International Journal of Science and Healthcare Research
Vol.7; Issue: 3; July-Sept. 2022
Website: ijshr.com
Review Article *ISSN: 2455-7587*

Iris Melanoma: Genetic Pathway, Staging, Histopathology, Clinical Features, Diagnostic Imaging, Treatment and Management

Areeb Rehmani[1], Labishetty Sai Charan[2], Tara Rani[3], Salal Khan[4], Sana Falak[5]

[1, 4, 5] M. Optometry Scholar, Department of Optometry, Galgotias University, Greater Noida, U.P (India).
[3]Assistant Professor, Department of Optometry, Galgotias University, Greater Noida, U.P (India).
[2]Assistant Professor, Department of Optometry, Chandigarh University, Mohali, Punjab (India).

Corresponding Author: Salal Khan

DOI: https://doi.org/10.52403/ijshr.20220707

ABSTRACT

Introduction- Iris melanomas mainly grow in the anterior chamber or along the iris surface, and by local extension; they commonly invade the anterior chamber angle and anterior ciliary body. Iris melanomas account for 2–3% of all uveal melanomas, with the diffuse variety accounting for about 10% of all iris melanomas.
Methodology-A systematic review is a technical tool that basically describes a more or less systematic way of collecting and synthesizing past research by integrating findings and perspectives from a variety of empirical findings. In this study, authors conducted a systematic assessment of 51 research articles on the subject of "Iris Melanoma" in order to examine and compare the various approaches and outcomes.
This comprehensive review summarizes all 51 research articles in the most accessible manner to discuss the Genetic pathway, Staging, Histopathology, Clinical features, Diagnostic Imaging, Treatment, and Management.
Results-Iris melanomas are discovered early and treated fast because they are apparent when they are little. As a result, patients with this tumor had a better prognosis than those with posterior uvea tumors.
Conclusion- Radiotherapy or surgical resection are usually used in this situation. A combination of radiotherapy and surgery may be employed in some circumstances. Conservative treatment is an excellent option for enucleation since it provides for effective tumor control locally.

Keywords- Iris melanoma, Diagnosis, Management, Stages, Eye-care.

INTRODUCTION

Iris melanomas account for 2–5% of all uveal melanomas. The size, shape, degree of pigmentation, and clinical behavior of iris melanomas vary. Radiotherapy or surgical resection are commonly used in this situation. Incomplete tumor excisions can result in recurrence, hemorrhage, vitreous loss, displaced lens, iridocyclitis, macular edema, retinal detachment, glaucoma, and cataract. A combination of radiotherapy and surgery may be employed in some instances.(1)

The tumor size (thickness and basal diameter), as well as intraocular and extraocular expansion, are used to classify uveal melanoma. With pseudo melanomas, the differential diagnosis is made based on the tumor's appearance and location. When opposed to choroidal melanoma, iris melanoma has a better prognosis and a lower fatality rate. (2)

Iris melanomas mainly grow in the anterior chamber or along the iris surface, and by local extension, they commonly invade the anterior chamber angle and anterior ciliary body. (3) Iris melanomas account for 2–3% of all uveal melanomas,

with the diffuse variety accounting for about 10% of all iris melanomas. (4)

A recorded increasing melanocytic iris mass of nodular or flat structure with or without spreading of the tumor onto the surrounding iris and into the anterior chamber angle are clinical characteristics suggestive of iris melanoma. (5) Because most iris melanomas are identified when they are tiny and have a low grade cell type, a favorable prognosis is usually expected, with just 5% metastasis at 10 years. (4) The incidence of iris melanoma varies between 0.2 and 0.9 per million persons. (6) The incidence of iris melanoma has been growing in recent decades, according to the literature, which is most likely due to the impact of solar radiation. (7)(8) The prevalence appears to be unaffected by geographic location. (9)

In other age groups, however, there is no statistically significant variation in incidence between genders. (7) The most common cause of iris melanoma is a pre-existing nevus. (10) The majority of persons who acquire a Uveal Melanoma are between the ages of 50 and 70, however the tumor can also occur in younger people. (11)

Anatomy of Eye and Iris

Iris blood vessels give nutrition and oxygen not just to the iris, but also to the entire anterior segment of the eye, thanks to numerous anastomotic linkages between arteries and veins.(12) Arterioles starting from the main circle and projecting radially from the base in the direction of the pupillary margin are visible on a typical iris angiography, with gradual thinning and a slightly twisted course.(13) The minor arterial circle of the iris is a vascular network formed of arteriovenous connections that can be seen next to the pupillary border. (14)In the stroma of the iris, veins are more numerous and deeply located, with a uniform distribution in the four quadrants similar to arterioles.(15)

