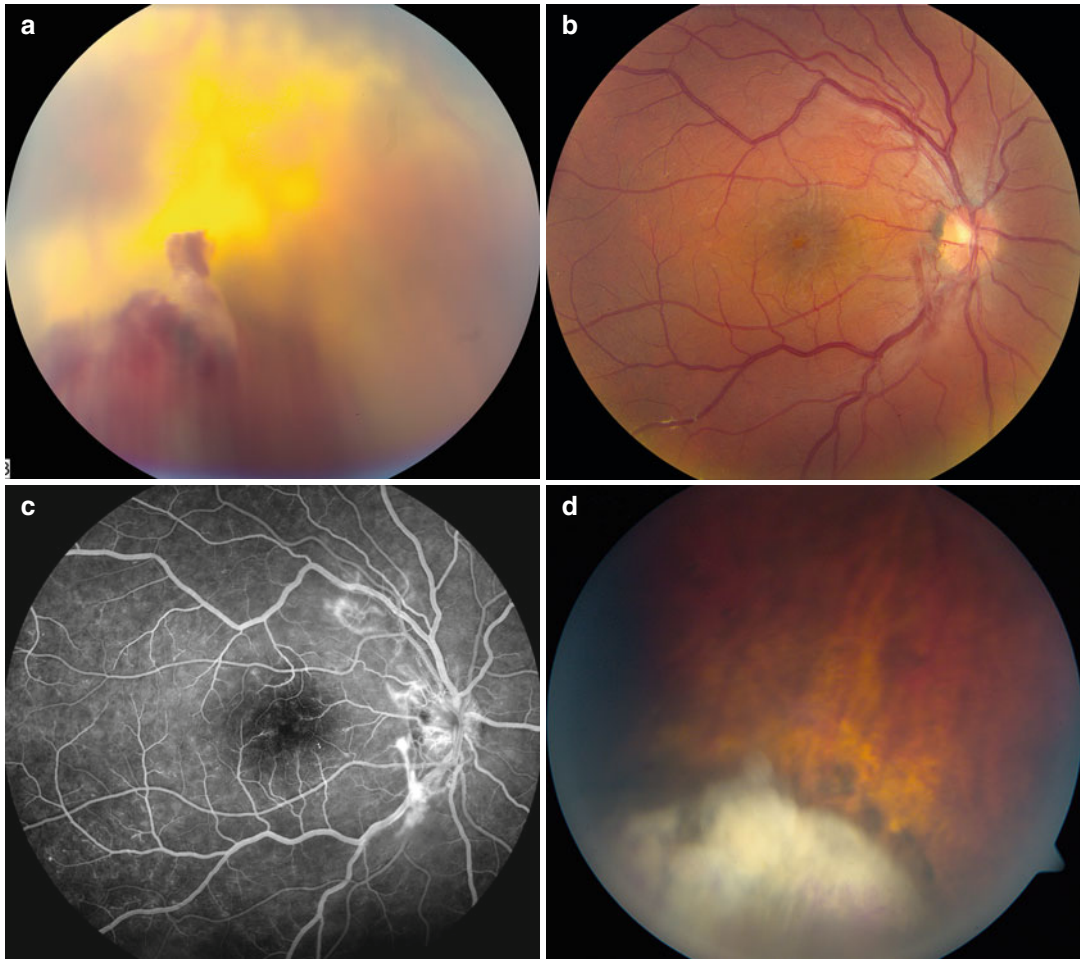

Fig. 3.8 Fundus appearance of a retinal vasoproliferative tumor. Note prominent retinal lipid exudation and peripheral hemorrhagic tumor (**a**). Following treatment with plaque radiation therapy (35 Gy), there was increase in secondary epiretinal membrane (**b**) with onset of retinal neovascularization (**c**) necessitating intravitreal injection of bevacizumab (1.25 mg. 0.05 ml). Four weeks later, the tumor appeared totally avascular and gliotic (**d**)

3.4.6.2 Cryotherapy

Vasoproliferative retinal tumors can be treated successfully with triple freeze-thaw transconjunctival cryotherapy, although repeat treatments may be required (Fig. 3.7) [9]. However, a large tumor may require heavy cryotherapy which in turn can result in significant complications and such tumors are probably best managed by other treatment modalities.

