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CASE REPORT

Iris Melanoma-A Rare Ocular Tumour

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ABSTRAK

Uveal melanoma adalah keadaan yang jarang berlaku, terutamanya dalam populasi Asia, dan boleh terlepas pandang sebagai pertimbangan diagnostik, menyebabkan pengenalpastian yang lewat. Kami melaporkan kes seorang lelaki Cina berumur 69 tahun yang mempunyai ketumbuhan iris yang pada awalnya dirawat sebagai sista. Ketumbuhan ini semakin membesar dan menimbulkan kecurigaan terhadap penyebab jangkitan lain atau kanser. Pemeriksaan awal uveitik menunjukkan positif QuantiFERON-TB. Penanda tumor dan X-ray dada tidak menunjukkan sebarang keabnormalan. Beliau dirawat sebagai granuloma iris sekunder kepada tuberkulosis. Walau bagaimanapun, ketumbuhan tersebut terus membesar dan telah mendorong kami untuk melakukan biopsi eksisional. Analisis histopatologi menunjukkan patologi sel campuran (spindle dan epithelioid). Jenis sel campuran mempunyai potensi metastasis yang lebih tinggi berbanding dengan jenis histopatologi lain. Kes ini menekankan kepentingan menyingkirkan etiologi yang lebih ganas dalam kes-kes lesi iris yang membesar untuk mengurangkan risiko komplikasi lanjutan.

Kata kunci: Biopsi eksisional; melanoma iris; melanoma sel campuran

ABSTRACT

Uveal melanoma is a rare condition, especially in the Asian population that can be overlooked as a diagnostic consideration, leading to delayed identification. We reported the case of a 69-year-old Chinese man who presented with an iris mass that was initially

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treated as a cyst. The mass continued to grow in size, which raised suspicion of other infective causes or malignancy. Following the initial uveitic workup, the patient was found to be positive for QuantiFERON-TB test. Tumour markers and chest X-rays were unremarkable. The patient was treated for iris granuloma secondary to tuberculosis. However, the lesion continued to grow, prompting us to perform an excisional biopsy. Histopathological analysis demonstrated a mixed cellular (both spindle and epithelioid) pathology. The mixed cellular type has a higher metastatic potential compared to other histopathological types. This case highlighted the importance of ruling out malignant aetiology in cases of enlarging iris lesions to mitigate the risks of further complications.

Keywords: Excisional biopsy; iris melanoma; mixed cell melanoma

INTRODUCTION

Uveal melanoma is the most common primary intraocular malignancy in adults. It can arise in any part of the uveal tract, from the iris to the ciliary body and choroid (Krantz et al. 2017; Krohn et al. 2022). The incidence of uveal melanoma in different parts of Asia ranges from 0.42 to 0.64 per million (Manchegowda et al. 2021). Uveal melanoma accounts for only 3-5% of the total melanoma cases. In 95-98% of cases, uveal melanomas are observed in the choroid and ciliary body, while they are located in the iris in only 2-5% of cases (Krantz et al. 2017; Krohn et al. 2022). Therefore, the iris is the least common location for primary uveal melanoma. Iris melanomas are more common in Caucasians than in Asians. Liu et al. (2015) conducted a study in China and found that only 0.2% of the tumours were found in the iris. Owing to its rarity in the Asian population, uveal melanoma might be disregarded as a diagnostic consideration. We encountered diagnostic dilemma in a case of iris mass. Ultimately, a definitive diagnosis was attained following an excisional biopsy (sectoral iridectomy).

CASE REPORT

A 69-year-old Chinese man with no known medical illness presented with blurry vision in the right eye (OD) for over a month. There was no antecedent history of trauma, flashes, or floaters, and no family history of malignancy. His vision was 6/9 bilaterally. There was an incidental finding of a cystic right iris mass, measuring 1 mm x 1 mm, with a reddish hue near the pupillary margin at 11 o'clock (Figure 1A). Other ocular examinations were normal with Grade 1 nuclear sclerosis was noted in both eyes. The lesion was treated as an iris cyst with periodic observation.