Risk factors

Iris melanomas are more common in the inferior area of the iris, where sunlight exposure is the most prominent. Direct sunlight does not reach the choroid or ciliary body. (16) Important risk factors for iris melanoma metastatic disease have recently been discovered, including older age at diagnosis, tumor involvement in the anterior chamber angle, elevated intraocular pressure (IOP), and extraocular extension of tumor. (17) Large tumor size, conspicuous tumor vascularity, tumor seeding, high intraocular pressure, and tumor-related ocular consequences such as hyphema are all worrisome clinical signs that necessitate excisional biopsy in our experience. (17) A light-colored iris and skin colour have also been linked to an increased risk of iris melanoma. (10)

Genetic pathway

The key regulatory route linked in melanoma is the RAS/RAF/MEK/ERK pathway, often known as the MAPK pathway (Figure-1). Cell growth, migration, differentiation, proliferation, and death are all regulated by this route.(18)

Binding of receptor tyrosine kinases (RTKs) or integrin adhesion between the cell membrane and the extracellular matrix can begin the MAPK pathway (ECM). By transforming RAS proteins from a GDP-bound state to a GTP-bound state, this binding activates them. RAS induces the phosphorylation of RAF proteins when it is activated. By phosphorylating MEK and, as a result, ERK, the activated form of RAF further stimulates downstream signaling. Activated ERK travels to the nucleus, where it controls the production of many transcription factors involved in cell cycle progression and differentiation.(19) Mutations in BRAF cause MEK and ERK to be activated all of the time. GTP disengagement from the RAS complex is caused by mutations in NRAS, resulting in constitutive activation of downstream signaling.(20)

As previously stated, NF1 tumor suppressor gene deletions result in uncontrolled cell proliferation and invasion.(21) Iris melanoma is caused by the deletion of chromosome 3 and

chromosomal region 9p21, which is analogous to the tumor suppressor gene CDKN2A. (22)Furthermore, investigations suggest that the chromosomal changes seen in iris melanoma differ from those seen in posterior uveal melanoma. (10)

