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Review

Hamartomas of the Retina and Optic Disc

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Abstract

Hamartomas are local malformation of cells that demonstrate abnormal proliferation in the area where they are normally present. Retinal and optic disc hamartomas include astrocytic hamartoma, congenital hypertrophy of the retinal pigment epithelium (CHRPE), simple congenital hamartoma of the retinal pigment epithelium (CSHRPE), combined hamartoma of the retina and retinal pigment epithelium (CHRRPE), retinal hemangioblastoma (retinal capillary hemangioma), and retinal cavernous hemangioma. Retinal and optic disc hamartomas can be observed sporadically as well as with systemic associations. Astrocytic hamartoma usually appears as a flat, transparent yellowish lesion. CHRPE is a round, pigmented, and flat lesion. CSHRPE usually presents as a dark black macular tumor. CHRRPE consists of vascular, glial, and pigment epithelial components, which can demonstrate peripapillary, macular, and peripheral localization. Retinal hemangioblastoma is a vascular tumor, red-pink in color with tortuous and dilated afferent and efferent vessels, typically located in the peripheral retina or optic disc. Retinal cavernous hemangioma is characterized by the formation of thin-walled saccular angiomatous structures in the retina or optic nerve head resembling concord grapes. Ultrasonography, fundus autofluorescence, optical coherence tomography, optical coherence tomography angiography, and fluorescein angiography methods are used in the diagnosis of retinal and optic disc hamartomas. Some retinal and optic disc hamartomas do not require treatment. However, complications including vitreous hemorrhage, macular exudation, retinal detachment, macular hole, epiretinal membrane, and choroidal neovascularization require treatment.

Keywords: Astrocytic hamartoma, congenital hypertrophy of the retinal pigment epithelium, simple congenital hamartoma of the retinal pigment epithelium, combined hamartoma of the retina and retinal pigment epithelium, retinal hemangioblastoma, retinal cavernous hemangioma

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Introduction

The term hamartoma is derived from the Greek word "hamartia," meaning error. Hamartomas are malformations formed by the abnormal proliferation of cells in the region where they are normally found.[1] Unlike neoplasms, which are caused by mutation in a single cell, multiple cells are affected in hamartomas. They are benign, slow-growing lesions that resemble normal tissue, but malignant transformation may occur. Hamartomas are usually associated with a genetic syndrome. They can occur in different parts of the body.[1] Most cases are asymptomatic and are detected incidentally during evaluation for other medical conditions.[2]

Retinal and optic disc hamartomas include astrocytic hamartoma, congenital hypertrophy of the retinal pigment epithelium (CHRPE), congenital simple hamartoma of the retinal pigment epithelium (CSHRPE), combined hamartoma of the retina and retinal pigment epithelium (CHRPE), retinal hemangioblastoma (retinal capillary hemangioma), and retinal cavernous hemangioma. Retinal and optic disc hamartomas can be observed sporadically or with systemic associations (Table 1). Possible syndromic associations include tuberous sclerosis complex (TSC), neurofibromatosis type 1, retinitis pigmentosa, Usher syndrome, and Stargardt disease for astrocytic hamartoma; familial adenomatous polyposis (FAP) syndrome for CHRPE; neurofibromatosis types 1 and 2, Gorlin-Goltz syndrome, Poland anomaly, and branchio-oculo-facial syndrome for CHRRPE; Von Hippel-Lindau (VHL) syndrome for retinal hemangioblastoma; and cerebral and dermal hemangiomas for retinal cavernous hemangioma.[3,4,5,6,7]

There has been no previous publication reviewing retinal and optic disc hamartomas in the literature. Our aim in this article was to collectively examine rare retinal and optic disc hamartomas.

Astrocytic Hamartomas of the Retina and Optic Disc

Clinical Features

Astrocytic hamartomas of the retina and optic disc are benign lesions. They are most commonly seen in patients with TSC. They can also occur in isolation or secondary to other diseases. Approximately 50% of patients with TSC have optic disc and retinal astrocytic hamartoma, and approximately 30% of TSC patients with astrocytic hamartoma develop bilateral tumors.[8] Astrocytic hamartoma is less commonly associated with neurofibromatosis type 1, retinitis pigmentosa, Usher syndrome, and Stargardt disease.[8]

Astrocytic hamartoma develops from glial cells. Tumorgenesis is caused by mutations in the *TSC1* and *TSC2* genes, which encode hamartin and tuberin, respectively.[9,10] Retinal astrocytic hamartoma, facial angiofibromas, and depigmented macules on the skin resembling vitiligo are the typical triad of patients with TSC.[8]

Astrocytic hamartoma usually presents as a flat, round, transparent lesion (Figure 1a). The lesion then grows into a nodular structure and becomes calcified.[11,12] Sometimes the central part of the lesion is calcific, while the peripheral part may be transparent. There may be hard exudates around astrocytic hamartomas.[13] Hard exudates are generally absent in untreated retinoblastoma/retinocytoma.[13,14] In contrast, changes in the retinal pigment epithelium (RPE) observed in retinoblastomas and retinocytomas do not usually occur in astrocytic hamartomas.[14] Calcification in astrocytic hamartomas is bright yellow with an appearance similar to fish eggs.[15] However, the calcification in retinoblastoma is chalky white.[15] Other diseases that should be considered in the differential diagnosis include optic nerve head drusen, acquired retinal astrocytomas, reactive gliosis, and conditions that cause optic disc edema.

