

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

186,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Glaucoma Related to Ocular and Orbital Tumors

Sonal P. Yadav

Abstract

Secondary glaucoma due to ocular and orbital tumors can be a diagnostic challenge. It is an essential differential to consider in eyes with a known tumor as well as with unilateral, atypical, asymmetrical, or refractory glaucoma. Various intraocular neoplasms including iris and ciliary body tumors (melanoma, metastasis, lymphoma), choroidal tumors (melanoma, metastasis), vitreo-retinal tumors (retinoblastoma, medulloepithelioma, vitreoretinal lymphoma) and orbital tumors (extra-scleral extension of choroidal melanoma or retinoblastoma, primary orbital tumors) etc. can lead to raised intraocular pressure. The mechanisms for glaucoma include direct (tumor invasion or infiltration related outflow obstruction, trabecular meshwork seeding) or indirect (angle closure from neovascularization or anterior displacement or compression of iris) or elevated episcleral venous pressure secondary to orbital tumors. These forms of glaucoma need unique diagnostic techniques and customized treatment considerations as they often pose therapeutic dilemmas. This chapter will review and discuss the mechanisms, clinical presentations and management of glaucoma related to ocular and orbital tumors.

Keywords: ocular tumors, secondary glaucoma, orbital tumors, angle infiltration, neovascular glaucoma, neoplastic glaucoma

1. Introduction

With the advent of constantly evolving and advancing ophthalmic imaging techniques as well as surgical modalities in the field of ophthalmic diseases, diagnostic accuracy, and treatment outcomes of ocular as well as orbital tumors have improved remarkably over the past few years. Raised intraocular pressure (IOP) is known to be one of the presenting features or associated finding for numerous ocular as well as orbital tumors. Ocular and orbital tumors can cause secondary glaucoma due to various mechanisms. They often pose a diagnostic challenge as well as a therapeutic dilemma owing to the complex pathophysiology involved. A thorough clinical evaluation, appropriate index of suspicion and optimum use of ancillary testing can lead to a proper diagnosis and management in such scenario.

Intraocular tumors that can lead to secondary glaucoma are malignancies like iris melanoma, iris metastasis, iris lymphoma, ciliochoroidal melanoma, retinoblastoma as well as benign pathologies like iris melanocytoma, benign ciliary body medulloepithelioma, diffuse choroidal hemangioma. [1] Indicators for a possible underlying intraocular tumor are, markedly elevated and often asymmetric level of IOP, acquired iris heterochromia, glaucoma non-responsive to optimum treatment or accompanying distinctive ocular features. [1, 2] The mechanism by which these

tumors can cause secondary glaucoma varies with tumor type, size, and extent of the main tumor as well as seeding, tumor location, growth pattern, ongoing treatment along with secondary features related to the tumor. [3] Iris and predominantly ciliary body tumors located in anterior segment can cause glaucoma by direct infiltration of anterior chamber angle or because of iris neovascularization; while large tumors originating in retina or choroid are likely to cause glaucoma following iris neovascularization because of long standing or total retinal detachment or secondary angle closure. [1, 2]

Orbital tumors which can be congenital, traumatic, inflammatory, vascular, or neoplastic in origin may cause secondary glaucoma due to mass effect or anatomical and vascular changes leading to raised IOP [4] Orbital tumors causing raised orbital pressure may directly increase the IOP by increasing hydrostatic pressure around the globe or indirectly by raising the episcleral venous pressure.

Management of secondary glaucoma due to ocular and orbital tumors depends on both tumor characteristics and glaucoma related factors. Treatment of primary tumor may lead to IOP control in some cases while for others, management options include medical management, laser trabeculoplasty, transscleral cyclophotocoagulation, anti-VEGF injections, minimally invasive glaucoma surgery (MIGS), filtering or shunting surgery or enucleation. Glaucoma surgery like filtering or shunting procedure can be performed with due caution in proven benign or completely regressed tumors post-treatment. Such surgeries in an eye with suspected but unproven benign/malignant ocular tumor must be avoided to prevent unintended iatrogenic tumor dispersion or seeding especially in cases with iridociliary tumors or retinoblastoma.

2. Mechanisms of glaucoma secondary to ocular and orbital tumors

A. Direct mechanism-

- a. Solid tumor invasion- related outflow obstruction
- b. Infiltrative tumor -related outflow obstruction
- c. Trabecular meshwork seeding

B. Indirect mechanism-

- a. Angle closure from neovascularization
- b. Angle closure (compressive and rotational)
- c. Ghost cell- Hemolytic
- d. Elevated episcleral venous pressure

3. Ocular tumor related glaucoma

3.1 Anterior segment tumors

Anterior uveal tumors known to cause secondary glaucoma are iris/ciliary body melanocytoma, iris melanoma (nodular or diffuse), ciliary body melanoma

(nodular or ring melanoma), iris lymphoma and iris metastasis. Direct invasion of the anterior chamber angle by infiltration followed by neovascularization and trabecular meshwork tumor seeding are the common etiologies of raised IOP in iris tumors; while pigment dispersion followed by direct angle invasion are the common etiologies for same in pigmented ciliary body tumors. [1, 2, 5, 6]

Iris melanocytoma, a variant of melanocytic iris nevus is a deeply pigmented benign tumor which is well circumscribed, often dark brown to black dome shaped lesion with cobblestone surface and feathery edges showing echogenic nodular thickening of iris on ultrasound biomicroscopy (UBM). (**Figure 1A–C**) [2, 7] Melanocytoma can undergo spontaneous necrosis with pigment dispersion leading to pigment-laden melanophages seeding the angle causing secondary glaucoma. [8] (**Figure 1D**) Secondary glaucoma has been reported in 11% of cases in a series of 47 iris melanocytoma where pigmented keratic precipitates and anterior chamber inflammation were identified as factors predictive of development of raised IOP emphasizing the role of macrophages in the anterior chamber angle. [7]

Suspected melanocytoma can be observed cautiously. They are very rarely known to show malignant transformation. [9] Clear corneal approach fine needle aspiration biopsy, minimally invasive Finger Iridectomy technique (FIT), iridectomy or iridogoniocyclectomy can be utilized to obtain histopathological diagnosis in atypical iris nevi and suspected melanocytoma. [7, 10] Secondary glaucoma demonstrating melanocytoma eyes can be treated medically, by transscleral photocoagulation, by sector iridectomy or with glaucoma filtration surgery. [7, 8, 11, 12] However, a diagnostic confirmation of the lesion by prior biopsy and histopathology