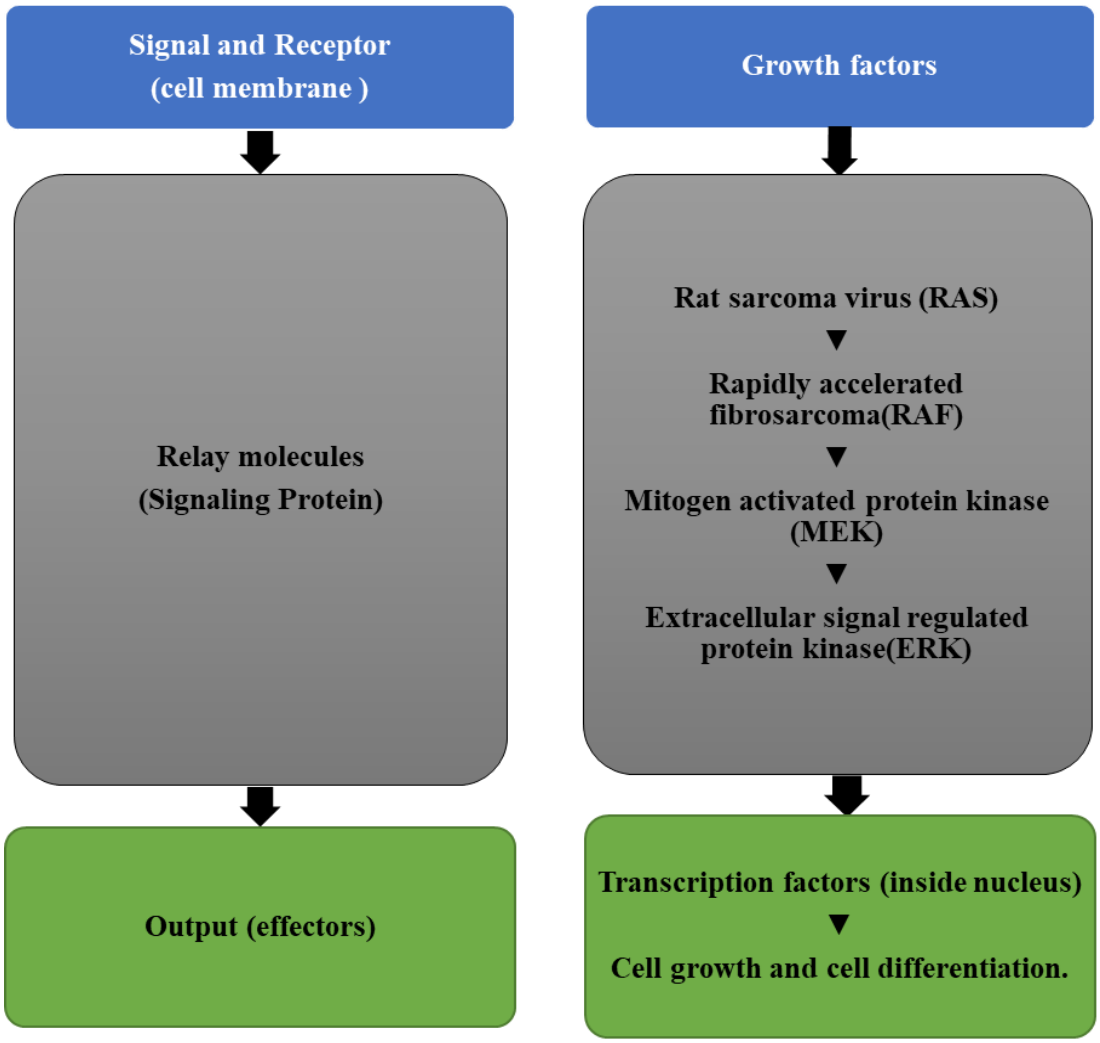

Figure 1: Schematic cellular events in MAPK pathway (mitogen activated signaling cascade)

Stages

The TNM classification of the American Joint Committee on Cancer (AJCC), which is based on original tumour characteristics as well as the existence of regional nodal and distant metastases (DM), has been widely employed. (23)

The seventh edition of the American Joint Committee on Cancer–Union for International Cancer Control (AJCC-UICC) TNM system(Table-1),clinical and pathologic staging guidelines are based on a multicenter retrospective evaluation of more than 8000 patients and document tumor size and extension, secondary glaucoma, regional lymph nodes, and distant metastasis: T0-No indication of the initial tumor. ; T1-Iris-limited tumor; T1a-Iris-limited tumor (not more than three clock hours in size); T1b-Iris-limited tumor (more than three clock hours in size); T1c-Iris-limited tumor with secondary glaucoma; T2-Tumor spreading into or confluent with the ciliary body, choroid, or both; T2a-Secondary glaucoma tumor that is confluent with or extends into the ciliary body, choroid, or both; T3-Tumor confluent with or extending into the ciliary body, choroid, or both with scleral extension; T3a-Tumor confluent with or extending into the ciliary body, choroid, or both with scleral extension and secondary glaucoma; T4-Tumor with

extraocular extension; T4a-Tumor with extra scleral extension <5 mm in diameter; T4b-Tumor with extra scleral extension >5 mm in diameter; (24) NX-It is not possible to analyze regional lymph nodes; N0-no regional lymph node metastases; N1-regional lymph node metastasis; MX-It is impossible to assess distant metastasis; M0-No distant metastases; M1-Distant metastasis, M1a-largest diameter of the largest metastasis (less than 3 cm); M1b-largest diameter of the largest metastasis (3.1-8.0 cm); M1c-largest diameter of the largest metastasis (greater than 8 cm);large GX-It is impossible to assign a grade; Spindle cell melanoma (G1), mixed cell melanoma (G2), and epithelioid cell melanoma (G3) are the three types of melanoma. (25)(26)

Metastatic spread

Although metastatic illness in confined iris melanoma is uncommon, it is more common in DIM, possibly due to the epithelioid cells' low cohesiveness, which causes tumor dispersion on the iris and into the angle. (1) At the age of six years, the incidence was observed to be around 13%. (27)

Table -1: Iris melanoma stages based on AJCC seventh edition classification (TNM)

Category		Criteria	References
T category	**T1**	**Iris limited tumor**	(23),(24),(25), (26),(27)
	T1a	Iris limited tumor (not more than three clock hour in size)	
	T1b	Iris limited tumor (more than three clock hour in size)	
	T1c	Iris limited tumor with secondary glaucoma	
	T2	**Tumor spreading into or confluent with the ciliary body, choroid or both**	
	T2a	Secondary glaucoma tumor that is confluent with or extends into the ciliary body, choroid or both	
	T3	**Tumor confluent with or extending into the ciliary body, choroid or both with scleral extension**	
	T3a	Tumor confluent with or extending into the ciliary body, choroid or both with scleral extension and secondary glaucoma.	
	T4	**Tumor with extraocular extension**	
	T4a	Tumor with extra scleral extension <5mm in diameter	
	T4b	Tumor with extra scleral extension >5mm in diameter	
N category	NX	It is not possible to analyze the regional lymph nodes.	(23),(24),(25), (26),(27)
	N0	No regional lymph node metastasis	
	N1	regional lymph node metastasis	
M category	MX	It is impossible to assess distant metastasis	(23),(24),(25), (26),(27)
	M0	No distant metastasis	
	M1	**Distant metastasis**	
	M1a	Largest diameter of largest metastasis (less than 3 cm)	
	M1b	Largest diameter of largest metastasis (3.1-8.0 cm)	
	M1c	Largest diameter of largest metastasis (greater than 8 cm)	