Although astrocytic hamartomas generally have a stable course, giant cell astrocytomas can show progressive growth and cause secondary glaucoma and globe destruction.[15] These tumors are considered malignant but do not metastasize.[15]

Examination Methods

Astrocytic hamartomas appear on ultrasonographic examination as an acoustically solid mass and intralesional calcification is detected. On fundus autofluorescence (FAF) imaging, astrocytic hamartomas demonstrate

Table 1. Systemic diseases associated with retinal and optic disc hamartomas

Retinal and optic disc hamartomas	Associated systemic diseases
Astrocytic hamartoma	Tuberous sclerosis complex Neurofibromatosis type 1 Retinitis pigmentosa Usher syndrome Stargardt disease
Congenital hypertrophy of the retinal pigment epithelium	Familial adenomatous polyposis
Combined hamartoma of the retina and retinal pigment epithelium	Neurofibromatosis type 1 Neurofibromatosis type 2 Gorlin-Goltz syndrome Poland anomaly Branchio-oculo-facial syndrome
Retinal hemangioblastoma	Von Hippel-Lindau disease
Retinal cavernous hemangioma	Coexistence with cerebral and skin hemangiomas

hyperautofluorescence, depending on their calcium content (Figure 1b).[16] Optical coherence tomography (OCT) shows a dome- or plateau-shaped lesion with moderate to high reflectivity and choroidal shadowing (Figure 1c,d).[16] The choriocapillaris is preserved and "moth-eaten" cavities may be visible. OCT angiography (OCTA) reveals a well-defined, hyperreflective lesion and finely branching tumor vessels.[16,17] Retinal flow signals within the tumor can be detected on B-mode angiography (Figure 1e). The tumor vasculature is seen in the superficial and deep retina (Figure 1f,g). The outer retina and choriocapillaris show hyporeflective changes due to shadowing/masking caused by calcium or high blood flow within the lesion (Figure 1h,i). Because of the moth-eaten cavities within the lesion, areas of nonperfusion are seen in the deep retinal plexus and projection artifacts can be observed in the outer retina and choriocapillaris.[16] The lesion is hyporeflective in the full macular composite image (Figure 1j). Hyperreflective signals in the lesion center are due to the tumor vasculature in the deep capillary plexus. On fluorescein angiography (FA), early blockage can be seen in the choroidal phase, while the intrinsic tumor vessels begin filling and hyperfluorescence gradually increases during the arterial phase. There may be leakage in the late venous phase. The differential diagnosis of astrocytic hamartoma includes retinoblastoma, retinocytoma, myelinated nerve fibers, and massive retinal gliosis.[11,12,18]

Based on clinical and OCT findings, four types of retinal astrocytic hamartoma have been identified (Pichi classification).[19] Type 1 appears as a flat retinal lesion (<500 µm) on OCT, with no clinical signs of retinal traction. Type 2 appears as a mildly raised retinal lesion (>500 µm) on OCT, with clinical signs of retinal traction. Type 3 appears as a raised lesion (>500 µm) with calcification in the inner retina on OCT and "mulberry-like" calcification is observed clinically. Type 4 appears as a raised lesion with optically hollow cavities on OCT and the clinical