However, the iris mass gradually increased in size over the past 5 months. Therefore, further workup was conducted to rule out infectious causes and malignancies. QuantiFERON-TB test was found to be positive, while other investigations, such as complete blood count, renal function test, liver function test, erythrocyte sedimentation rate, tumour markers, Venereal Disease Research Laboratory test, and chest X-rays, were normal. Anterior segment optical coherence tomography showed a cystic iris lesion. Ultrasound of the abdomen

and magnetic resonance imaging (MRI) of the brain and orbit did not indicate metastases.

He was then treated for iris granuloma, presumably secondary to tuberculosis (TB). However, even after the initiation of oral anti-TB drugs for two weeks, the iris mass continued to grow (Figure 1B), with whitish deposits in the anterior chamber and cells 1+. The OD intraocular pressure was mildly elevated to 23 mmHg. There was also the development of a OD hyperaemic disc with a blot retinal haemorrhage inferior to the disc (Figure 2A). A OD fundus fluorescein angiography (FFA) was performed. However, it only revealed a hot disc and minimal angiographic cystoid macular oedema. The left eye (OS) remained normal. No occlusive vasculitis or choroiditis was noted in either eye. The patient's condition was treated as a paradoxical worsening of ocular TB due to inflammation. Topical steroids and oral prednisolone were added.

Despite continuing anti-TB treatment for two months, the OD iris mass continued to grow, forming a pigmented pedunculated mass measuring 4 mm x 2 mm with a reddish hue (Figure 1C & 1D). The optic disc swelling and blot haemorrhage gradually resolved. Ultrasound biomicroscopy (UBM) was performed to determine the possibility of a solid mass. The UBM of the anterior segment demonstrated a mixed

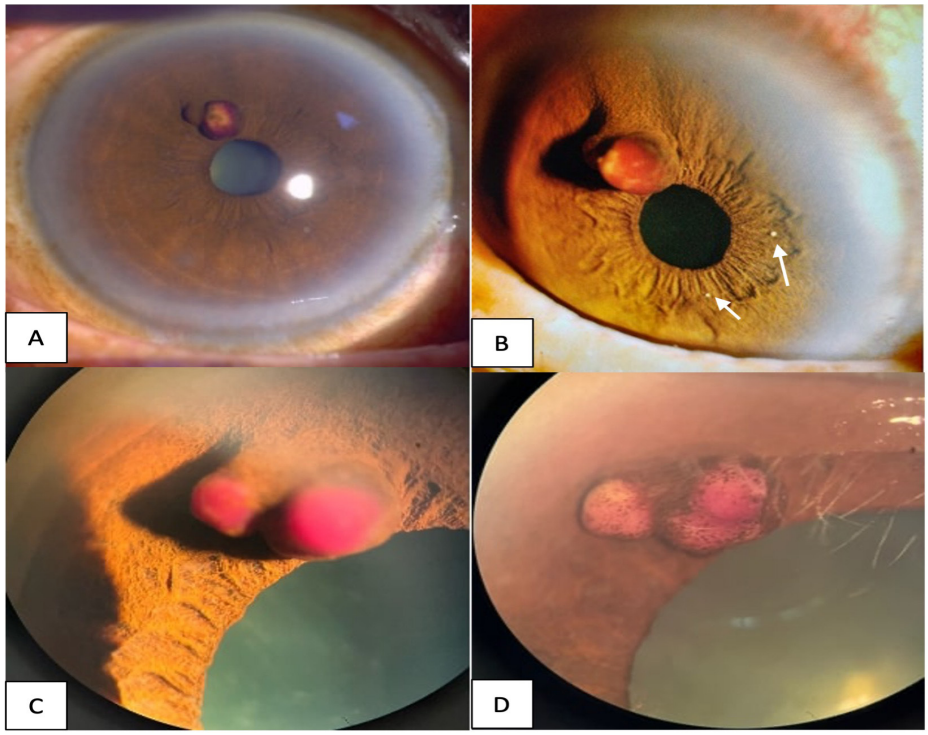

FIGURE 1: Right eye iris mass near the pupillary margin at 11 o'clock with (A) At first presentation; (B) 2 weeks post anti-TB drugs with whitish deposits in the anterior chamber (indicated by white arrows) ; (C & D) Iris mass increased in size despite anti-TB treatment