Histological findings and histopathology

Medina et al. suggested bending the needle tip to 90 degrees and entering the tumor obliquely rather than radially to reduce the likelihood of a negative biopsy.(28) Iris melanomas are less pigmented than choroidal and ciliary body melanomas and can range from entirely amelanotic to highly pigmented. Iris melanomas are classified into three kinds based on their histology: Spindle cell, mixed cell, and epithelioid cell melanomas are 3 kinds of melanomas. Spindle cells or epithelioid cells are seen morphologically. Nuclei with linear interdigitation linked to a chromatin strip, tiny nucleoli (spindle B cells), or no evidence of nucleoli are identified in the first (spindle A cells). Epithelioid cells are bigger, polygonal cells with a defined cell boundary and copious, glassy cytoplasm.(29)In the literature, most reported iris melanomas are spindle cell melanomas, whereas diffuse iris tumors tend to be of the epithelioid cell type with a resultant higher risk of metastasis than circumscribed ones.(29)

Clinical features

Pigmentation may change between being heavily diffuse, variable or amelanotic. The areas of origin-from the most to the least frequent-are the peri-pupillary iris, the midzone and the iris periphery.(30)

They can extend to the anterior and/or the posterior chamber, commonly being limited

by the lens.(31) In sequential order, the most affected quadrant is the inferior (between the positions of 5 and 7 o'clock), followed by the temporal, nasal and then superior quadrant.(30) Ten percent of all iris melanomas are diffuse iris melanoma (DIM). DIM appears as a flat, infiltrating tumor with possible seeding that progressively changes the iris coloration and rate of invasion to the angle, resulting in a secondary glaucoma that responds poorly to hypotensive eye drops, causing severe disc cupping and functional loss. (31)
According to Shields, to correctly diagnose an iris melanoma, the lesion should replace the stroma of the iris, should be larger than 3 mm in diameter and 1 mm in thickness and should present at least three of the following five features: photographic evidence of growth, secondary cataract, glaucoma, conspicuous vascularity and iris ectropion.(27)
Jakobiec and Silbert believe that ectropion uvea, vascularity, pupil distortion, involvement of the angle and glaucoma could be evident in other types of lesions (nevus or melanoma).(32) They propose only the involvement of the ciliary body as the most indicative aspect of malignancy, while Shields is of the opinion that documented growth is the most important sign to diagnose iris melanoma.(27) After the evaluation of 1611 eyes, Shields et al. constructed an ABCDEF guide(Table-2) to remember the risk factors that are predictive of iris nevus growth to melanoma, where A is age (young), B is blood (past episodes of hyphema), C is the clock hour (a tumor location from 4 o'clock to 9 o'clock), D is a diffuse configuration, E is ectropion and F is a feathery margin. These key clinical features help to identify iris melanoma at a time in which therapy could be life-saving. (27)
The main local clinical complications of iris melanomas are tumor vascularization (in terms of sentinel episcleral vessel and posterior iris feeder vessel), ectropion uvea, pupillary distortion, pigment dispersion, sector cataract, chronic uveitis , hyphema and glaucoma with irreversible optic nerve damage.(32)

Table 2: ABCDEF GUIDE to remember risk factors for iris nevus growth to melanoma constructed by Shields et al.