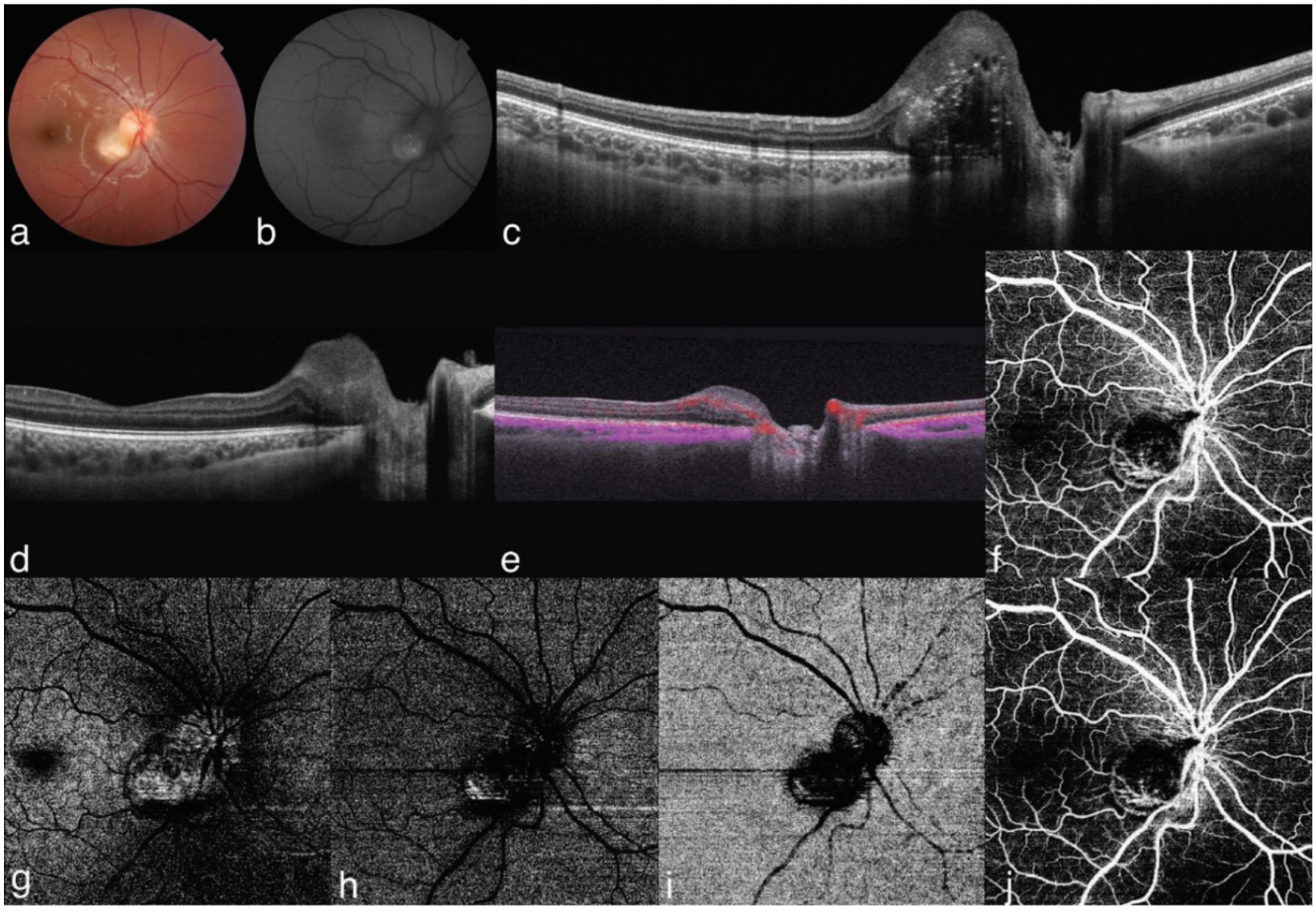

Figure 1. Fundus autofluorescence, optical coherence tomography, and optical coherence tomography angiography findings of a patient with retinal astrocytic hamartoma. a) Color fundus photograph shows a juxtapapillary astrocytic hamartoma in the lower temporal of the optic disc in the right eye. b) Fundus autofluorescence imaging demonstrates hyperautofluorescence due to the presence of calcium in the lesion. c-d) Swept-source optical coherence tomography depicts a moderately reflective, dome-shaped lesion with a base diameter of 1.0x1.0 mm and thickness of 1.1 mm, originating from the retinal nerve fiber layer and compressing the outer retina. Hyperreflective spots caused by the presence of calcium are observed (c). The lesion appears to be associated with the optic disc (d). e) B-mode angiography shows retinal flow signals within the tumor. f-j) Swept-source optical coherence tomography angiography demonstrates minimal hyperreflectivity related to the tumor in the superficial plexus (f). The tumor vascular network is visible in the deep retina (g). The outer retina (h) and choriocapillaris (i) demonstrate hyporeflective alterations due to shadowing/masking caused by intralesional calcium or high blood flow. The lower border of the lesion features a projection artifact from the retinal vessels (h,i). In the full macular composite image, the lesion appears hyporeflective, with hyperreflective signals centrally originating from the vascular network in the deep retinal plexus (j)

appearance is a flat, non-calcified lesion in the inner retina. Type 2 retinal astrocytic hamartoma is significantly more common in TSC patients with fibrous skin plaques, Type 3 in those with subependymal giant cell astrocytic hamartoma, and Type 4 in those with lung lymphangiomyomatosis.[19]

Treatment and Prognosis

Astrocytic hamartoma is generally stable and does not require treatment. Rarely, spontaneous regression may occur.[20] Periodic monitoring is important because of the risk of vitreous hemorrhage, retinal exudation, retinal detachment, and neovascular glaucoma. Laser photocoagulation can be applied to small lesions. Photodynamic therapy can be attempted for tumors that are larger and symptomatic (if exudates and fluid are present). Anti-vascular endothelial growth factor (anti-VEGF) injections can be administered in cases with secondary choroidal neovascularization. If vitreous hemorrhage from intratumoral fine vessels or neovascularization occurs, pars plana vitrectomy surgery may be required. Giant cell astrocytic hamartoma may show an aggressive course, and enucleation may be necessary due to tumor necrosis, vitreous hemorrhage, subretinal hemorrhage, massive exudation, and the development of neovascular glaucoma.[21] Neovascular glaucoma occurs as a result of intratumoral necrosis or chronic retinal detachment. TSC patients with subependymal giant cell astrocytoma and renal angiomyolipoma can be treated with m-TOR inhibitors (rapamycin, everolimus, sirolimus).[22]

Congenital Hypertrophy of the Retinal Pigment Epithelium (CHRPE)

Clinical Features

These are flat, round, and pigmented fundus lesions that are not raised from the surface. They are located at the RPE level. There are three variants: solitary, multifocal, and atypical (Figure 2a). Histopathologically, CHRPE lesions are composed of hypertrophic RPE cells containing excessive pigment granules. The choriocapillaris and choroid are normal. The photoreceptor layer over the RPE may be normal or atrophic. Photoreceptor atrophy fully manifests as the lesion becomes chronic.[23] Patients with photoreceptor atrophy exhibit absolute scotomas on visual field examination.[24]

The margins of CHRPE lesions are usually smooth but can occasionally be irregular. They often occur in the peripheral fundus; peripapillary localization is less common. There may be depigmented lacunae within the lesion and a hypopigmented halo around the lesion (Figure 2a). CHRPE lesions can show minimal growth, especially in myopic eyes.[23] Rarely, lesions such as RPE adenoma/adenocarcinoma may develop from CHRPE.[25]

CHRPEs are occasionally amelanotic.[26] These types of lesions are called amelanotic CHRPE. The retina and retinal vessels overlying the CHRPE are normal.[26] Focal intraretinal pigmentation may be present. In rare cases, neovascularization may occur at the edge of CHRPE.[27]