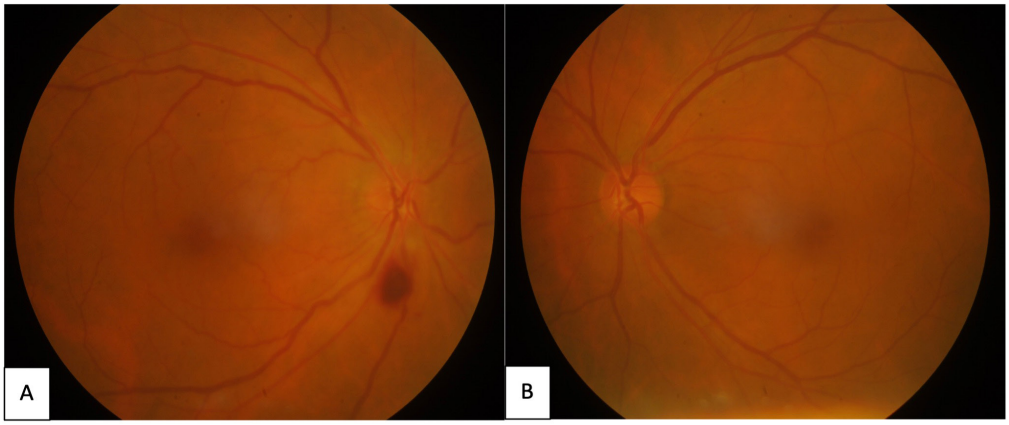

FIGURE 2: Fundus photo of the (A) OD showing hyperemic optic disc with blot hemorrhage inferior to the disc; (B) OS showing normal fundus examination

solid and cystic lesion (Figure 3). In view of the presence of a heterogeneous solid and cystic iris mass with rapid growth, there was a high clinical suspicion of malignant transformation. A sectoral iridectomy (Figure 4) was performed three months after anti-TB treatment, and the specimen was sent for biopsy purposes. It was an uneventful operation with no complications. Histopathology (HPE) reported atypical melanocytic proliferation that favours iris melanoma with mainly pleomorphic oval to epithelioid-shaped nuclei. Some showed elongated spindle nuclei (Figure 5). Postoperative reviews were conducted after two weeks, one month, two months, six months, and one year. There was no recurrence of iris tumour growth. Currently, the patient is under surveillance. His OD vision remained good at 6/9.

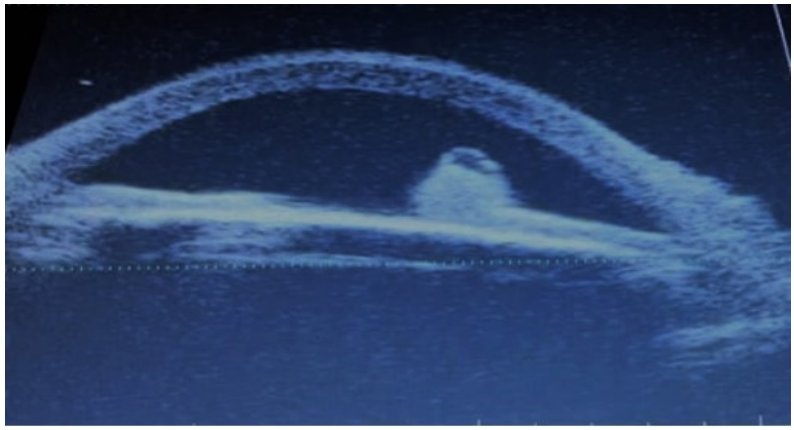

FIGURE 3: Right eye iris mass with a mixed component of cystic and solid lesion were shown in UBM