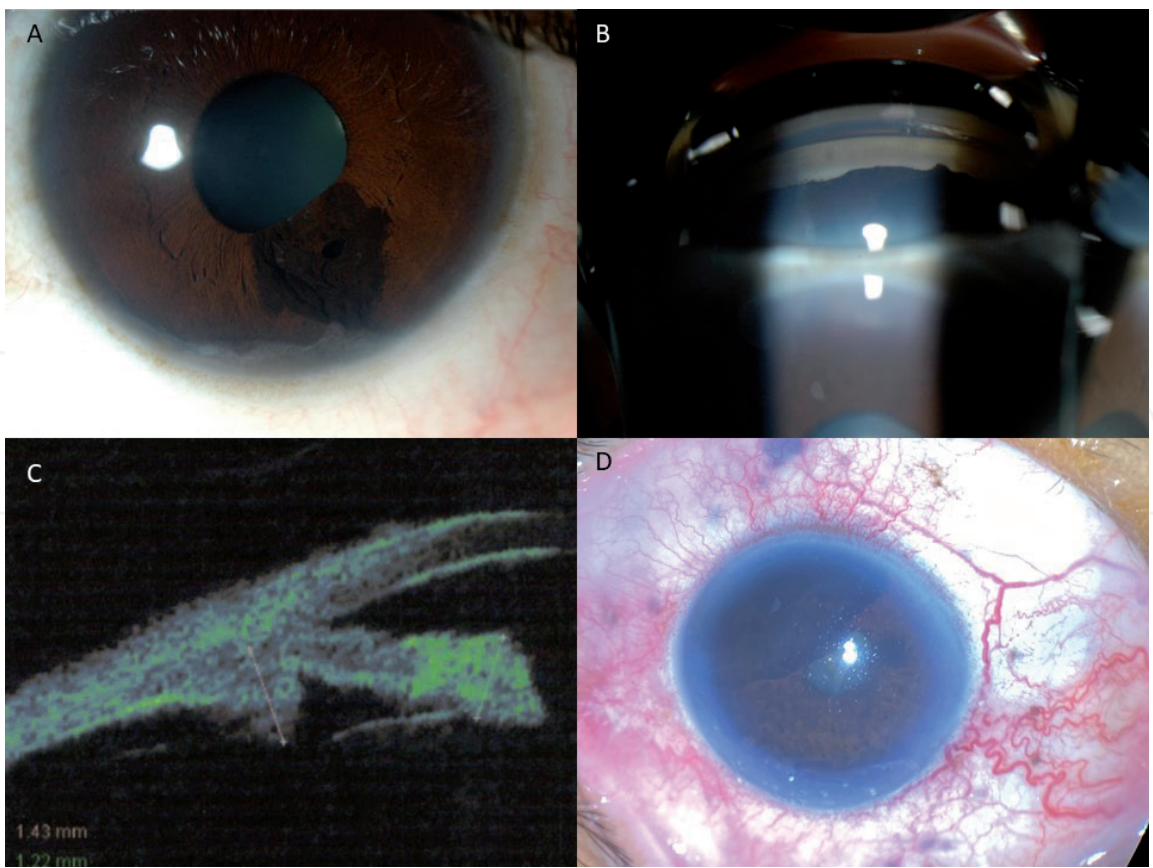


Figure 1.
(A) Slit lamp image of iris melanocytoma; (B) Gonioscopy image of iris melanocytoma with extension of pigmentation up to the angle, (C) ultrasound biomicroscopy (UBM) image of iris melanocytoma appearing as irregular hyperreflective lesion on iris surface; (D) large iris melanocytoma leading to raised IOP due to angle closure glaucoma (compressive angle closure) {image credit for **Figure 1A–C** Dr. Paul T Finger MD, FACS, Director, The New York Eye Cancer Center, New York USA}.

is mandated before planning a filtering surgery. Local surgical resection can be used to treat the secondary glaucoma caused by necrotic iris melanocytoma. [8, 13] Enucleation is reserved for painful blind eyes or eyes with absolute glaucoma.

Iris and iridociliary melanoma are the least common variant of uveal melanoma constituting only 2–3% of cases and have documented metastatic rate of 10.7–11%. [14–16]. Iris melanoma presents as a variably pigmented lesion (melanotic or amelanotic) which can be well circumscribed- nodular type, flat pigmented on iris surface- diffuse type and rarer predominantly trabecular meshwork involving type. (**Figure 2**) Secondary glaucoma has been reported in 33% of cases with iris melanoma while, with 100% of those with trabecular meshwork melanoma. [6, 17] Mechanisms include direct angle invasion (infiltration), iris neovascularization and trabecular meshwork seeding (melanomalytic glaucoma). [2, 3, 6] Unilateral findings of markedly elevated IOP, heterochromia iridis along with pigment dispersion onto the corneal endothelium, anterior iris surface and into the angle point towards melanomalytic glaucoma. [2, 18] Diffuse iris melanoma should be suspected in all cases of iris heterochromia and unilateral glaucoma. (**Figure 2B and D**) [2, 19] Morphological features of iris melanoma such as diffuse tumor location (>1 quadrant), posterior tumor margin involving the angle, reduced median tumor thickness (flat configuration) and greater extent of tumor seeding on the iris stroma and angle have been statistically related to presence of glaucoma at presentation. [6] Patients with iris melanoma and secondary glaucoma are at significantly higher risk of systemic metastasis with a hazard ratio of 4.51 compared to iris melanoma without