One type of CHRPE is associated with FAP. The gene responsible for FAP is called the *APC* (adenomatous polyposis coli) gene, located in the 5q21-q22 region. CHRPEs associated with FAP are generally oval-shaped and have tail-like extensions.[28] These lesions are called pigmented ocular fundus lesions (POFL) to distinguish them from other CHRPEs.[29] Their tails may be depigmented and they may contain lacunae. Histopathologically similar to CHRPE, they have pathological appearances of RPE hypertrophy, hyperplasia, and hamartoma.[29] POFLs usually have a base diameter smaller than 5 mm.[30]

POFL can be associated with Gardner syndrome and Turcot syndrome.[29] In Gardner syndrome, hundreds of polyps appear in the colon and give rise to adenocarcinoma of the colon. Prophylactic colectomy is recommended. Extracolonic cancers in Gardner syndrome occur in the thyroid, adrenal gland, and liver. Benign lesions include head and orbit osteomas, sebaceous cysts, lipomas, and fibromas. Opaque jaw lesions can also be observed. In general, detection of 4 or more POFLs is a strong indicator of FAP.[29] In Turcot syndrome, patients develop brain tumors in addition to POFL.[31]

Examination Methods

On ultrasonographic examination, CHRPE lesions appear as flat or minimally raised (<0.5 mm), acoustically solid lesions. FAF imaging typically shows hypoautofluorescence due to the lesions' high melanin content (Figure 2b).[16] Non-pigmented halos or cavities may show autofluorescence.[32] On OCT they are flat lesions at the RPE level that contain hyperreflective deposits and cause choroidal shadowing (Figure 2c,d).[16] The inner retinal layers are normal, but the outer retinal layers exhibit thinning.[16] On OCTA, CHRPEs are generally well-defined and hyperreflective in the superficial and deep retinal plexi.[16] B-mode angiography demonstrates flow signals in the retina overlying the tumor.[16] Masking of the outer retina and choriocapillaris causes the appearance of "signal void" areas.[16] On FA, leakage is not observed.[24] The underlying choroidal fluorescence is blocked in areas other than depigmented halos or cavities.[24]

Treatment and Prognosis

CHRPE lesions generally do not require treatment. However, long-term follow-up is essential. Rarely, RPE adenoma/adenocarcinoma may arise from CHRPE. This type of RPE tumor can be confused with choroidal malignant melanoma. RPE tumors are darker brown/near black in color. However, as they are indistinguishable from choroidal malignant melanoma, RPE adenoma/adenocarcinoma is usually treated by enucleation. The use of proton beam therapy for CHRPE-derived RPE adenocarcinoma was reported in one case.[33]

Congenital Simple Hamartoma of the Retinal Pigment Epithelium (CSHRPE)

Clinical Features

CSHRPE usually appears as a unilateral and dark black tumor with irregular margins. They are black nodules 0.5-1

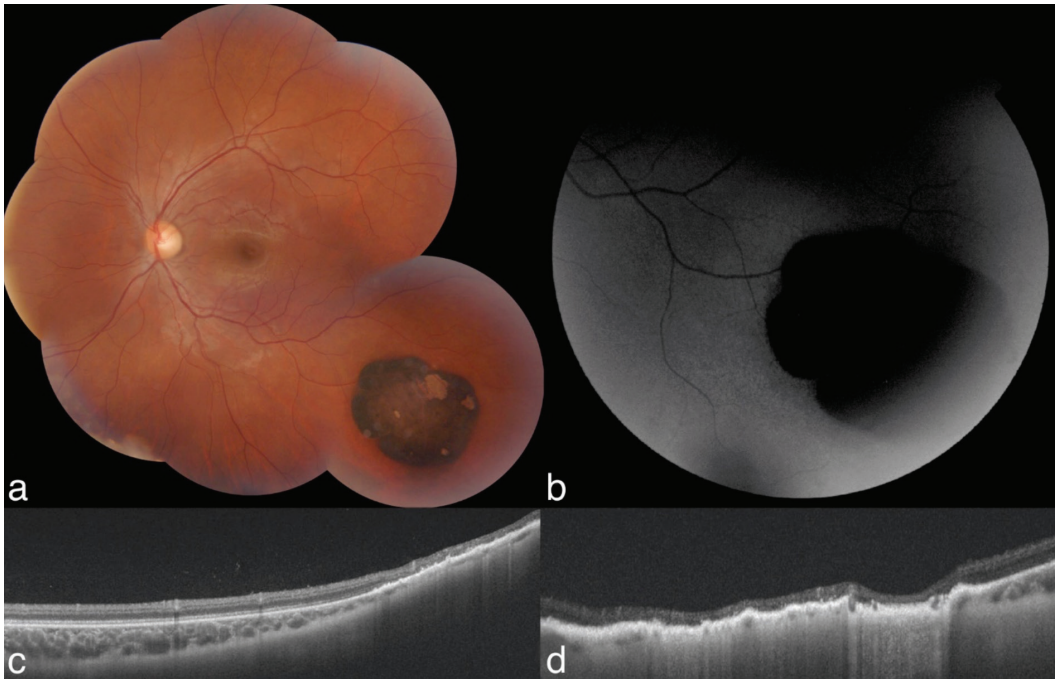

Figure 2. Congenital hypertrophy of the retinal pigment epithelium (CHRPE). a) Composite colored fundus image reveals an inferotemporal CHRPE in the left eye. b) Fundus autofluorescence imaging shows a hypoautofluorescent lesion due to its high melanin content. c-d) Swept-source optical coherence tomography depicts a flat, highly reflective lesion causing choroidal shadowing. Proliferation and high reflectivity are noted at the level of the retina pigment epithelium. The outer retina is thinned. Increased optical transmission is observed in the lacunae within the lesion (d)

