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Recurrent Ciliary Body Melanoma after Inadequate Systemic Adjuvant Chemotherapy

Ardy Gisnawan[1], HalimahPagarra[1], Suliati P. Amir[1], Andi Pratiwi[1], Andi Mukramin Amran[2]

[1]Department of Ophthalmology, Faculty of Medicine, Hasanuddin University WahidinSudirohusodo Hospital, Makassar, Indonesia

[2]Faculty of Medicine, Al-Khairaat University, Palu, Indonesia

ABSTRACT

Ciliary body melanoma is diagnosed rarely because of its location and unclear associated symptoms. The existence of orbital recurrent depends on several factors including the width of the intraocular tumor, the diameter, the tumor location and degree of intraocular tumor necrosis. A sixty-year-old man presented with black mass at the perilimbal area of the left eye since 2 years prior with a decrease in visual acuity. History of incisional biopsy at the same site 1 year before, with pathology presented Malignant Melanoma. The patient rejected enucleation but then completed chemotherapy for 8 months with dacarbazine 1300mg. After consulted to haemato-oncologist. Recurrent hiperpigmented mass with 8 x 9 x 5 mm in sized, appeared at limbus area 4 months later, and followed by enucleation 1 month in advanced. Gross macroscopic section displayed the mass arose from the ciliary body area, filling in the anterior part of the left eye. Microscopic result was consistent for malignant melanoma. Metastatic workup remains normal, without any lymph node enlargement. The efficacy of systemic chemotherapy alone in intraocular melanoma was still controversy.Dacarbazine is ineffective as a single therapy and reduce the metastasis. Patients with large tumors had more than double the risk of recurrence of patients with smaller tumors.Enucleation still the best therapy for large tumor.Single adjuvant chemotherapy in ciliary body melanoma may be considered inadequate in large size ciliary body melanoma.

Keywords: Ciliary body Melanoma, uveal melanoma, Pathology Anatomy

INTRODUCTION

Melanomas of the uvea and conjunctiva arise from the structure of ocular and adnexa 5% of all melanomas. 95% of ocular melanomas arise in uvea. The incidence of uveal melanoma in the United States is 5.2 per million per year and 0.2 to 0.3 cases per 1 million in Africa and Asia. The incidence of uveal melanoma has remained stable for the last 50 years. There is a strong racial variation in the incidence, with the white population mostly affected. Clinical, epidemiological, physiological, and genetic data argue against a major role of UV light in the causation of uveal melanoma. Oculo-dermal melanocytotic predisposes to uveal melanoma (Singh et al., 2014).

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To determine the precise therapy in this case, it is important to diagnose accurately with ultrasonography, ultrasound biomicroscopy, and biopsy if necessary. The main goal of therapy is to save lives, other than that the treatment can be done depending on the size of the tumor and the risk of metastasis in older patients and loss of chromosome 3. Types of therapy are proton beam radiotherapy and brachytherapy (episcleral plaque radiotherapy) for tumor size that is small and enucleate at a large size (Damato, 2019). The size of the tumor can be measured with ultrasonography to know the diameter and depth of the mass. It is considered as a large mass if the diameter ≥ 15 mm and depth ≥ 10 mm (Kim et al., 2018).

Recurrent choroidal melanoma may exist to the extension of tumor to adjust scleral tissue despite complete chemotherapy. However, chemotherapy as a single treatment is still controversial and enucleation is still the golden standard for ciliary body melanoma (Kim et al., 2018; Damato& Singh, 2019).

Some studies report the possibility of recurrences in ciliary body melanoma may occupy in months to years after complete chemotherapy/radiotherapy, and mortality rate increase in metastasis lesion, related to some factors including the diameter of mass that attached to extraocular or to the posterior equator. Kim J H, et. al (2018), showed 226 patients with stage I-III uveal melanoma located in the choroid (220 patients) and ciliary body (6 patients), treated with Brachytherapy, Trans-pupillar thermotherapy (TTT), Enucleation (based on suze of tumors). median recurrence rate at 151.6 months with metastases in the liver (87.7%), bone (22.4%) and lung (12.2%).