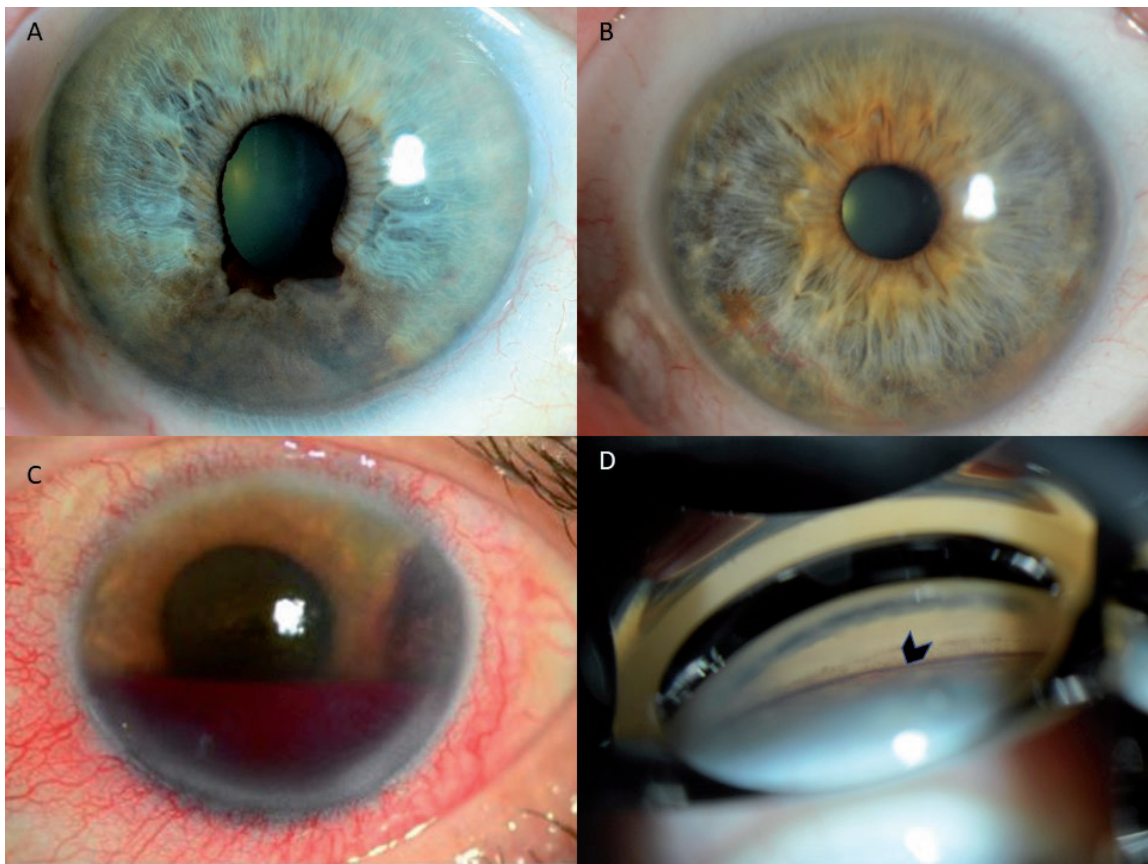


Figure 2. (A) Slit lamp image of iris melanoma showing correctopia, ectropion uveae and extension up to the angle, (B) slit lamp image of diffuse iris melanoma presenting with angle closure, (C) slit lamp image of ciliary body melanoma with iris infiltration presenting as secondary glaucoma with hyphema. (D) Gonioscopy image of blood vessel (black arrowhead) at the anterior chamber angle in a case of diffuse iris melanoma with angle closure depicted in **Figure 1B**. {image credit for **Figure 1 A, B, D**- Dr. Paul T Finger MD, FACS, Director, The New York Eye Cancer Center, New York USA and for **Figure 2C**- Dr. Santosh G Honavar MD FACS, Director, Ocular Oncology Services, Centre For Sight Hospital, Hyderabad, India}.

glaucoma. [3, 6] Possible explanation being-tumor location and its dis cohesive nature along with raised IOP that enables the egress of tumor cells into emissary veins leading to distant metastasis. [2, 6, 20].

Management of iris and iridociliary melanoma depends upon tumor size, location or extent, tumor seeding and presence of tumor related glaucoma. [15, 20] Local resection (iridectomy, iridocyclectomy), plaque brachytherapy, proton beam radiotherapy and enucleation are available treatment options for both nodular as well as diffuse iris melanoma. [6, 15, 20, 21] Secondary glaucoma in association with iris melanoma can be managed with medications, trans-scleral photocoagulation or laser trabeculoplasty. [22] Antivascular endothelial growth factor (anti-VEGF) injections can be tried in neovascular glaucoma. [23] Cases with refractory glaucoma resulting in blind painful eyes may warrant enucleation. [24] Filtering, shunting surgery or MIGS should be avoided in eyes with untreated tumor to prevent tumor spread outside of the globe. Diffuse iris melanoma or trabecular meshwork melanoma if misdiagnosed or missed prior to performing above named procedures can warrant enucleation for further tumor control. [3, 19]

Ring melanoma of the iris and ciliary body are a rare entity constituting only 0.3% of all uveal melanomas while having a poor prognosis owing to metastatic rate of up to 50%. [25]. The later could be likely due to delayed diagnosis as ring melanoma tend to grow circumferentially involving iris and entire ciliary body making them less obvious on ophthalmic examination. Prominent episcleral (sentinel) vessels, anterior chamber shallowing, multinodular tumor configuration, unilateral lens changes and occasional extra-scleral extension, light blockage on transillumination and ultrasonographic hollowness with intrinsic vascular pulsations are salient diagnostic features suggestive of ring melanoma. [25, 26] They tend to initially manifest with low intraocular pressure and later develop secondary glaucoma and secondary retinal detachment. Secondary glaucoma has been reported in 35% of cases. [25] The mechanisms involved are direct angle infiltration, trabecular meshwork seeding, angle closure and neovascularization of iris. [2, 3, 27–29] Plaque radiotherapy, proton beam radiotherapy or enucleation are available management options for the tumor. [25, 26, 30] Medical management, transscleral cyclophotocoagulation to uninvolved ciliary body or laser trabeculoplasty to uninvolved angle can be tried to control glaucoma in salvaged eyes. However, refractory cases require enucleation. [3] High index of suspicion is warranted when examining a case of unilateral refractory glaucoma with multinodular thickening of angle structures to avoid misdiagnosis as uveal effusion. Ultrasound biomicroscopy in such a case can help in identifying the tumor. Hurried shunting or filtering surgery for IOP control in tumor containing eyes can lead to tumor spread and further necessitate enucleation. [29, 31]

Iris and ciliary body metastasis constitute 8% and 2% of all cases of uveal metastasis respectively with breast and lung cancers being the most common primary tumors. [32] They tend to appear as solitary or multiple yellow, white, or pink stromal nodules with hyphema or pseudo hypopyon. They may present as ill-defined iris or ciliary body thickening in a setting of iridocyclitis. Ultrasound biomicroscopy (UBM) is useful in suspicious cases. (**Figure 3A and B**) Secondary glaucoma has been reported in about 37% of iris metastasis with angle invasion and iris neovascularization as mechanisms for raised IOP. [33] Treatment of primary, plaque brachytherapy, external beam radiotherapy (EBRT) or systemic chemotherapy are management options for iris and ciliary body metastasis. [2, 3, 33] Medical management, transscleral laser photocoagulation or laser trabeculoplasty can be useful for IOP control in these eyes. Anti VEGF injections may help in neovascular glaucoma. [3, 33–35]