mm in size and involve the macula (Figure 3).[34,35] A slightly dilated afferent arteriole and efferent venule are present. Vision is generally preserved. There is retinal traction around the lesion in most cases (80%).[34,35] Pigmented cells may be detected in the vitreous (20%).[35] The development of full-thickness macular hole associated with CSHRPE has been reported.[36] Loss of vision occurs as a result of foveal traction and central foveal involvement.[35]

Examination Methods

On ultrasonographic examination, CSHRPE appears as a nodular lesion with moderate internal reflectivity.[35] The lesion is hypoautofluorescent on FAF.[37] OCT demonstrates a lesion with a hyperreflective surface that shows full-thickness retinal involvement and choroidal shadowing.[37,38] Intratumoral vessels can be detected on OCTA.[39,40] On FA, there is hypofluorescence starting in the early phase and continuing throughout the entire angiography, with no leakage.[35,38]

Treatment and Prognosis

As the lesion is not progressive, treatment is generally not necessary but periodic monitoring is recommended. Vision loss is inevitable with lesions involving the macula. Vitreoretinal surgery can be performed if macular hole or tractional epiretinal membrane develop.[36]

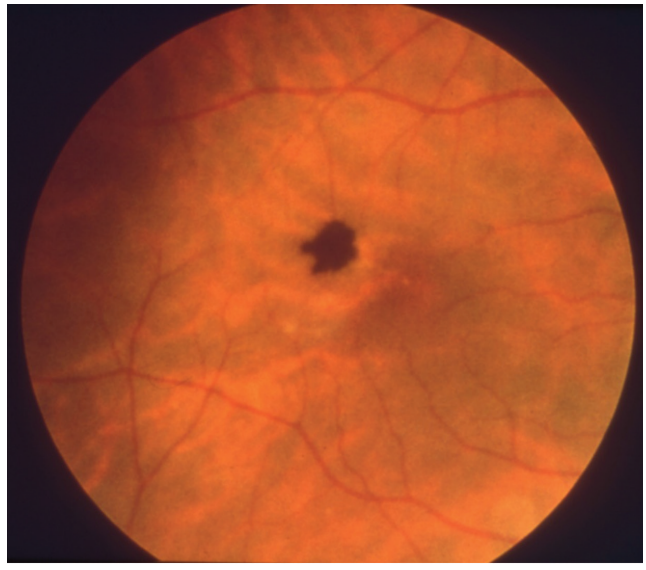

Figure 3. Congenital simple hamartoma of the retinal pigment epithelium. Fundus photograph shows a congenital simple hamartoma of the retinal pigment epithelium located in the macula

Combined Hamartoma of the Retina and Retinal Pigment Epithelium (CHRRPE)

Clinical Features

CHRRPE is a rare benign lesion.[41,42,43,43] It presents between the ages of 1 and 74 years and the mean age at diagnosis is 23 years.[44] Combined hamartoma is usually unilateral and most cases are sporadic.[24] It has been reported to occur more frequently in patients with neurofibromatosis type 2. Less common associations include neurofibromatosis type 1, Poland syndrome, Gorlin syndrome, and branchio-oculo-facial syndrome.[24] Combined hamartoma consists of vascular, glial, and pigment epithelial components.

It can occur in the optic disc or other areas of the fundus (Figure 4a). CHRRPE is classified into three groups according to location: peripapillary, macular, and peripheral. CHRRPE is believed to originate from the inner retina and progress towards the outer retina over time, and an increase in macular thickness may occur regardless of tumor location.[44] Young patients exhibit partial involvement, mainly of the inner retina, and full-thickness retinal involvement is more often seen in older patients. Preretinal fibrosis is more common in young patients, while pigmentary changes are more frequently detected in older patients. An increase in average macular thickness is more common in macular lesions than with those in other locations.[44] There are three stages of CHRRPE according to the anatomical condition of the retina: 1) no retinal traction, 2) retinal traction or retinoschisis is present, and 3) retinal detachment is present.[45] Pigmentation, full-thickness retinal involvement, intraretinal cystic cavities, ellipsoid zone/RPE disruption, and choroidal neovascularization are more common in peripapillary CHRRPE lesions compared to macular CHRRPE lesions.[46] Vision loss varies depending on optic disc, papillomacular bundle, and foveal involvement.[41,42] Tractional distortion occurs in the macula due to epiretinal membrane formation. They usually do not show malignant transformation. Choroidal neovascularization may cause vitreous hemorrhage, retinoschisis, and macular hole.[47]

Examination Methods

Combined hamartoma is diagnosed by indirect ophthalmoscopy. On ultrasonographic examination, CHRRPE lesions appear as slightly raised, acoustically solid lesions with moderate to high internal reflectivity. Peripapillary pigmented lesions exhibit hyperautofluorescence on FAF.[46] On OCT, CHRRPE is divided into three groups according to lesion anatomy: A) epiretinal component only, B) partial retinal involvement, and C) full retinal and RPE involvement.[45] The pathogenesis involves focal vitreoretinal traction. The inner retina exhibits a "sawtooth" pattern (mini-peak) and "omega sign" (maxi-peak).[48,49] The sawtooth and omega signs are usually detected in young patients (Figure 4c).[44] OCTA demonstrates retinal vascular alterations and a "filigree" pattern in the intratumoral vessels.[50,51] On FA, the lesion is hyperfluorescent (Figure 4b). Despite increased pigmentation in the RPE, early