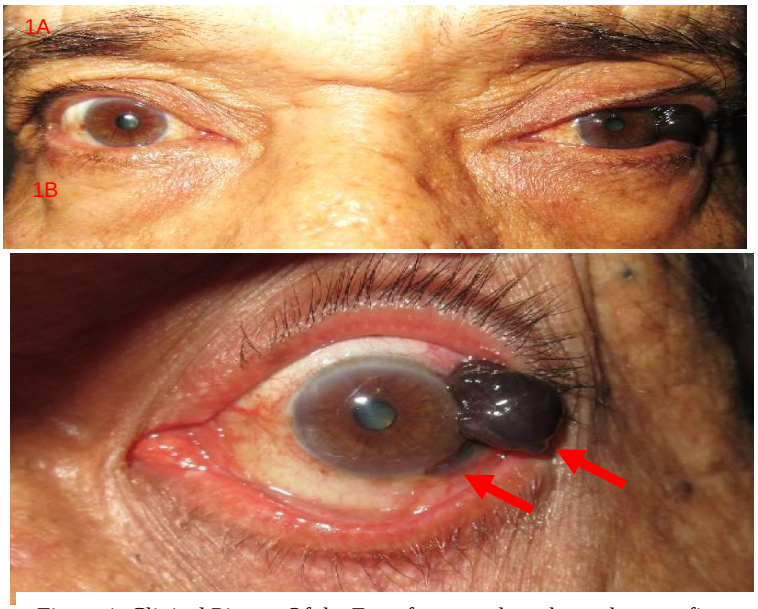

Figure 1. Clinical Picture Of the Eye after complete chemotherapy, figure 1a show the both eye and 1bshow the left eye (red arrow) showed hiperpigmentation mass.

This is also related to the large size of the tumor interpreted in tumor staging (Damato& Singh, (2019)Metastatic workup is mandatory for future management (Pach et al., 1986).Herein, we report a case of recurrent ciliary body melanoma after complete systemic chemotherapy.

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CASE PRESENTATION

A-60-year old male, came to the hospital with a chief complain of painless black mass in his left white eye for 2 years, along with a decrease in visual acuity. History of incisional biopsy for same lesion on the same site 1 year ago, with pathology result was malignant melanoma, but he rejected enucleation. The patient advised to

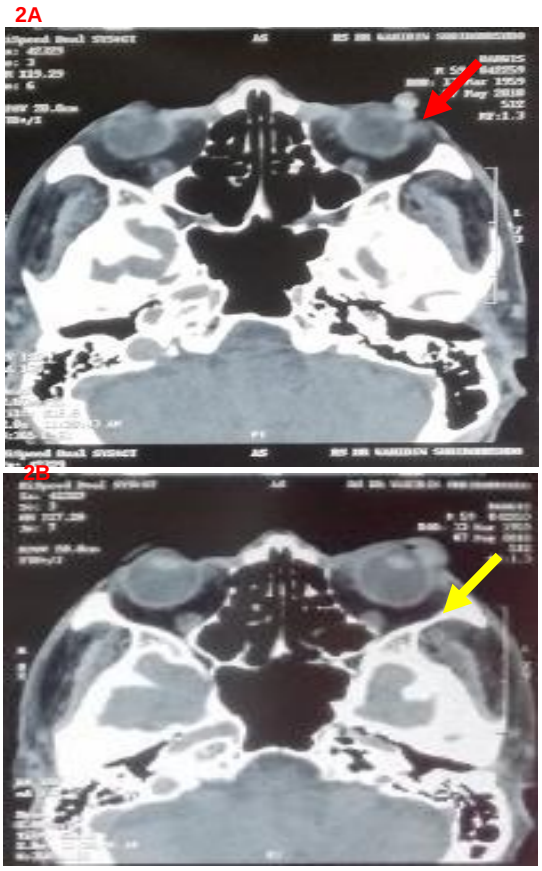

Figure 2. MSCT Orbital with Contrast
The red arrow (2A)showed the mass at leff eye attached from extraocular to intraocular. Yellow arrow (2B) showed the mass at extraocular