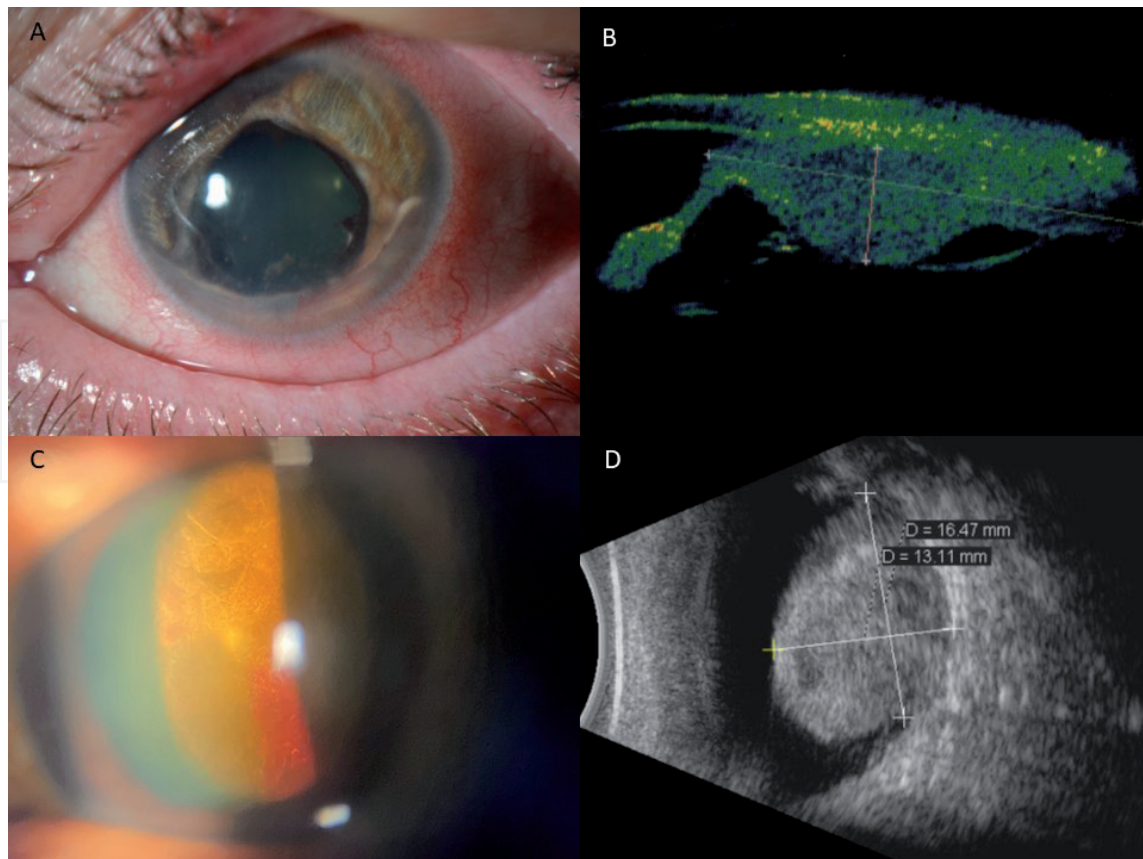


Figure 3.

(A) Slit lamp image of iris and ciliary body metastasis from lung adenocarcinoma showing correctopia, ectropion uveae, neovascularization of iris presenting with raised IOP (B) Ultrasound biomicroscopy image of iris metastasis with blunting of anterior chamber angle and thickened ciliary body (C) Slit lamp image of large choroidal melanoma presenting with intratumoral hemorrhage and raised IOP. (D) Ultrasound B scan of lesion in (C) showing low to moderately reflective choroidal melanoma with surrounding detached retina {image credit for **Figure 1** A, B- Dr. Paul T Finger MD, FACS, Director, The New York Eye Cancer Center, New York USA}.

Iris lymphoma, localized or diffuse is a differential diagnosis of iris melanoma or metastasis. Unilateral or bilateral presentation of diffuse non-granulomatous uveitis with raised IOP in open angles, uveitis- glaucoma- hyphema syndrome (UGH) or steroid resistant pseudo-uveitis are documented clinical manifestations of intraocular lymphoma. [36–38] The mechanism for raised IOP include angle infiltration, angle closure, hyphema. [3, 37] Plaque radiotherapy, EBRT, systemic chemotherapy have been used for management of iris lymphoma while, the raised IOP may respond to medical therapy, transscleral cyclophotocoagulation or laser trabeculoplasty. Enucleation is reserved for refractory cases. [2, 3]

Leukemic infiltration from acute lymphocytic leukemia (ALL) and acute myeloid leukemia (AML) in the anterior chamber, trabecular meshwork and Schlemm's canal can cause outflow obstruction and raised IOP. [2] ALL is the most common cause of both intraocular leukemia and secondary leukemia related glaucoma. Leukemia with central nervous system (CNS) involvement has been strongly associated with leukemic hypopyon and glaucoma. [2, 39] Treatment with systemic chemotherapy or EBRT is recommended for these. EBRT is known to show rapid resolution of angle infiltration in cases with secondary glaucoma. [2]

Other disorders like: Multiple myeloma, a malignant proliferation of plasma cells characterized by monoclonal production of immunoglobulins; Juvenile Xanthogranuloma, a benign histiocytic skin disorder can also affect anterior segment and lead to raised IOP. [2]

3.2 Posterior segment tumors

3.2.1 Choroidal tumors

Choroidal melanoma is the most common primary intraocular malignancy found in adults and the most common uveal melanoma encountered overall. Clinically it manifests as a dome shaped or mushroom shaped pigmented (melanotic) or non-pigmented (amelanotic) choroidal mass often associated with surrounding sub-retinal fluid, overlying orange pigmentation and exudative retinal detachment. (**Figure 3C**) The ultrasound B scan shows low to moderately reflective choroidal lesion with associated detached retina or occasional vitreous hemorrhage. (**Figure 3D**) Compared to anterior uveal melanomas, choroidal melanoma is less likely to cause secondary glaucoma (2%). [2, 3] Secondary glaucoma has been reported in both known and previously undiagnosed cases of choroidal melanoma. [2, 3] Secondary glaucoma has also been termed as the 'masquerading sign' for uveal melanomas in the literature. [40, 41] The reported mechanisms for raised IOP include iris neovascularization, direct angle invasion, angle closure, hyphema and suprachoroidal hemorrhage. [1, 3] Globe sparing episcleral plaque brachytherapy is commonly used modality of treatment followed by proton beam radiotherapy and local resection. Enucleation is warranted for large melanomas not amenable to radiotherapy or those causing absolute glaucoma. For control of IOP, medical management, transscleral cyclophotocoagulation or laser trabeculoplasty can be tried. In contrast to anterior uveal melanomas, for choroidal melanoma not involving ciliary body or iris root MIGS, filtering and shunting surgery can be considered in eyes where complete tumor regression has been achieved. [3]

Contrary to traditional thinking, a recent study of analysis of glaucoma drainage device surgery for control of IOP in treated (totally regressed) uveal melanoma (both anterior as well as posterior) did not find a greater risk of local or extraocular recurrence after a median follow up of 2 years. [42] However, further analysis with larger sample size and longer follow up duration is warranted, and caution needs to be exercised while deciding regarding treatment options for control of IOP in such cases.