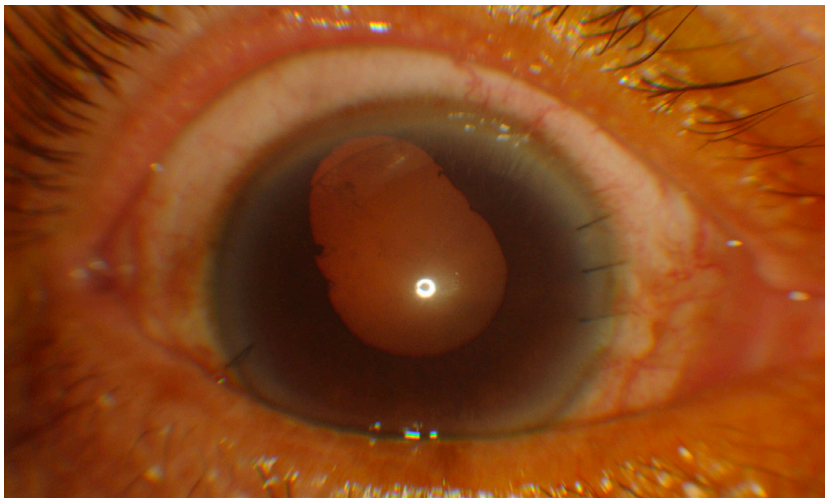

FIGURE 4: Right eye post-excisional biopsy of iris mass. A sectoral iridectomy from 10 to 11 o'clock was perfomed

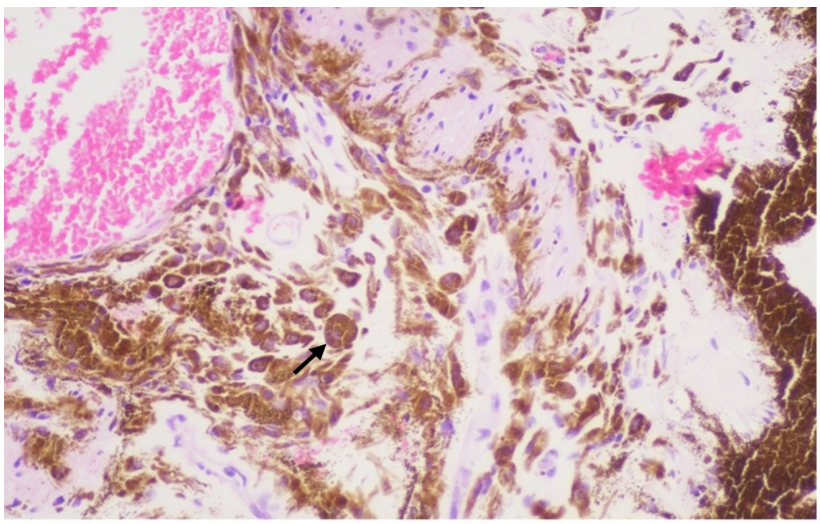

FIGURE 5: HPE showed heavily pigmented cells arranged in irregular nests (indicated by the black arrow). The cells exhibited pleomorphic oval to epithelioid-shaped nuclei, irregular nuclear membranes, and inconspicuous to small nucleoli with moderate cytoplasm and coarse brown pigments. Some cells showed elongated spindle nuclei

DISCUSSION

Iris melanomas are rare, and there is a lack of recently published data on their vast clinical spectrum. Due to its rarity in the Asian population, it is seldom considered and is prone to misdiagnosis. The overall estimated incidence of iris melanoma is in the range of 0.4-0.6 cases per 1 million people per year (Cherkas et al. 2024). As opposed to individuals with posterior uveal melanoma, individuals diagnosed with iris melanoma commonly have a younger age at diagnosis, typically between 45 to 65 years. They generally face a lower risk of metastasis compared to posterior uveal melanoma approximately 5% within 10 years and 10% within 20 years (Krohn et al. 2022; Shields et al. 2001). There is also no sexual predilection (Starr et al. 2004). Individuals with a fair complexion and a light iris color (such as blue, grey, or green) are at a greater risk of developing iris melanoma (Cherkas et al. 2024).