Mnemonics	Risk factor	References
A	Age (young)	(27)
B	Blood (hyphema)	
C	Clock Hour (tumor location)	
D	Diffuse configuration	
E	Ectropion	
F	Feathery margin	

Diagnostic Imaging

Anterior segment (AS) optical coherence tomography (OCT), and ultrasound biomicroscopy. These (UBM) are used in the differential diagnosis of iris cysts.(33)
These techniques are important in ruling out solid tumors such as nevus or melanoma.(34)Ultrasound Bio Microscopy (UBM) is a high-resolution ultrasound technique that allows noninvasive in vivo imaging of structural details of the anterior ocular segment at near-light microscopic resolution. It allows for a detailed assessment of anterior segment structures, allowing for the differentiation of solid iris lesions from iris cysts (acoustically empty), as well as the detection of anterior chamber angle and ciliary body involvement. Furthermore, a "lion's paw" look, described as a posterior extension of the iris circumscribed by the lens, might be seen during this examination.(35)
When imaging anterior segment lesions, AS-OCT is compared to UBM in the literature. Anterior Segment Optical Coherence Tomography, according to Hau et al., can be employed in mild iris tumors with low pigmentation, but UBM is recommended for ciliary body tumors and those with excessive pigmentation.(36)
Although vascular patterns of the melanocytic lesions were distinct from healthy tissue, no differentiating OCTA features were found between nevi and melanoma of either the conjunctiva or iris.(37)
Study showed that OCTA can be used in anterior segment ocular oncology, but better software and enhanced imaging techniques are needed before conclusions about its

clinical utility can be drawn. Imaging techniques that are not dependent on light (such as ultrasound biomicroscopy, using sound waves) may be more suitable to depict tumor size.(38) AS-OCTA may provide an additional parameter for differentiating disease (e.g., providing reassurance when no abnormal vessels are seen).With better techniques, a prognostic value of angiography may be established. (39) Some studies have described the technique in iris pathological conditions, such as rubeosis iridis and melanomas, using commercially available spectral domain OCTA.(40) Swept source technology, which is only used for research purposes. Swept source technology employed in AS-OCTA has demonstrated increased capacity of light penetration, and may be applicable in cases of densely pigmented iris.(41)

Differential diagnosis

Overall, iris melanoma has a better prognosis and lower mortality rate, with metastases occurring in just 2 to 7% of cases, with a greater rate (10%) if mixed cellularity or ciliary body involvement. (2)

It might be difficult to tell the difference between benign and malignant iris abnormalities. Larger tumor size with a mean basal dimension of 6mm and 2.3mm thickness, seeding to other areas on the iris or adjacent trabecular meshwork, secondary glaucoma, secondary cataract, confirmed enlargement, and conspicuous vascularity are all characteristics that distinguish melanoma from nevus. (42)

Treatment

External beam irradiation is recommended when chemotherapy fails to provide adequate local tumor control. (43)

Surgical excision

Because many primary iris lesions have a favorable prognosis, many writers prefer to treat smaller iris tumors (those with a basal diameter of less than 3 mm) conservatively. (10)

At least 1 to 2 mm of safety margins must be resected. A partial lamellar iridocyclectomy with a more posterior scleral flap, big incision, and excision of the entire iris mass surrounded by the normal iris and ciliary body may be preferred in cases of restricted malignancies with iris root invasion but no seeding. If the seeding is contained within one or two clock hours of the tumor, the entire mass and seeding are carefully removed, usually followed by the placement of a radioactive plaque at the resection site. (17)

Smaller tumors (diameter 5 mm) are more likely to be handled by surgery alone, according to Samira Khan et al., while larger tumors (diameter 5 mm) are more likely to be controlled by radiotherapy.(44)

Proton beam and plaque radiotherapy

If a charged particle accelerator is available, this approach is a common conservative alternative to brachytherapy or enucleation for the treatment of unresectable or diffuse iris melanoma and medium-sized or larger posterior melanomas. (2)

Plaque radiotherapy involves suturing a radioactive disc to the globe's surface for a period of time to allow radiation of the iris melanoma through the cornea. (45)

It can be given without prior resection, following a high-degree resection of a malignant iris melanoma, or when tumor cells reach the resection specimen's margin. (17)

Irradiation therapies/ Brachytherapy

It is also successful in the treatment of iris melanoma; however, it causes cataracts and eyelid scarring at a much greater rate. The plaques come in a variety of sizes and forms, and they must be 2 mm larger than the tumor's maximum basal diameter. (46). To radioactively charge the plaques, different isotopes with good tissue penetration are utilized. (2)

DISCUSSION

The most crucial component in making a good diagnosis of Iris Melanoma is being aware of its clinical appearance. Careful surveillance of a lesion is the treatment of choice. (47)

Because the radiation dose provided to the tumor volume is homogeneous, plaque

radiotherapy is more suited than plaque brachytherapy. The dose supplied at the base of the irradiated tumor with brachytherapy is substantially higher than the required dose at the apex, resulting in an overdose at the base of the lesion. (5) A stromal nodule, ill-defined iris thickening, discomfort, iridocyclitis, or hyphema are all signs of iris metastases. (48) Iris cysts are most commonly found on the iris's periphery and in the lower quadrants, with a preference for the temporal area. Cysts cannot be distinguished from solid tumors by their anatomical location. There is no substantial rise in cyst size during long-term surveillance, indicating that these changes are benign and harmless. The majority of cysts are asymptomatic and don't need to be treated. (49)