Choroidal metastasis represents around 90% of total uveal metastasis. Breast, lung, kidney, gastrointestinal tract, and cutaneous melanoma are the leading sites of primary malignancies. [32] (**Figure 4A**) Secondary glaucoma has been reported in 1% of cases with mechanism being angle closure and iris neovascularization. [24] Plaque brachytherapy, photodynamic therapy, EBRT, systemic chemotherapy or enucleation are available management options for choroidal metastasis. Secondary glaucoma can be managed like choroidal melanoma related secondary glaucoma described above.

Choroidal hemangioma is a benign vascular hamartoma presenting as an orange-red mass showing hyperreflectivity on ultrasound B scan. It can be solitary or 'circumscribed' or 'diffuse'. (**Figure 4C**) Circumscribed tumors cause secondary glaucoma in 1% of cases of due to angle closure and iris neovascularization due to total retinal detachment. [43] Diffuse choroidal hemangiomas appear as diffuse choroidal thickening and have been said to give 'tomato-catsup' fundus impression. They are known to be associated with Sturge-Weber syndrome (SWS). The raised IOP found in SWS has been found to be due to developmental anomalies of anterior chamber and raised episcleral venous pressure and often unrelated to diffuse choroidal hemangioma. Total retinal detachment and iris neovascularization can rarely cause secondary glaucoma in such eyes. [3] Management options include plaque brachytherapy (for circumscribed as well as to the nodular component if any, in the diffuse variant), photodynamic therapy or EBRT to halt tumor growth and control



Figure 4.

(A) Montage fundus image of choroidal metastasis from breast carcinoma presenting with multifocal lesions, retinal detachment and raised IOP. (B) Posterior pole fundus image of the same patient (A) showing radiation retinopathy after stereotactic radiotherapy (45Gy) (C) Fundus picture showing circumscribed choroidal hemangioma.

of subretinal fluid to achieve stabilization of visual acuity. [44, 45] For control of IOP, medical management, transscleral cyclophotocoagulation, laser trabeculoplasty, MIGS, filtering or shunting surgeries can be performed.

3.2.2 Retinal tumors

Retinoblastoma is the most common primary intraocular malignancy found in pediatric population with estimated incidence of 1:16,000–18,000 live births. [46] White reflex or ‘leukocoria’ is the most common presenting feature of retinoblastoma. Presence of an intraocular mass with presence of intratumoral calcifications demonstrated on ultrasound B scan and/or computed tomography (CT) scan is pathognomic of the malignancy. Retinoblastoma can show endophytic, exophytic, diffuse or mixed growth pattern with presence of vitreous seeds. Secondary glaucoma is reported in 17% of cases due to iris neovascularization (5%), angle closure (1%), anterior tumor seeding (<1%) or related to hyphema (<1%). [24] Retinoblastoma is an important differential diagnosis to be considered in any pediatric uveitis or glaucoma. Delayed presentation and often misdiagnosis as either only intraocular inflammation or glaucoma can result in delay in retinoblastoma treatment and greater risk of metastasis with poor prognosis. [1, 2] Neovascular glaucoma is the most common cause of retinoblastoma related raised IOP which is postulated to be mediated by vascular endothelial growth factor (VEGF) produced by necrotic and hypoxic tumor cells. [47] (**Figure 5A and B**) Other causes include pupillary block and tumor seeding in anterior chamber angle. Glaucoma in retinoblastoma has been reported to be associated with metastasis related to optic nerve invasion by tumor cells. [48] Presence of secondary glaucoma at presentation has

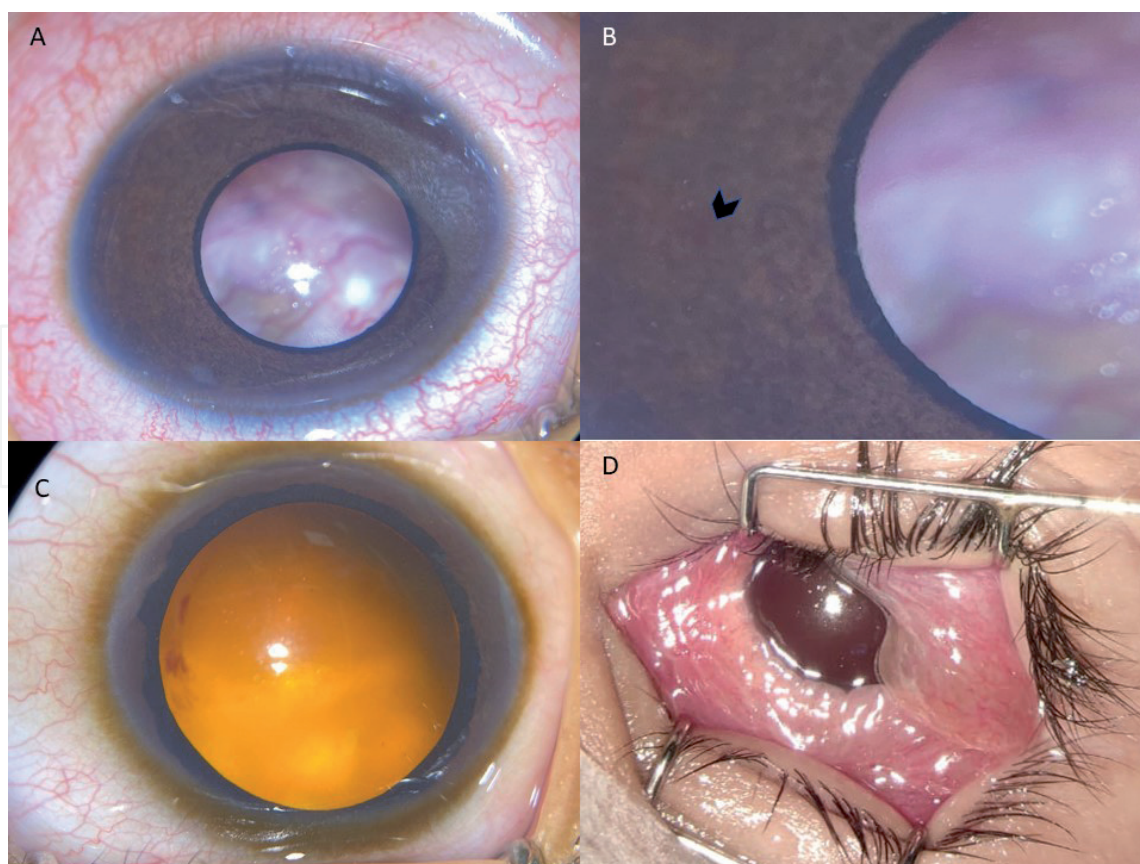


Figure 5.
 (A) Group E retinoblastoma presenting with total retinal detachment, iris neovascularization and neovascular glaucoma (clinical risk factors) (B) iris neovascularization (black arrowhead) (C) post chemotherapy tumor necrosis induced vitreous hemorrhage and secondary glaucoma in an eye with retinoblastoma (D) secondary glaucoma and sterile orbital inflammation in a case of retinoblastoma on systemic chemotherapy.