3.4.6.3 Plaque Brachytherapy

Large lesions can be managed effectively using either ruthenium or iodine plaque brachytherapy (Fig. 3.8) [9, 43–45].

3.4.6.4 Photothrombotic and Photodynamic Therapy

Indocyanine green-mediated photothrombotic therapy [46] and photodynamic therapy have

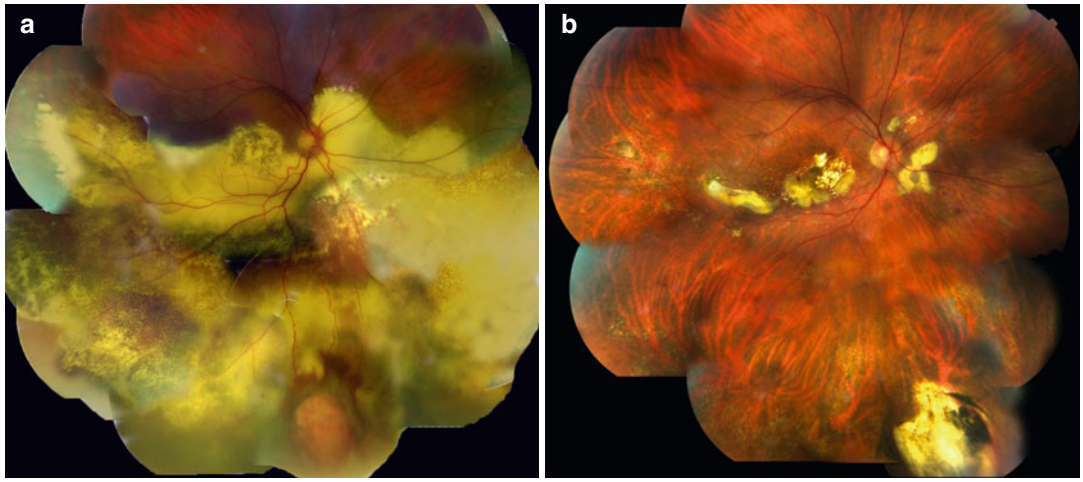

Fig. 3.9 31-year-old female patient presented with history of decreased vision (20/200) in her right eye. Fundus examination revealed a vasoproliferative tumor in the inferior nasal periphery, causing massive subretinal exudation extending to the macula (**a**). Ten months after treatment with indocyanine green-mediated photothrombosis (**b**). Note almost complete absorption of the exudates, RPE and choroidal atrophy, as well as RPE hyperplasia in the site of the lesion (Reproduced with permission from Bertelli and Pernter [46])

been shown to be effective in the treatment of vasoproliferative tumors (Fig. 3.9) [47, 48].

3.4.6.5 Anti-VEGF Agents

May be used as an adjunct to cryotherapy (Figs. 3.8 and 3.10) [49, 50].

3.4.7 Association with Vasoproliferative Tumors

About 25 % of all vasoproliferative tumors are secondary to a preexisting congenital, inflammatory, vascular, traumatic, dystrophic, and degenerative ocular disease such as intermediate uveitis, retinitis pigmentosa, and ocular toxoplasmosis [9]. Rare occurrence in monozygotic twins [51], Waardenburg syndrome [52], and neurofibromatosis 1 [50] and possible association with systemic hypertension and hyperlipidemia have been reported (Fig. 3.8) [9].

3.4.8 Prognosis

In a large series of 103 patients, up to one-third of cases were initially managed by observation [9]. However, even small peripherally located vasoproliferative tumors may be associated with a significant loss of vision. Advanced cases can progress to neovascular glaucoma requiring enucleation.