Shields et al. presented a clinically based review of 40 cases of iris metastasis over a 20-year span in 1995, noting hazy vision, ocular pain, and eye redness as the patients' principal complaints. Secondary glaucoma, iridocyclitis, or tumor scleral invasion were all suspected causes of ocular pain. In the example at hand, ocular pain was assumed to be linked to secondary glaucoma and iridocyclitis. (50)

The most common presenting complaint in patients with iris metastases (32 percent) was ocular pain, according to a recent study by Shields et al.(50)

CONCLUSION

Although the therapy choices for primary tumors, which rely on various surgical excision procedures and/or irradiation therapies, provide acceptable local tumor control, the treatment options for metastatic illness, despite being numerous, are still insufficient in preventing a catastrophic outcome. (2) Furthermore, a melanocytic iris nevus is usually monitored until it shows signs of advancement. Radiotherapy or surgical resection are usually used in this situation. A combination of radiotherapy and surgery may be employed in some circumstances. Conservative treatment is an excellent option to enucleation since it provides for effective tumor control locally. Iris melanomas are discovered early and treated fast because they are apparent when they are little. As a result, patients with this tumor had a better prognosis than those with posterior uvea tumors. This could be due to posterior tumors' larger size and more malignant cytology. (51)

Acknowledgement: None
Conflict of Interest: None

REFERENCES

1. Russo A, Avitabile T, Reibaldi M, Bonfiglio V, Pignatelli F, Fallico M, et al. Iris melanoma: Management and prognosis. Appl Sci. 2020;10(24):1–10.
2. Branisteanu D, Bogdanici C, Branisteanu D, Maranduca M, Zemba M, Balta F, et al. Uveal melanoma diagnosis and current treatment options (Review). Exp Ther Med. 2021 Oct 11;22(6):1428.
3. Conway RM, Chua WC, Qureshi C, Billson FA. Primary iris melanoma: diagnostic features and outcome of conservative surgical treatment. Br J Ophthalmol. 2001 Jul;85(7):848-54. doi: 10.1136/bjo.85.7.848. PMID: 11423461; PMCID: PMC1724056.
4. CL S, MA M, JA S, E G, AD S, A S. Factors associated with elevated intraocular pressure in eyes with iris melanoma. Br J Ophthalmol. 2001;85(6):666–9.
5. Leblanc A, Rouic LL-L, Desjardins L, Dendale R, Cassoux N. Diffuse Iris Melanoma: Conservative Treatment with Proton Beam Therapy after Limbal Stem Cell Preservation or Enucleation? Ocul Oncol Pathol. 2019 Oct 1;5(6):396.
6. Gokhale R, Medina CA, Biscotti C V., Singh AD. Diagnostic fine-needle aspiration biopsy for iris melanoma. Asia-Pacific J Ophthalmol. 2015;4(2):89–91.
7. Krohn J, Dahl O. Incidence of iris melanoma in western Norway. Acta Ophthalmol. 2008 Feb 1;86(1):116–7.
8. McGalliard JN, Johnston PB. A study of iris melanoma in Northern Ireland. Br J Ophthalmol. 1989 Aug 1;73(8):591–5.
9. Singh AD, Topham A. Incidence of uveal melanoma in the United States: 1973–1997. Ophthalmology. 2003 May 1;110(5):956–61.
10. McLaughlin CC, Wu X-C, Jemal A, Martin HJ, Roche LM, Chen VW. Incidence of noncutaneous melanomas in the U.S. Cancer. 2005 Mar 1;103(5):1000–7.