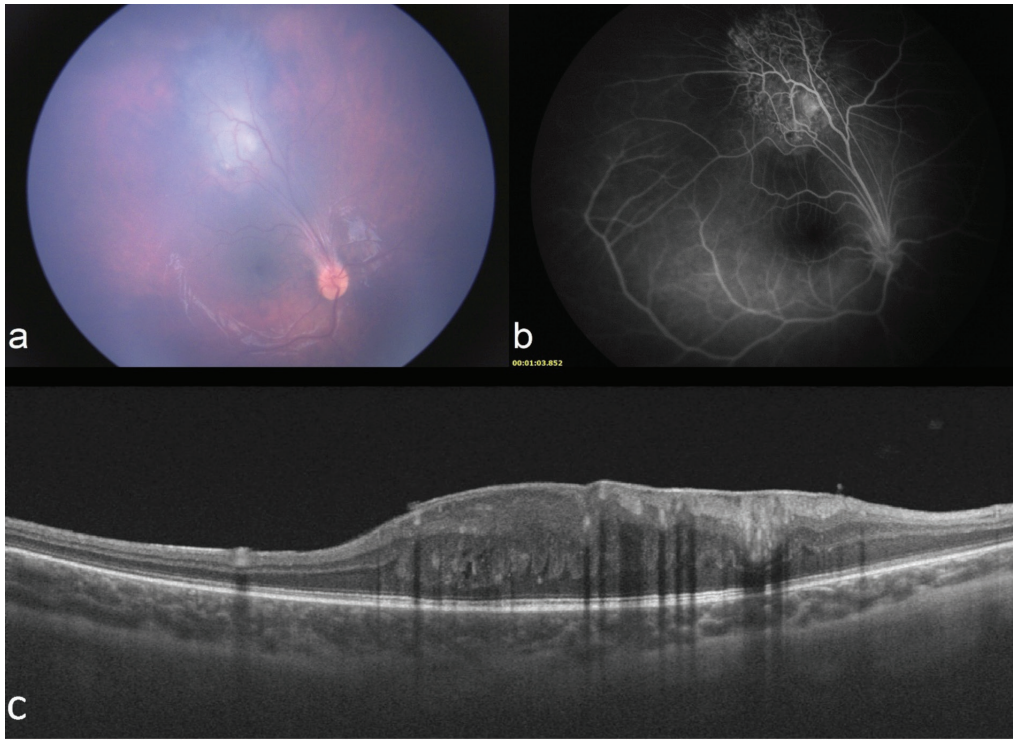

Figure 4. Combined hamartoma of the retina and retinal pigment epithelium (CHRRPE). a) Retcam 3 fundus photograph of a superotemporal amelanotic CHRRPE. b) Retcam 3 fluorescein angiography shows that the lesion is hyperfluorescent. Microaneurysms and non-leaking telangiectatic vessels are observed. c) Swept-source optical coherence tomography demonstrates retinal thickening, intraretinal hyperreflective foci, epiretinal membrane, and the CHRRPE-specific "omega sign" and "sawtooth" pattern

and late hyperfluorescence is observed because of RPE atrophy and cell migration. Microaneurysms and telangiectatic vessels are observed. Although there is usually no leakage from the telangiectatic vessels, minimal leakage from the tortuous vessels may be seen in the late phase.[51,52]

Treatment and Prognosis

Periodic monitoring is recommended for treatment. The role of epiretinal membrane peeling surgery is controversial. In some cases, visual improvement has been reported with vitrectomy and membrane peeling.[53,54] Intravitreal anti-VEGF injection can be administered in eyes with secondary choroidal neovascularization.[55] Amblyopia treatment should also be provided.[24] However, visual improvement is rarely achieved. Vision loss occurs in most cases.[24]

Retinal Hemangioblastoma (Retinal Capillary Hemangioma)

Clinical Features

Retinal hemangioblastomas are benign vascular tumors.[56] They are red-pink tumors typically located in the peripheral retina or optic disc (Figure 5a). Their afferent and efferent vessels are tortuous and dilated.[56] They may be single or multiple. The disease has two types, exudative and tractional.[56] The exudative type is characterized by intraretinal and subretinal exudation, the tractional type by retinal gliosis, vitreoretinal traction, vitreous hemorrhage, and tractional retinal detachment. They may exhibit exophytic and endophytic growth.[56]

Retinal hemangioblastomas may be isolated or occur as part of VHL syndrome. Patients presenting with solitary retinal hemangioblastoma before the age of 10 years have a 45% risk of developing VHL syndrome, while the risk is <1% in those over 60 years of age.[57] Pheochromocytoma, renal cell carcinoma, central nervous system hemangioblastomas, pancreatic cysts, and neuroendocrine tumors may be seen in VHL syndrome. The VHL Alliance recommends dilated fundus examination every 6-12 months until the age of 30 and annually after the age of 30 for patients with VHL syndrome (https://www.vhl.org/patients/clinical-care/screening). Retinal hemangioblastoma is often the initial sign of VHL syndrome (50%) and is seen in VHL patients at an average age of 25 years.[58] Approximately 58% of cases are bilateral.[59] Central nervous system hemangioblastoma is seen in patients aged >20 years, pheochromocytoma in patients aged >40 years, and renal cell carcinoma in patients aged >50 years.[58] Renal cell carcinoma is the most common cause of death.[58]