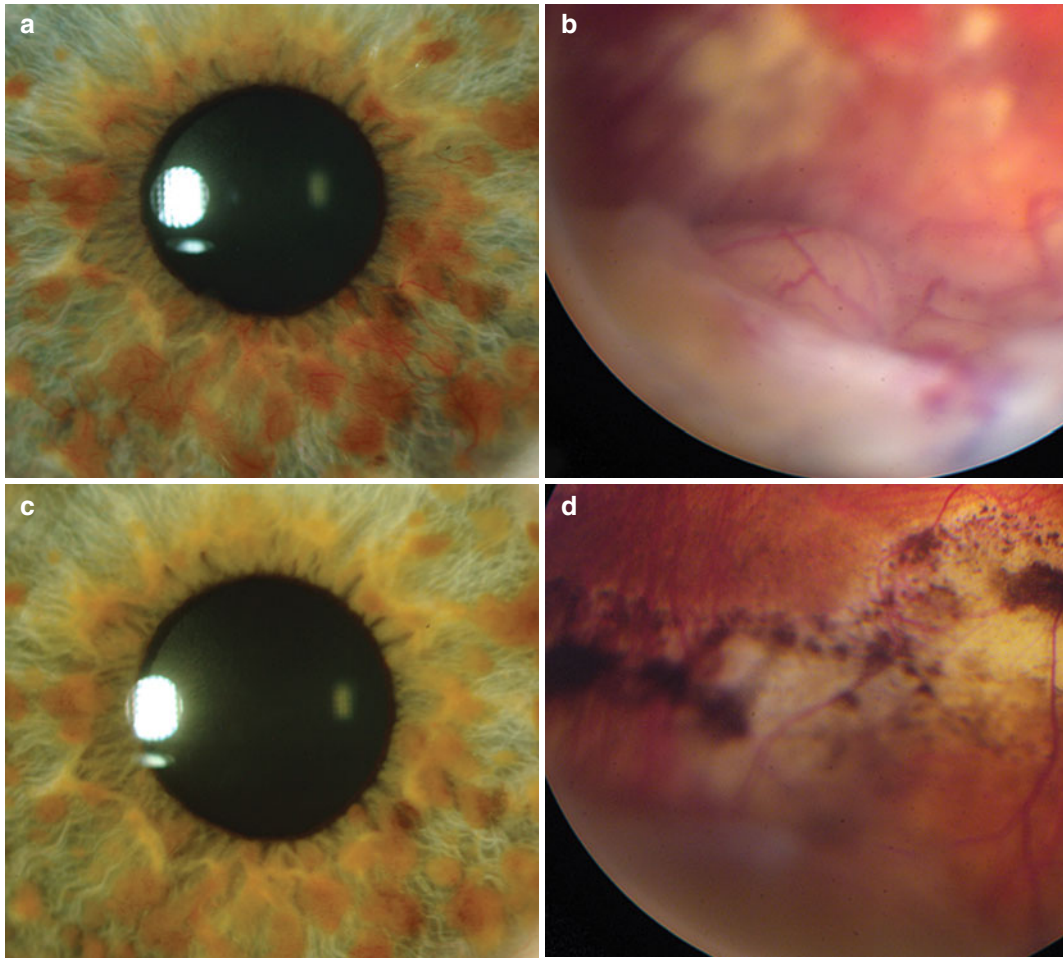

Fig. 3.10 Slit lamp photograph of the right eye at presentation demonstrating multiple Lisch nodules and florid neovascularization of the iris (**a**). On gonioscopic examination, there was 360° neovascularization of the angle. In the inferior fundus, there was a pink, elevated vascular mass with surrounding lipid exudate, consistent with vasoproliferative tumor (**b**). After treatment with cryotherapy and two intravitreal injections of bevacizumab, the neovascularization of the iris resolved almost completely (**c**). The vasoproliferative tumor appeared less vascular with chorioretinal atrophy and hyperpigmentation of the posterior margin (**d**). Note resolution of lipid exudates (Reproduced with permission from Hood et al. [50])

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