also been identified as a predictor for high-risk histopathological features of retinoblastoma along with prolonged duration of symptoms. [49] Management options for retinoblastoma depend upon age at presentation, laterality as well as grouping and staging of the disease. Modalities used are systemic chemotherapy, intra-arterial chemotherapy, intravitreal chemotherapy, focal lasers, cryotherapy, plaque radiotherapy and Orbital radiotherapy. Non-salvageable and advanced tumor containing eyes need enucleation. The IOP can get controlled as tumor regression is achieved in some eyes precluding any need of separate management for the glaucoma. Medical management, laser trabeculoplasty or cyclophotocoagulation can be tried in selected eyes post-tumor treatment. Any filtering surgeries, shunting procedures, MIGS should be avoided in tumor containing eyes to avoid extra-scleral extension of tumor.

4. Glaucoma associated with management of ocular tumors

Radiotherapy associated glaucoma- Radiotherapy is increasingly being used for management of intraocular tumors as means of eye and vision salvage. The modalities in practice are plaque brachytherapy (Iodine¹²⁵, Palladium¹⁰³, Ruthenium¹⁰⁶), proton beam radiotherapy, stereotactic radiotherapy, and external beam radiotherapy. Glaucoma has been reported as one of the common side effects of radiation. The common cause of radiation induced raised IOP is development of iris neovascularization and subsequent neovascular glaucoma (NVG). Pathogenesis of iris neovascularization is multifactorial, including increased release angiogenic factors, anterior and posterior segment ischemia, vascular occlusion, tumor hypoxia, radiation retinopathy (**Figure 4D**) and optic neuropathy. [50] Secondary open angle glaucoma

has also been noted in radiotherapy treated tumor eyes apart from NVG. After Iodine ¹²⁵ plaque brachytherapy for uveal melanoma reported Kaplan–Meier estimated risk of secondary open angle glaucoma was 15% at 5 years with higher incidence in earlier postoperative period, whereas estimated incidence of NVG was 13% at 5 years. [51] The risk factors for development of radiation induced secondary glaucoma (both open angle and NVG) include larger tumor size, higher radiation dose, involvement of iris and ciliary body and presence of retinal detachment. [2, 51–53] Proton beam radiotherapy for uveal melanoma has reported NVG rate of 12–31% at 5 years with greater tumor height, older age at presentation and larger tumor diameter as identified risk factors. [54] Anti- VEGF injections as well as pan-retinal photocoagulation for treatment of ocular ischemia or radiation retinopathy might be useful to reduce rate of neovascular glaucoma induced by radiation retinopathy.

Tumor necrosis induced glaucoma- Hemolytic glaucoma (Ghost cell glaucoma) is known to occur in tumor containing eyes with vitreous hemorrhage following systemic chemotherapy or focal tumor treatments. It occurs due to obstruction of trabecular meshwork by red blood cells, their debris and macrophages filled with hemorrhagic components from phagocytosis of vitreous hemorrhage. It can be observed in retinoblastoma eyes showing tumor necrosis as well as vitreous hemorrhage post chemotherapy. (**Figure 5C and D**).

4.1 Special considerations

In instances where patient seeks attention with glaucoma as the presenting feature, a detailed work up involving slit lamp examination, dilated fundus examination, gonioscopy of anterior chamber angle, high frequency ultrasound microscopy (UBM) and ultrasound B scan of posterior segment will provide essential clues about diagnosis of possible intraocular tumor. Initial management with IOP lowering medications should be the first line treatment with simultaneous investigation for underlying cause. [2] When the tumor presents with atypical features or causes diagnostic uncertainty, a diagnostic biopsy is warranted in managing such case of secondary glaucoma. [55] Systemic work up with the help of positron emission tomography (PET) CT scan can come in handy while evaluating a case of possible secondary ocular metastasis by highlighting an existing primary malignancy elsewhere.

4.2 Orbital tumor related glaucoma

The orbit is a pyramidal structure limited by bony walls except from anteriorly where it is limited by soft tissue i.e., orbital septum and eyelids. Thus, any instances of increased orbital volume may lead to increased hydrostatic pressure in the orbit. This increased orbital pressure can have a direct effect of IOP by raised hydrostatic pressure around the eye or indirect effect by compression of episcleral and orbital veins raising venous pressure. The episcleral venous system mainly empties into the anterior ciliary and superior ophthalmic veins and eventually draining into cavernous sinus. Thus, any disease process that might affect this drainage pathway due to structural, occlusive, compressive, or destructive pathophysiology can alter and raise IOP causing secondary glaucoma. [4] Focal mass effect due to tumors or swollen extraocular muscles may directly compress the eye globe leading to raised IOP while, vascular changes affecting venous pressure due to compression of episcleral veins or altered arterio-venous flow may also increase IOP indirectly.

Table 1 summarizes the broad etiological classes of orbital tumors leading to rise in IOP and secondary glaucoma. Open angle glaucoma is more common in the listed diseases however, angle closure along with acute angle closure glaucoma has also been reported in variety of pathologies.

Sr. No	Etiology	Example
1	Inflammatory	Non-specific Orbital Inflammatory Disease (NSOID) Thyroid eye disease Orbital granulomatous disease Orbital Foreign Body granuloma Juvenile Xanthogranuloma (orbital histiocytosis)
2	Vascular	Carotid-cavernous fistula (Direct or Indirect) Arterio-venous malformations Orbital varix Cavernous hemangioma Orbital lymphangioma
3	Neoplastic	Orbital osteoma Lymphoproliferative disorders Optic nerve glioma Optic nerve meningioma Neurofibromatosis Lacrimal gland tumors Primary orbital melanoma
4	Secondary	Orbital metastasis (from breast, lung carcinoma) Orbital chloroma (Acute myeloid leukemia) Multiple myeloma Invasive (secondary) ocular melanoma Extra-scleral (orbital) extension of retinoblastoma Invasive (secondary) squamous cell carcinoma
5	Miscellaneous	Orbital amyloidosis Mucopolysaccharidoses Phakomatosis (Neurocutaneous syndromes) Collagen tissue disorders (Lupus erythematosus, Wegener granulomatosis)

Table 1.
Etiologic classification of orbital tumors causing secondary glaucoma.