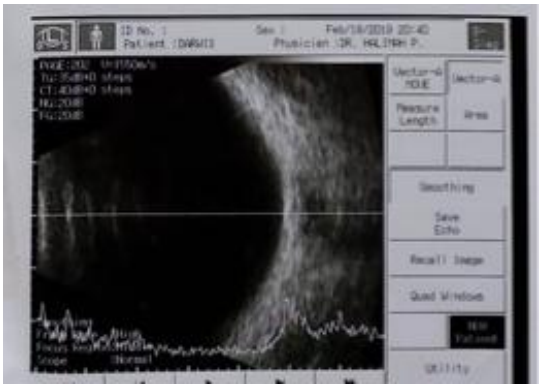

Figure 3. Ultrasonography images showed no

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enucleation but he rejected. He ask for another option to kept the eye. The patient consulted to internist for chemotherapy. He completed 5 cycles of systemic chemotherapy with Dacarbazine 1300mg. The mass reappeared 4 months after he finished the chemotherapy. Visual acuity in Right eye and left eye was 20/20 and 20/50, respectively. Anterior segment evaluation in Left Eye showed a painless hyperpigmented mass, 8 mm x 9 mm x 5 mm in size, attached precisely at the limbal area from 1-4 o'clock, rubbery consistency and fine surface, surrounded by enlarged vascularization in the conjunctiva beneath it. (Figure 1)

Dilated posterior segment was within normal limits. Contrast Orbital CT-Scan showed a slight hyperdense lesion (84 HU) with relatively firm, irregular margins, without calcification at the anterior side of the left eye, suggesting an intraocular mass (Figure 2).

The patient was suspected with recurrent ciliary body melanoma based on the clinical and ancillary examination. Metastatic workup including a chest x-ray and the whole abdomen ultrasonography was normal and there was no sign of metastatic.

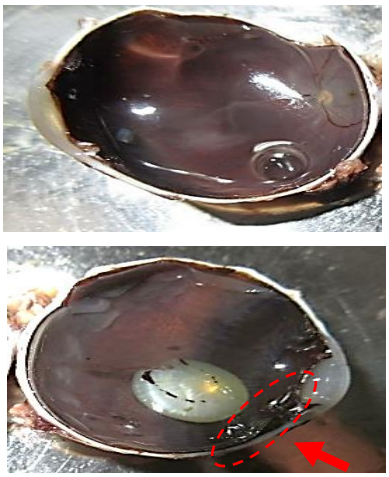

Figure 4. Gross Macroscopic of Left eye in formalin for

Enucleation was performed, and gross macroscopic showed a hyperpigmented mass arose from ciliary body area, filling in the anterior part of the left eye (figure 4). Pathology result of tissue preparation was a tumor mass composed of proliferation of melanocyte cells with atypical nuclei, pleomorphic, crude chromatin nuclei, with cytoplasm containing brownish pigments (melanin), consistent with malignant melanoma (figure 5).

The patient was diagnosed with Ciliary Body Melanoma based on two times pathology exam and the site of the tumor.

DISCUSSION

Ciliary body melanoma is a rare condition. Mostly, it is found secondarily after melanoma in iris or choroid was diagnosed. This patient presented a recurrent ciliary body melanoma after a complete 5 cycles of systemic chemotherapy with Dacarbazine 1300mg as single adjuvant therapy. We assume that this kind of management may become the risk factor of recurrent

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ciliarybody melanoma, as reported in several studies that the efficacy of systemic chemotherapy alone was still controversy because of the limited evidence that supports the use of this regiment, also the patients rarely exhibit clinical responses (Kim et al., 2018).Some studies also reported that there are no significant survival outcome for those treated with adjuvant therapy (Binkley et al., 2020).Furthermore, some literature reported that ciliary body melanoma therapy depends on the size of the tumor, visual potential and metastatic. It is important to measure the tumor size by radiologic examination such as ultrasonography and Contrast Computed Tomography Scan.