Examination Methods

FAF shows a hypoautofluorescent lesion (Figure 5b). On OCT, a hyperreflective lesion originating from the retina with compression of the outer retina, retinal edema, and localized retinal detachment is observed (Figure 5c,d). On ultrasonographic examination, retinal hemangioblastoma appears as a raised lesion with moderate to high internal reflectivity (Figure 5e). On FA, the lesion shows hyperfluorescence in the arterial phase that increases in the late phase, with dye leakage into the vitreous (Figure 5f). The afferent and efferent vessels are better detected with OCTA than with FA, because leakage and pooling are not seen on OCTA.[60] However, peripheral tumors cannot be imaged with OCTA.[60,61]

Treatment and Prognosis

For some small, asymptomatic masses, periodic monitoring can be sufficient and spontaneous regression may be observed in some cases.[62] Tumors with limited retinal exudation or retinal detachment can be treated with laser photocoagulation (Figure 5g,i), cryotherapy, transpupillary thermotherapy, and photodynamic therapy and advanced tumors may be treated with plaque radiotherapy or external beam therapy.[63] Successful treatment results in shrinkage of the lesion, narrowing of the afferent vessels, and regression of exudative symptoms in the macula (Figure 5h,j). If vitreous traction and retinal detachment occur, pars plana vitrectomy can also be performed. Endoresection may also be attempted for some tumors.[64] The United States Food and Drug Administration (FDA) recently approved the use of belzutifan, a hypoxia-inducible factor inhibitor, in patients with VHL-associated renal cell carcinomas, central nervous system hemangioblastomas, or pancreatic neuroendocrine tumors (https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-belzutifan-cancers-associated-von-hippel-lindau-disease).

Retinal Cavernous Hemangioma

Clinical Features

Retinal cavernous hemangioma is a unilateral, benign vascular hamartomatous lesion. Ninety percent of cases are unifocal.[65] The lesions are characterized by the formation of thin-walled saccular angiomatous structures in the retina or optic nerve head that resemble a bunch of concord grapes (Figure 6). Malignant transformation has not been reported. It is usually sporadic but can also show autosomal dominant inheritance. In this syndromic association, it may co-exist with cerebral and skin hemangiomas.[66] *KRIT1/CCM1, CCM2/MGC4607, CCM3/PDCD10,* and 7q mutations may be present.[67] The *CCM3* mutation is associated with intracranial hemorrhage.[68]

Examination Methods

On ultrasonographic examination, retinal cavernous hemangioma appears as a raised lesion with high internal reflectivity. On FA, the tumor exhibits hypofluorescence in the early phase and slow filling in the late venous phase. Dye accumulation in the upper half of the saccule and the presence of hypofluorescence underneath give the appearance of a "fluorescein cap."[69] This pattern is the result of hypofluorescence caused by erythrocyte sedimentation at the bottom of the saccule and hyperfluorescence caused by free fluorescein in the plasma at the top.[69]

Treatment and Prognosis

Most cases do not require treatment. Recurrent vitreous hemorrhage can be treated with pars plana vitrectomy.[70] Membrane peeling can be performed in cases with severe traction and vision loss.[71]