Iris melanomas typically present as either pigmented or non-pigmented masses. They usually originate from the peri-papillary iris, mid zone, or iris periphery in that order of frequency. The inferior quadrant is the most affected (between 5 and 7 o'clock), followed by the temporal, nasal, and superior quadrants (Russo et al. 2020). There are two growth patterns: circumscribed and diffuse. Circumscribed iris melanomas have a yellow, tan, or brown coloration and a flat or rounded anterior contour. On the other hand, diffuse melanoma is described as unilateral darkening of the iris (heterochromia) without focal thickening (Henderson & Margo 2008). In our patient, the iris mass was localised and well-circumscribed, originated from the least frequent site in superior quadrant. It caused an elevated intraocular pressure with whitish deposits in anterior chamber. Other associated features reported in the literature include corectopia (62%), ectropion uvea (44%), intrinsic tumour vessels (43%), iris sentinel vessels (25%), tumour-induced cataract (14%), and hyphema (9%) (Starr et al. 2004).

In the present case, during the initial presentation, the patient was treated as iris cyst due to its cystic appearance and absence of other associated features suggestive of malignancy. However, as the iris mass continued to grow, workups were done to rule out infectious causes and malignancy. TB was considered in view of its high prevalence in the Southeast Asian countries, with more than 45% of the global burden of annual TB incidence (World Health Organization 2023). Since the QuantiFERON-TB test was positive and other non-invasive tests for malignancy were negative, he was then treated for iris granuloma presumably secondary to TB. Subsequent development of anterior chamber reaction, fundus findings of a hyperaemic disc with a blot retinal haemorrhage inferior to the disc and FFA findings of hot disc with angiographic cystoid macular oedema raised suspicion of paradoxical worsening of ocular TB. Paradoxical worsening, known as the Jarisch-Herxheimer reaction, is believed to occur due to the liberation of mycobacterial antigens following anti-TB therapy, the enhancement of the host immune response, and the reduction of immunosuppressive mechanisms. It has been observed in both immunocompromised and immunocompetent individuals (Basu et al. 2013). It causes progressive inflammation,

and in our case, it manifested as papillitis, as demonstrated by the hot disc on FFA, and also cystoid macular oedema. These findings were resolved with tropical and systemic steroids. However, the continued growth of the iris mass prompted further investigations to rule out malignancy.

In line with the results of other series, iris melanocytic lesions that replaced the iris stroma locally and/or exceeded 3 mm in diameter or 1 mm in thickness are clinically diagnosed as iris melanomas or lesions suggestive of iris melanoma. The diagnosis may be supported by one or more associated features, such as (i) notable vascularity, (ii) ectropion uvea, (iii) secondary cataract, (iv) secondary glaucoma, and (v) documented growth evidence (Henderson & Margo 2008; Russo et al. 2020; Shields et al. 1983; Shields et al. 2001). Shields et al. (1983) recommended that it needs to fulfill at least three out of the listed five features to be classified as malignant melanoma. Our case exhibited an accelerated growth and secondary glaucoma which prompted us to carry out a biopsy of the lesion to confirm our diagnosis. The most crucial indicator in diagnosing iris melanoma is the presence of documented growth (Russo et al. 2020).