IOP evaluation should be routinely performed when evaluating a case of suspected orbital tumor or pathology. Gonioscopic examination can provide essential information regarding the status of the anterior chamber angle as well as show evidence of blood in Schlemm’s canal as the distinguishing feature of elevated venous pressure. The treatment of primary orbital pathology along with medical management of raised IOP is indicated for control of orbital tumor related secondary glaucoma.

In sum, glaucoma can be associated with various ocular as well as orbital tumors. It may constitute one of the many manifesting clinical features or be the sole presenting feature of these pathologies. Appropriate diagnosis and timely management of these tumors can help eye and vision salvage; however, a misdiagnosis or delayed diagnosis due to initial presentation as secondary glaucoma can lead to catastrophic sequel necessitating enucleation and can pose a greater risk to life. A thorough clinical evaluation, use of ancillary testing and stepwise management can help achieve optimum visual outcome and overall survival in cases with ocular or orbital tumors.

Acknowledgements

The author acknowledges contributions from Dr. Paul T Finger MD, FACS, Director- The New York Eye Cancer Center, New York, USA and Dr. Santosh G Honavar MD, FACS, Director- Ocular Oncology Services, Centre For Sight Hospital, Hyderabad, India for select clinical images used in this chapter.

IntechOpen

IntechOpen

Author details

Sonal P. Yadav

Dept of Ophthalmic Plastic Surgery, Orbit and Ocular Oncology, PBMA's H V Desai Eye Hospital, Pune, Maharashtra, India

*Address all correspondence to: sonal.yadav@hvdeh.org

IntechOpen

© 2021 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. 

References

- [1] Shields CL, Shields JA, Shields MB, Augsburger JJ. Prevalence and mechanisms of secondary intraocular pressure elevation in eyes with intraocular tumors. *Ophthalmology* 1987; 94:839-846
- [2] Radcliffe NM, Finger PT. Eye cancer related glaucoma: current concepts. *Survey of ophthalmology*. 2009 Jan 1; 54(1):47-73.
- [3] Camp DA, Yadav P, Dalvin LA, Shields CL. Glaucoma secondary to intraocular tumors: mechanisms and management. *Current Opinion in Ophthalmology*. 2019 Mar 1;30(2):71-81.
- [4] Nassr MA, Morris CL, Netland PA, Karcioğlu ZA. Intraocular pressure change in orbital disease. *Survey of ophthalmology*. 2009 Sep 1;54(5):519-44.
- [5] Foulds WS, Lee WR. The significance of glaucoma in the management of melanomas of the anterior segment. *Trans Ophthalmol Soc UK*. 1983;103 (Pt 1):59—63
- [6] Shields CL, Shah SU, Bianciotto CG, Emrich J, Komarnicky L, Shields JA. Iris melanoma management with iodine-125 plaque radiotherapy in 144 patients: impact of melanoma-related glaucoma on outcomes. *Ophthalmology*. 2013 Jan 1;120(1):55-61.
- [7] Demirci H, Mashayekhi A, Shields CL, et al. Iris melanocytoma: clinical features and natural course in 47 cases. *Am J Ophthalmol* 2005; 139: 468-475.
- [8] Fineman MS, Eagle RC Jr, Shields JA, et al. Melanocytolytic glaucoma in eyes with necrotic iris melanocytoma. *Ophthalmology* 1998; 105: 492-496.
- [9] Cialdini AP, Sahel JA, Jalkh AE, et al. Malignant transformation of an iris melanocytoma. A case report. *Graefes Arch Clin Exp Ophthalmol*. 1989;227(4):348—5
- [10] Finger PT, Latkany P, Kurli M, et al. The Finger iridectomy technique: small incision biopsy of anterior segment tumours *British Journal of Ophthalmology* 2005;89:946-949.
- [11] Fountain TR, Goldberg MF, Green WR. Glaucoma and a melanocytic iris lesion in an 18-year-old. In: Schachat AP, editor. *Current practice in ophthalmology*. St. Louis: Mosby, 1992:371-380.
- [12] Chen MJ, Liu JL, Li WY, et al. Diode laser transscleral cyclophotocoagulation in the treatment of refractory glaucoma with iris melanocytoma. *J Chin Med Assoc* 2008; 71:546-548.
- [13] Shields JA, Annesley WH Jr, Spaeth GL. Necrotic melanocytoma of iris with secondary glaucoma. *Am J Ophthalmol* 1977;84:826-829.
- [14] Shields CL, Shields JA, Materin M, et al. Iris melanoma: risk factors for metastasis in 169 consecutive patients. *Ophthalmology*. 2001;108:172-178.
- [15] Khan S, Finger PT, Yu GP, et al. Clinical and pathologic characteristics of biopsy-proven iris melanoma: a multicenter international study. *Arch Ophthalmol*. 2012;130(1): 57-64.
- [16] Singh AD, Turell ME, Topham AK. Uveal melanoma: trends in incidence, treatment, and survival. *Ophthalmology* 2011; 118:1881-1885.
- [17] Demirci H, Shields CL, Shields JA, et al. Ring melanoma of the anterior chamber angle: a report of fourteen cases. *Am J Ophthalmol* 2001; 132: 336-342.
- [18] Van Buskirk EM, Leure-duPree AE. Pathophysiology and electron microscopy of melanocytolytic glaucoma. *Am J Ophthalmol*. 1987;85(2):160—6