11. Al-Jamal RT, Cassoux N, Desjardins L, Damato B, Konstantinidis L, Coupland SE, et al. The Pediatric Choroidal and Ciliary Body Melanoma Study: A Survey by the European Ophthalmic Oncology Group. Ophthalmology. 2016 Apr 1;123(4):898–907.
12. Morrison JC, Michael Van Buskirk E. Anterior collateral circulation in the primate eye. Ophthalmology. 1983;90(6):707–15.
13. Zett C, Stina DMR, Kato RT, Novais EA, Allemann N. Comparison of anterior segment optical coherence tomography angiography and fluorescein angiography for iris vasculature analysis. Graefes Arch Clin Exp Ophthalmol. 2018 Apr 1;256(4):683–91.
14. Parodi MB, Bondel E, Saviano S, Ravalico G. Iris fluorescein angiography and iris indocyanine green videoangiography in pseudoexfoliation syndrome. Eur J Ohthalmol. 1999;9(4):284–90.
15. Maruyama Y, Kishi S, Kamei Y, Shimizu R, Kimura Y. Infrared angiography of the anterior ocular segment. Surv Ophthalmol. 1995;39 Suppl 1(SUPPL. 1).
16. Houtzagers LE, Wierenga APA, Ruys AAM, Luyten GPM, Jager MJ. Iris colour and the risk of developing uveal melanoma. Int J Mol Sci. 2020 Oct 1;21(19):1–17.
17. Shields CL, Shields JA, Materin M, Gershenbaum E, Singh AD, Smith A. Iris melanoma: Risk factors for metastasis in 169 consecutive patients. Ophthalmology. 2001;108(1):172–8.
18. Dhillon AS, Hagan S, Rath O, Kolch W. MAP kinase signalling pathways in cancer. Oncogene 2007 2622. 2007 May 14;26(22): 3279–90.
19. Burotto M, Chiou VL, Lee J-M, Kohn EC. The MAPK pathway across different malignancies: A new perspective. Cancer. 2014 Nov 15;120(22):3446–56.
20. Platz A, Egyhazi S, Ringborg U, Hansson J. Human cutaneous melanoma; a review of NRAS and BRAF mutation frequencies in relation to histogenetic subclass and body site. Mol Oncol. 2008 Apr 1;1(4):395–405.
21. Mehnert JM, Kluger HM. Driver Mutations in Melanoma: Lessons Learned From Bench-to-Bedside Studies. Curr Oncol Reports 2012 145. 2012 Jun 22;14(5):449–57.
22. Mensink HW, Vaarwater J, Keizer RJW de, Wolff-Rouendaal D de, Mooy CM, Klein A de, et al. Chromosomal aberrations in iris melanomas. Br J Ophthalmol. 2011 Mar 1;95(3):424–8.
23. Sa HS, Rubin ML, Ning J, Li W, Tetzlaff MT, McGovern SL, et al. Association of T and N Categories of the American Joint Commission on Cancer, 8th Edition, with Metastasis and Survival in Patients with Orbital Sarcoma. JAMA Ophthalmol. 2020 Apr;138(4):374–81.
24. Shields CL, Nicola M Di, Bekerman VP, Kaliki S, Alarcon C, Fulco E, et al. Iris Melanoma Outcomes Based on the American Joint Committee on Cancer Classification (Eighth Edition) in 432 Patients. Ophthalmology. 2018 Jun 1;125(6):913–23.
25. Shields CL, Kaliki S, Furuta M, Fulco E, Alarcon C, Shields JA. American Joint Committee on Cancer classification of posterior uveal melanoma (tumor size category) predicts prognosis in 7731 patients. Ophthalmology. 2013 Oct;120(10):2066–71.
26. Shields CL, Kaliki S, Al-Dahmash SA, Lally SE, Shields JA. American joint committee on cancer (AJCC) clinical classification predicts conjunctival melanoma outcomes. Ophthal Plast Reconstr Surg. 2012 Sep;28(5):313–23.
27. Shields CL, Kaliki S, Hutchinson A, Nickerson S, Patel J, Kancherla S, et al. Iris nevus growth into melanoma: Analysis of 1611 consecutive eyes: The ABCDEF guide. Ophthalmology. 2013 Apr;120(4):766–72.
28. Medina CA, Biscotti C V., Singh N, Singh AD. Diagnostic Cytologic Features of Uveal Melanoma. Ophthalmology. 2015 Aug 1;122(8):1580–4.
29. Henderson E, Margo CE. Iris melanoma. Arch Pathol Lab Med. 2008 Feb;132(2):268–72.
30. Marigo FA, Finger PT. Anterior segment tumors: Current concepts and innovations. Surv Ophthalmol. 2003;48(6):569–93.
31. Demirci H, Shields CL, Shields JA, Eagle RC, Honavar SG. Diffuse iris melanoma: A report of 25 cases. Ophthalmology. 2002;109(8): 1553–60.
32. Jakobiec FA, Silbert G. Are Most Iris 'Melanomas' Really Nevi? A Clinicopathologic Study of 189 Lesions. Arch Ophthalmol. 1981;99(12):2117–32.
33. Shields CL, Arepalli S, Lally EB, Lally SE, Shields JA. Iris stromal cyst management with absolute alcohol-induced sclerosis in 16 patients. JAMA Ophthalmol. 2014;132(6):703–8.
34. Köse HC, Gündüz K, Hoşal MB. Iris cysts: Clinical features, imaging findings, and treatment results. Turkish J Ophthalmol. 2020;50(1):31–6.
35. He M, Wang D, Jiang Y. Overview of ultrasound biomicroscopy. J Curr Glaucoma Pract. 2012;6(1):25–53.
36. Hau SC, Papastefanou V, Shah S, Sagoo MS, Restori M, Cohen V. Evaluation of iris and