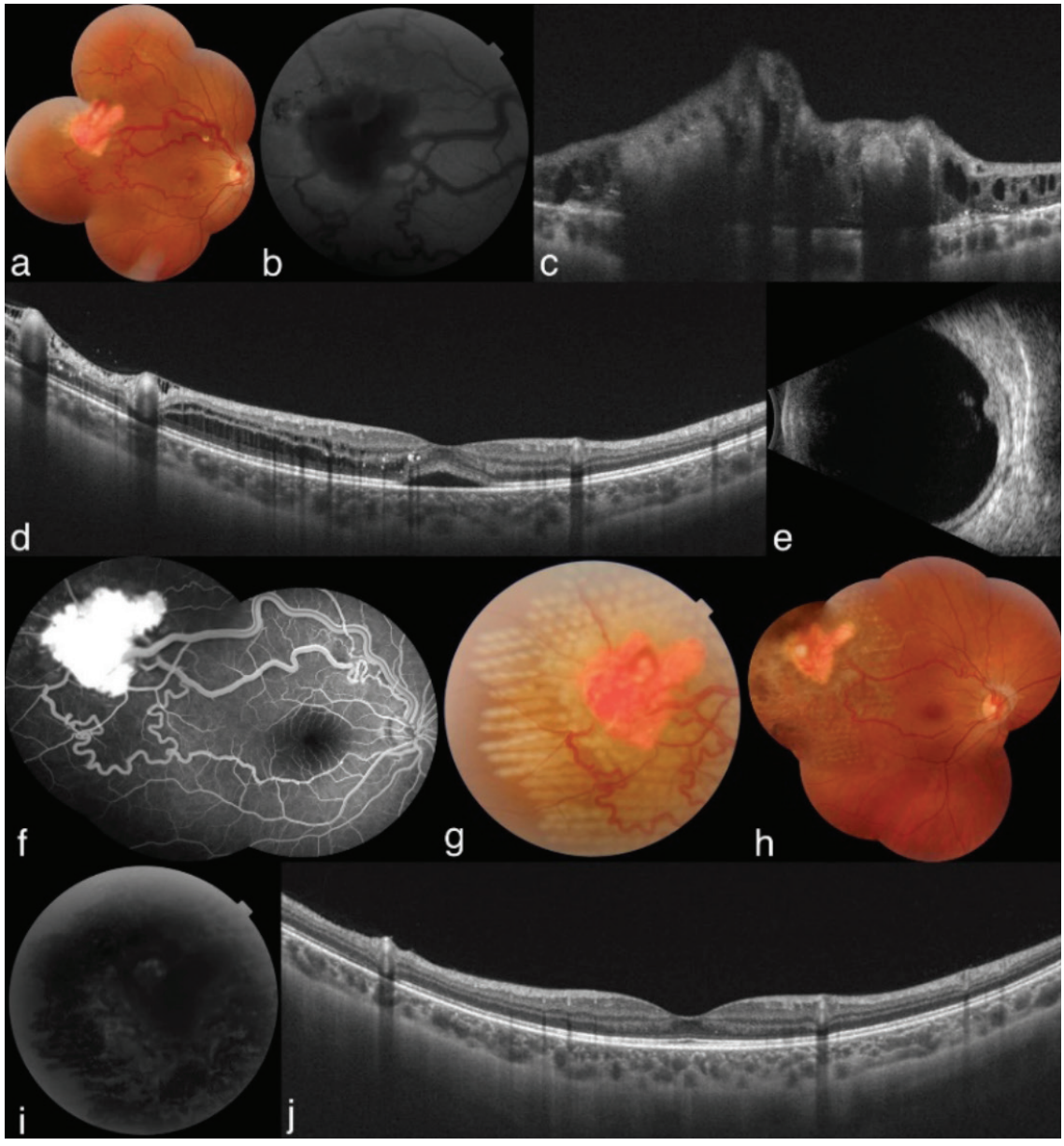

Figure 5. Retinal hemangioblastoma. a) Composite colored fundus photograph shows a temporally located retinal hemangioblastoma with tortuous and dilated afferent and efferent vessels. b) The lesion is hypoautofluorescent on fundus autofluorescence (FAF) imaging. c) Swept-source optic coherence tomography (SS-OCT) through the tumor demonstrates moderate reflectivity causing choroidal shadowing and intraretinal edema. d) In the SS-OCT section passing through the macula, subretinal fluid, retinal schisis, and choroidal shadowing from dilated tumor vessels are observed. e) B-mode ultrasonogram shows that tumor has acoustic solidity, basal diameter of 4.5x4.5 mm, and thickness of 1.9 mm. f) Fluorescein angiography demonstrates an intensely hyperfluorescent lesion with dilated vessels and vascular beading. g) After performing scatter laser photocoagulation to the tumor and surrounding tissue, pattern laser spots are observed on fundus photography. h) Composite color fundus photograph 2 months after 3 sessions of laser photocoagulation therapy demonstrates narrowing of the afferent vessels and areas of fibrosis over the tumor. i) FAF imaging 2 months after 3 sessions of laser photocoagulation shows the hypoautofluorescent lesion as well as hypoautofluorescent areas corresponding to the laser photocoagulation spots. j) Two months after 3 laser photocoagulation sessions, the subretinal fluid has resolved and the retinal schisis is almost completely regressed on SS-OCT

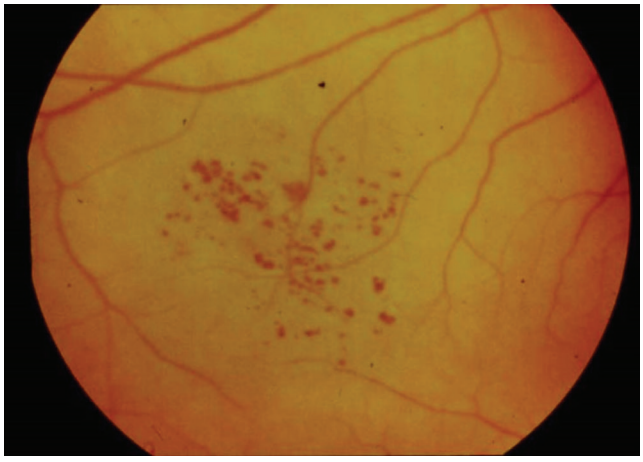

Figure 6. Retinal cavernous hemangioma. Color fundus photograph shows a retinal cavernous hemangioma resembling clusters of red grapes

Conclusions

Hamartomas of the retina and optic disc include astrocytic hamartoma arising from glial cells; CHRPE, CSHRPE, and CHRRPE arising from the RPE and retina; and the vascular tumors retinal hemangioblastoma and retinal cavernous hemangioma. Most of these lesions are asymptomatic and detected incidentally in patients presenting for routine eye examination. Macular lesions may cause findings such as reduced visual acuity and visual field loss.

Retinal and optic disc hamartomas may be isolated or associated with systemic diseases As they may be the initial sign of systemic diseases, the ophthalmologist must know the syndrome/diseases associated with these hamartomas.

Most retinal and optic disc hamartomas do not require treatment but should be monitored periodically. While they are generally benign and slow-growing lesions, malignant transformation can occur in rare cases. Treatment can be provided for complications secondary to the tumors.

Ethics

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: I.M., A.K.G., Concept: I.M., A.K.G., Design: I.M., A.K.G., Data Collection or Processing: I.M., A.K.G., Analysis or Interpretation: I.M., A.K.G., Literature Search: I.M., A.K.G., Writing: I.M., A.K.G.

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