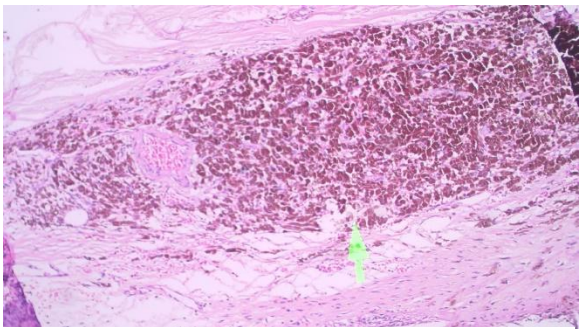

Figure 5.Microscopic Findings Melanoma Maligna

Size and location of the tumor also play important roles in recurrency of a melanoma. Patients with large tumors had more than double the risk of recurrence of patients with smaller tumors. Similarly, a patient's risk of treatment failure was more than doubled if the tumor involved the ciliary body rather than the choroid only (Gragoudas et al., 2002). Therefore, ultrasonography and ultrasound biomicroscopyis needed to identify specifically identify ciliary body mass (Pathan et al., 2018).In this case, we found a painless conjunctival mass with decrease of visual acuity and normal fundoscopy. As written in the literature, this condition may happen in small sized tumor. In addition, ciliary body melanoma hasnonspecific symptom, but mostly present with decreased visual acuity or blurred vision, primarily related to a progression of the serous retinal detachment. It is important to perform routine ocular fundus examination because in some cases the tumor/mass accidentally discovered with this examination (Zografos&Schalenbourg, 2019; Hamal et al., 2019).Although this patient presented with small conjunctival mass, yet, the gross macroscopic section showed a circumferential ciliary body origin lesion, attached firmly to the sclera and extended extraocularly. This is also a potential cause of recurrences in ciliary body melanoma. Ciliary body melanoma can invade the anterior chamber and involve the iris and angle. The mass needs to be evaluated by using High-frequency ultrasound biomicroscopy to demonstrate the extend of anteroposterior and circumferential. When extension to extraocularoccured, the mass becoming visible as a subconjunctival nodule. Transpupillarytransillumination is useful for demonstrating the tumor location as well as the circumferential and anteroposterior extent. As with other tumors in thHis location, benign or malignant, uveal melanomas are invariably associated with sentinel episcleral vessels. They usually initiate serous retinal detachment, distortion of the lens, and cataract (Singh et al.,

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2014)Again, It is important for early diagnosis and treatment to avoid the metastasis (Macedo et al., 2019).

Our patient then underwent enucleation because the mass is recurrent and it extended from intraocular to the conjunctiva. Enucleationremains gold standard for uveal melanoma. Earlier studies reported that for the past 3 decades, treatment for uveal melanoma is divided into 2 groups: for eye-conserving treatment possibility (for small tumors such as proton beam radiotherapy and brachytherapy) and to remove the tumor mass by enucleation (for large tumors) (Baily et al., 2019).Primary enucleation was performed for large tumors. Patients who strongly refused enucleation underwent brachytherapy (Kim et al., 2018).

The prognosis for this case could be high risk metastasis to other organ. There are some literature said the uveal tumors mostly can metastasis into the liver, followed by the bone and lung.

Metastasisworkupinclude chest x-ray, whole abdomen ultrasonography were done, and resulted in a normal limit without any sign of metastases. This result is consistent with Baily C, et. al (2018) and Hamal D et al (2019). They reported zero metastases for uveal melanoma after using the treatment such as brachytherapy, proton beam radiotherapy, and enucleation. Some of their patients underwent brachytherapy followed by enucleation, and there was no recurrence after enucleation (Hamal et al., 2019; Baily et al., 2019).Metastatic outcomes do not correlate with type of treatment as reported in the Collaborative Ocular Melanoma Study (COMS) (Chévez-Barrios & Espinosa, 2020).