- [19] Demirci H, Shields CL, Shields JA, et al. Diffuse iris melanoma: a report of 25 cases. *Ophthalmology* 2002; 109: 1553-1560.
- [20] Shields CL, Kaliki S, Furuta M, et al. Iris melanoma features and prognosis in children and adults in 317 patients. *J Am Assoc Pediatr Ophthalmol Strabismus* 2012;16:10-6.
- [21] Chaugule SS, Finger PT. Regression patterns of iris melanoma after palladium-103 (103Pd) plaque brachytherapy. *Ophthalmology*. 2017 Jul 1;124(7):1023-30.
- [22] Girkin CA, Goldberg I, Mansberger SL, et al. Management of iris melanoma with secondary glaucoma. *J Glaucoma* 2002; 11:71-74.
- [23] Bianciotto C, Shields CL, Kang B, Shields JA. Treatment of iris melanoma and secondary neovascular glaucoma using bevacizumab and plaque radiotherapy. *Arch Ophthalmol* 2008; 126:578-579.
- [24] Shields JA, Shields CL, Shields MB. Glaucoma associated with intraocular tumors. In: Ritch R, Shields MB, Krupin T, editors. *The glaucomas*, 2nd ed. St. Louis, MO: Mosby; 1996. pp. 1131-1139.
- [25] Demirci H, Shields CL, Shields JA, Honavar SG, Eagle RC Jr: Ring melanoma of the ciliary body: report on twenty-three patients. *Retina* 2002;22:698-706; quiz 852-853
- [26] Gunduz K, Shields CL, Shields JA, et al. Plaque radiotherapy of uveal melanoma with predominant ciliary body involvement. *Arch Ophthalmol* 1999;117:170-177
- [27] Zhao M, Mu Y, Dang Y, Zhu Y. Secondary glaucoma as initial manifestation of ring melanoma: a case report and review of the literature. *Int J Clin Exp Pathol* 2014; 7:8163-8169.
- [28] Lee V, Cree IA, Hungerford JL. Ring melanoma—a rare cause of refractory glaucoma. *Br J Ophthalmol* 1999; 83:194-198.
- [29] Kaliki S, Eagle RC, Grossniklaus H, et al. Inadvertent implantation of aqueous tube shunts in glaucomatous eyes with unrecognized intraocular neoplasms: report of 5 cases. *JAMA Ophthalmol* 2013; 131:925-928.
- [30] Gragoudas ES, Lane AM, Munzenrider J, Egan KM, Li W: Long-term risk of local failure after proton therapy for choroidal/ciliary body melanoma. *Trans Am Ophthalmol Soc* 2002; 100: 43-48; discussion 48-49.
- [31] Pasternak S, Erwenne CM, Nicolela MT: Subconjunctival spread of ciliary body melanoma after glaucoma filtering surgery: a clinicopathological case report. *Can J Ophthalmol* 2005; 40: 69-71
- [32] Shields CL, Welch RJ, Malik K, et al. Uveal metastasis: clinical features and survival outcomes of 2214 tumors in 1111 patients based on primary tumor origin. *Middle East Afr J Ophthalmol* 2018; 25:81-90.
- [33] Shields CL, Kaliki S, Crabtree GS, et al. Iris metastasis from systemic cancer in 104 patients: the 2014 Jerry A. Shields Lecture. *Cornea* 2015; 34:42-48.
- [34] Seidman CJ, Finger PT, Silverman JS, Oratz R. Intravitreal bevacizumab in the management of breast cancer iris metastasis. *Retin Cases Brief Rep* 2017; 11:47-50
- [35] Aydin A, Tezel TH. Use of intra-vitreous bevacizumab for the treatment of secondary glaucoma caused by metastatic iris tumor. *J Glaucoma* 2018; 27:e113–e116.
- [36] Chan CC, Buggage RR, Nussenblatt RB. Intraocular lymphoma. *Curr Opin Ophthalmol*. 2002;13(6): 411—8

- [37] Gauthier AC, Nguyen A, Munday WR, et al. Anterior chamber non-Hodgkin lymphoma of the iris masquerading as uveitis-glaucoma-hyphema syndrome. *Ocul Oncol Pathol* 2016; 2:230-233
- [38] Bawankar P, Das D, Bhattacharjee H, et al. Systemic diffuse large B-cell lymphoma masquerading as neovascular glaucoma. *Indian J Ophthalmol* 2018; 66:317-319.
- [39] Matano S, Ohta T, Nakamura S, et al. Leukemic hypopyon in acute myelogenous leukemia. *Ann Hematol*. 2000;79(8): 455—8
- [40] Othman IS, Assem M, Zaki IM. Secondary glaucoma as initial manifestation of uveal melanoma. *Saudi Journal of Ophthalmology*. 2013 Jul 1;27(3):203-8.
- [41] Vempuluru VS, Jakati S, Krishnamurthy R, Senthil S, Kaliki S. Glaucoma as the presenting sign of intraocular tumors: beware of the masquerading sign. *International ophthalmology*. 2020 Mar 20:1-7.
- [42] Fatehi N, McCannel T, A, Giaconi J, Caprioli J, Law S, K, Nouri-Mahdavi K: Outcomes of Glaucoma Drainage Device Surgery in Eyes with Treated Uveal Melanoma. *Ocul Oncol Pathol* 2019;5:20-27. doi: 10.1159/000488056
- [43] Shields CL, Honavar SG, Shields JA, et al. Circumscribed choroidal hemangioma: clinical manifestations and factors predictive of visual outcome in 200 cases. *Ophthalmology* 2001; 108:2237-2248.
- [44] Finger PT. Radiation therapy for exudative choroidal hemangioma. *Indian journal of ophthalmology*. 2019 May;67(5):579.
- [45] Sen M, Honavar SG. Circumscribed choroidal hemangioma: An overview of clinical manifestation, diagnosis and management. *Indian journal of ophthalmology*. 2019 Dec;67(12):1965.
- [46] Kivela T. The epidemiological challenge of the most frequent eye cancer: retinoblastoma, an issue of birth and death. *Br J Ophthalmol* 2009; 93:1129-1131.
- [47] Kvanta A, Steen B, Seregard S. Expression of vascular endothelial growth factor (VEGF) in retinoblastoma but not in posterior uveal melanoma. *Exp Eye Res*. 1996;63(5): 511—8
- [48] Shields CL, Shields JA, Baez K, et al: Optic nerve invasion of retinoblastoma. Metastatic potential and clinical risk factors. *Cancer* 73:692-8, 1994
- [49] Kaliki S, Srinivasan V, Gupta A, Mishra DK, Naik MN. Clinical features predictive of high-risk retinoblastoma in 403 Asian Indian patients: a case-control study. *Ophthalmology*. 2015 Jun 1;122(6):1165-72.
- [50] Sivak-Callcott JA, O'Day DM, Gass JD, et al. Evidence-based recommendations for the diagnosis and treatment of NVG. *Ophthalmology* 2001;108:1767-1776
- [51] Kim EA, Salazar D, McCannel CA, Kamrava M, Demanes DJ, Lamb J, Caprioli J, McCannel TA. Glaucoma After Iodine-125 Brachytherapy for Uveal Melanoma: Incidence and Risk Factors. *Journal of glaucoma*. 2020 Jan 8;29(1):1-0.
- [52] Finger PT. Plaque radiation therapy for malignant melanoma of the iris and ciliary body. *Am J Ophthalmol*. 2001; 132(3):328—35
- [53] Finger PT. Radiation therapy for choroidal melanoma. *Surv Ophthalmol*. 1997;42(3):215—32
- [54] Mishra KK, Daftari IK, Weinberg V, Cole T, Quivey JM, Castro JR, Phillips TL, Char DH. Risk factors for neovascular

glaucoma after proton beam therapy of uveal melanoma: a detailed analysis of tumor and dose–volume parameters. *International Journal of Radiation Oncology* Biology* Physics*. 2013 Oct 1;87(2):330-6.

[55] Gombos D.S. (2019) Localised Therapy and Biopsies of Intraocular Tumors. In: Chaugule S., Honavar S., Finger P. (eds) *Surgical Ophthalmic Oncology*. Springer, Cham.