iridociliary body lesions with anterior segment optical coherence tomography versus ultrasound B-scan. Br J Ophthalmol. 2015 Jan 1;99(1):81–6.
37. Brouwer NJ, Marinkovic M, Bleeker JC, Luyten GPM, Jager MJ. Anterior Segment OCTA of Melanocytic Lesions of the Conjunctiva and Iris. Am J Ophthalmol. 2021 Feb 1;222:137–47.
38. Bianciotto C, Shields CL, Guzman JM, Romanelli-Gobbi M, Mazzuca D, Green WR, et al. Assessment of anterior segment tumors with ultrasound biomicroscopy versus anterior segment optical coherence tomography in 200 cases. Ophthalmology. 2011 Jul;118(7):1297–302.
39. Nanji AA, Sayyad FE, Galor A, Dubovy S, Karp CL. High-Resolution Optical Coherence Tomography as an Adjunctive Tool in the Diagnosis of Corneal and Conjunctival Pathology. Ocul Surf. 2015 Jul 1;13(3):226–35.
40. Roberts PK, Goldstein DA, Fawzi AA. Anterior Segment Optical Coherence Tomography Angiography for Identification of Iris Vasculature and Staging of Iris Neovascularization: A Pilot Study. Curr Eye Res. 2017 Aug 3;42(8):1136–42.
41. Skalet AH, Li Y, Lu CD, Jia Y, Lee BK, Husvogt L, et al. Optical Coherence Tomography Angiography Characteristics of Iris Melanocytic Tumors. Ophthalmology. 2017 Feb 1;124(2):197–204.
42. Gapsis BC, Warren NA, Nutaitis MJ, Bonaparte LA, Cooper SL, Ashenafi M, et al. Iris melanoma presenting as childhood glaucoma. 2018;
43. JA S, CL S, H K, P de P. Metastatic tumors to the iris in 40 patients. Am J Ophthalmol. 1995;119(4):422–30.
44. Khan S, Finger PT, Yu GP, Razzaq L, Jager MJ, De Keizer RJW, et al. Clinical and pathologic characteristics of biopsy-proven iris melanoma: A multicenter international study. Arch Ophthalmol. 2012 Jan;130(1):57–64.
45. Shields CL, Naseripour M, Shields JA, Freire J, Cater J. Custom-designed plaque radiotherapy for nonresectable iris melanoma in 38 patients: Tumor control and ocular complications. Am J Ophthalmol. 2003 May 1;135(5):648–56.
46. Dogrusöz M, Jager MJ, Damato B. Uveal melanoma treatment and prognostication. Asia-Pacific J Ophthalmol. 2017;6(2):186–96.
47. AB R, BD K, V J. Iris melanocytoma. Srp Arh Celok Lek. 2016 Jan 1;144(1–2):74–6.
48. Celebi RC, Kilavuzoglu AE, Emrah Altiparmak U, Banu Cosar C, Ozkiris A. Iris metastasis of gastric adenocarcinoma. World J Surg Oncol. 2016;14(1).
49. Konopińska J, Lisowski Ł, Mariak Z, Obuchowska I. Clinical features of iris cysts in long-term follow-up. J Clin Med. 2021 Jan 2;10(2):1–9.
50. CL S, S K, GS C, A P, S M, RA A, et al. Iris metastasis from systemic cancer in 104 patients: the 2014 Jerry A. Shields Lecture. Cornea. 2015 Jan 12;34(1):42–8.
51. Shields CL, Kaliki S, Furuta M, Mashayekhi A, Shields JA. Clinical spectrum and prognosis of uveal melanoma based on age at presentation in 8,033 cases. Retina. 2012 Jul;32(7):1363–72.

How to cite this article: Areeb Rehmani, Labishetty Sai Charan, Tara Rani et.al. Iris melanoma: genetic pathway, staging, histopathology, clinical features, diagnostic imaging, treatment and management. *International Journal of Science & Healthcare Research.* 2022; 7(3): 34-42.
DOI: *https://doi.org/10.52403/ijshr.20220707*

******