Iris melanomas typically demonstrate local growth, extending into the anterior chamber or along the surface of the iris. They commonly invade the anterior chamber angle and the anterior ciliary body through local extension (Conway et al. 2001). At times, they exhibit diffuse growth, extending posteriorly to involve the ciliary body and giving rise to a "ring melanoma" (Henriquez et al. 2007). Iris melanoma generally grows in a locally aggressive manner but rarely metastasizes. Histopathologically, a subset of lesions that includes an epithelioid component, such as mixed or epithelioid melanomas, may exhibit more aggressive behaviour (Conway et al. 2001). Geisse and Robertson (1985), in their literature review of 1043 cases and a minimum follow-up of ten years, reported higher metastatic rates in mixed-cell melanomas (10.5%) as compared to epithelioid melanomas (6.9%) and spindle B variant (2-6%). The biopsy results in our case demonstrated a mixed cell melanoma. Therefore, patient was advised for close monitoring every 6 monthly and for yearly MRI orbit and brain and ultrasound abdomen surveillance for early detection of recurrence and metastasis. However, iris melanoma usually has a better prognosis than lesion involving ciliary body. The clinical analysis of more than 8,000 cases by Shields et al. (2012), revealed that the 10-year metastatic rate from iris melanoma was approximately 6.9%, which is significantly lower compared to ciliary body melanoma (33.4%). In general, more than half of all iris melanomas reported are low-grade spindle cell melanomas (Russo et al. 2020). This iris melanoma's mixed cellular pathology (including both spindle cells and epithelioid cells), as reported in this case, has a higher metastatic rate than tumours composed entirely of either. Metastases mostly affect the liver and this occurs in 2.4-5% of cases (Starr et al. 2004). Hence, even though the tumour is excised, it is important for the patient to have yearly monitoring for tumour recurrence. Monitoring with ultrasound abdomen is crucial for its higher sensitivity. Liver function tests (LFTs) lack reliability in early liver metastasis detection as elevated levels are not specific to uveal melanoma

and may indicate various conditions, including inflammation, infection, other malignancies, or liver diseases related to alcohol and drugs (Francis et al. 2013).

The management of iris melanoma is a subject of controversy due to several factors. The majority of lesions are discovered in middle-aged individuals when they are still small, and patients often show no symptoms, maintaining good vision as described in our case. Additionally, these melanomas generally follow a natural course of benign, gradual growth (Conway et al. 2001). Because many primary iris lesions are benign, many clinicians prefer to treat smaller iris tumours (less than 3 mm basal diameter) conservatively. However, excision has traditionally been the treatment of choice for growing lesions (Russo et al. 2020). According to Cherkas et al. (2024) and Khan et al. (2012) smaller tumours (diameter <5 mm) are more likely to be treated with surgery alone, while larger tumours (diameter >5 mm) are more likely to be managed with radiotherapy. On the other hand, enucleation was recommended for eyes with bigger tumours (>4 clock hours of iris invasion), substantial tumour seeding (>2 clock hours), or secondary glaucoma refractory to treatment (>40 mmHg on maximal medicines) (Cherkas et al. 2024). As for our patient, the maximum diameter of the lesion is 4 mm. However, due to the rapid growth of the tumour, and also the secondary increase in intraocular pressure, the patient opted for surgical excision and biopsy to obtain the final diagnosis, despite the possible complications of surgery. The wide opening of the iris can lead to various disadvantages, including diplopia, photophobia, glare, and cosmetic changes to the appearance of the iris (Russo et al. 2020).

CONCLUSION

Iris melanoma, being uncommon among Asians, may be overlooked as a diagnostic consideration. It is crucial for clinicians to rule out uveal melanoma from other benign entities when diagnosis is in doubt, as misdiagnosis can lead to significant morbidity. In cases of enlarging tumours, it is imperative to consider prompt excisional biopsy or further diagnostic testing to accurately assess the nature of the growth and mitigate the risks associated with delays in treatment.

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CONFLICT OF INTERESTS

No potential conflict of interest was reported by the author(s).

ETHICAL CLEARANCE

We obtained approval from the Medical Research and Ethics Committee (MREC) and the Ministry of Health Malaysia (MOH), registered under NMRR ID-23-02603-ONO. No ethical clearance is required as this is a case report.

AUTHORSHIP

All authors attest that they meet the current ICMJE criteria for Authorship.

DISCLOSURE

The authors hereby certify that the work shown here is genuine, original and not submitted anywhere, either in part or full. They transfer the full rights of the content of the case report to Medicine & Health.

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REFERENCES

Basu, S., Nayak, S., Padhi, T.R., Das, T. 2013. Progressive ocular inflammation following anti-tubercular therapy for presumed ocular tuberculosis in a high-endemic setting. *Eye* **27**(5): 657-62.