CONCLUSION

Ciliary body melanoma melanoma is a rare malignant tumor. Recurrences may occur due to several risk factors: generous size tumor, ciliary body involvement, extraocular extension, and inadequate management. Systemic chemotherapy as single adjuvant therapy may be considered ineffective. We must consider many segments based on size, location, and metastasis.

REFERENCES

1. Baily, C., O'Neill, V., Dunne, M., Cunningham, M., Gullo, G., Kennedy, S., ...&Horgan, N. (2019). Uveal melanoma in Ireland. *Ocular oncology and pathology*, *5*(3), 195-204.
2. Binkley, E., Triozzi, P. L., Rybicki, L., Achberger, S., Aldrich, W., & Singh, A. (2020). A prospective trial of adjuvant therapy for high-risk uveal melanoma: assessing 5-year survival outcomes. *British Journal of Ophthalmology*, *104*(4), 524-528
3. Chévez-Barrios, P., & Espinosa, L. A. C. (2020).Selective Pathology of Intraocular Tumors.In *Oncological Surgical Pathology* (pp. 461-469).Springer, Cham.
4. Damato, B. E. (2019). Management of Patients with Posterior Uveal Melanoma.In *Clinical Ophthalmic Oncology* (pp. 185-199). Springer, Cham
5. Damato, B. E., & Singh, A. D. (2019). *Clinical Ophthalmic Oncology*. Springer International Publishing

6. Gragoudas, E. S., Lane, A. M., Munzenrider, J., Egan, K. M., & Li, W. (2002).Long-term risk of local failure after proton therapy for choroidal/ciliary body melanoma. *Transactions of the American Ophthalmological Society*, *100*, 43

7. Hamal, D., Limbu, B., Sthapit, P. R., Pradhan, E., Shrestha, R., &Saiju, R. (2019).Choroidal melanoma: our experience. *Nepalese Journal of Ophthalmology*, *11*(1), 64-73

8. Kim, J. H., Shin, S. J., Heo, S. J., Choe, E. A., Kim, C. G., Jung, M., ... & Shin, S. J. (2018). Prognoses and clinical outcomes of primary and recurrent uveal melanoma. *Cancer research and treatment: official journal of Korean Cancer Association*, *50*(4), 1238.

9. Macedo, S. S., Teixeira, M., Correia, A., Novais, A., & Cabral, C. (2019).Ocular Melanoma Presenting as Masquerade Syndrome. *European journal of case reports in internal medicine*, *6*(7)

10. Pach, J. M., Robertson, D. M., Taney, B. S., Martin, J. A., Campbell, R. J., & O'Brien, P. C. (1986).Prognostic factors in choroidal and ciliary body melanomas with extrascleral extension. *American journal of ophthalmology*, *101*(3), 325-331

11. Pathan, A. H., Barash, A., Tena, L. B., & Finger, P. T. (2018).Palladium-103 plaque radiation therapy for ciliary body melanoma through a functioning glaucoma filtering bleb. *European journal of ophthalmology*, *28*(1), 119-122

12. Singh, N., Bergman, L., Seregard, S., & Singh, A. D. (2014). Uveal melanoma: epidemiologic aspects. *Clinical Ophthalmic Oncology*, 75-87

13. Singh, N., Bergman, L., Seregard, S., & Singh, A. D. (2014). Uveal melanoma: epidemiologic aspects. *Clinical Ophthalmic Oncology*, 75-87

14. Zerrouk, R., Khmamouche, M., Tarib, I., Chaoui, Y., Mouzari, Y., Elasri, F., ...&Oubaaz, A. (2019). Melanoma of the Ciliary Body: About a Case. *International Research Journal of Oncology*, 1-5

15. Zografos, L., &Schalenbourg, A. (2019).Uveal Melanoma: Clinical Features. In *Clinical Ophthalmic Oncology* (pp. 71-83).Springer, Cham.