Cherkas, E., Kalafatis, N.E., Marous, M.R., Shields, C.L. 2024. Iris melanoma: Review of clinical features, risks, management, and outcomes. *Clin Dermatol* **42**(1): 62-70.

Conway, R.M., Chua, W.C., Qureshi, C., Billson, F.A. 2001. Primary iris melanoma: Diagnostic features and outcome of conservative surgical treatment. *Br J Ophthalmol* **85**(7): 848-54.

Francis, J.H., Patel, S.P., Gombos, D.S., Carvajal, R.D. 2013. Surveillance options for patients with uveal melanoma following definitive management. *Am Soc Clin Onco Edu Book* 382-7.

Geisse, L.J., Robertson, D.M. 1985. Iris melanomas. *Am J Ophthalmol* **99**(6): 638-48.

Henderson, E., Margo, C.E. 2008. Iris melanoma. *Arch Pathol Lab Med* **132**(2): 268-72.

Henriquez, F., Janssen, C., Kemp, E.G., Roberts, F. 2007. The T1799A BRAF Mutation Is Present in Iris Melanoma. *Invest Ophthalmol Vis Sci* **48**(11): 4897-900.

Khan, S., Finger, P.T., Yu, G.P., Razzaq, L., Jager, M.J., de Keizer, R.J., Sandkull, P., Seregard, S., Gologorsky, D., Schefler, A.C., Murray, T.G., Kivelä, T., Giuliari, G.P., McGowan, H., Simpson, E.R., Corriveau, C., Coupland, S.E., Damato, B.E. 2012. Clinical and pathologic characteristics of biopsy-proven iris melanoma: A multicenter international study. *Arch Ophthalmol* **130**(1): 57-64.

Krantz, B.A., Dave, N., Komatsubara, K.M., Marr, B.P., Carvajal, R.D. 2017. Uveal melanoma: Epidemiology, etiology, and treatment of primary disease. *Clin Ophthalmol* **11**: 279-89.

Krohn, J., Sundal, K. V., Frøystein, T. 2022. Topography and clinical features of iris melanoma. *BMC Ophthalmol* **22**(1): 6.

Liu, Y.M., Li, Y., Wei, W.B., Xu, X., Jonas, J.B. 2015. Clinical characteristics of 582 patients with uveal melanoma in China. *PloS One* **10**(12): e0144562.

Manchegowda, P., Singh, A.D., Shields, C., Kaliki, S., Shah, P., Gopal, L., Rishi, P. 2021. Uveal melanoma in Asians: A review. *Ocul Oncol Pathol* **7**(3): 159-67.

Russo, A., Avitabile, T., Reibaldi, M., Bonfiglio, V., Pignatelli, F., Fallico, M., Caltabiano, R., Broggi, G., Russo, D., Varricchio, S., Spatola, C., Basile, A., Liardo, R.L.E., Milazzotto, R., Arena, F., Foti, P.V., Longo, A. 2020. Iris melanoma: Management and prognosis. *Appl Sci* **10**(24): 8766.

Shields, C.L., Kaliki, S., Shah, S.U., Luo, W., Furuta, M., Shields, J.A. 2012. Iris melanoma: Features and prognosis in 317 children and adults. *J AAPOS* **16**(1): 10-6.

Shields, C.L., Shields, J.A., Materin, M., Gershenbaum, E., Singh, A.D., Smith, A. 2001. Iris melanoma: Risk factors for metastasis in 169 consecutive patients. *Ophthalmology* **108**(1): 172-8.

Shields, J.A., Sanborn, G.E., Augsburger, J.J. 1983. The differential diagnosis of malignant melanoma of the iris. A clinical study of 200 patients. *Ophthalmology* **90**(6): 716-20.

Starr, O.D., Patel, D.V., Allen, J.P., McGhee, C.N. 2004. Iris melanoma: Pathology, prognosis and surgical intervention. *Clin Exp Ophthalmol* **32**(3): 294-6.

World Health Organization. 2023. WHO, global tuberculosis report. https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023 [18 February 2024].