CASE REPORT

Extensive Primary Orbital Malignant Melanoma Associated with Nevus of Ota

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ABSTRACT

Primary orbital malignant melanoma is an extremely rare condition to present alone without previous extension of choroidal or conjunctival involvement. We reported the first case of malignant orbital melanoma without ocular involvement in a patient with nevus of Ota. A 52-year-old man presented with left proptosis and extensive bluish black pigmentation on left side of the face classified as Tanino type II of nevus of Ota and left ocular melanocytosis from birth. CT scan imaging showed extensive orbital mass occupying most of the orbital space. Transconjunctival biopsy was performed and a very pigmented mass was discovered, confirming the histopathology result of malignant melanoma. The patient was given up to five cycles of chemotherapy regimen. On serial orbital CT Scan, 33% of the tumor mass has disappeared after completing three cycles.

Key-words: primary orbital malignant melanoma, ota nevus

INTRODUCTION

rimary orbital malignant melanoma is an extremely rare condition and can be associated with nevus of Ota.1 Nevus of Ota or nevus fuscoceruleus ophthalmomaxillaris, is dermal melanocytic hamartoma, mostly congenital, that presents as bluish hyperpigmentation along the first or second branches of the trigeminal nerve, which clinically present as a blue-black or gray-brown patchy pigmentation.¹ Nevus of Ota affects between 0.014%-0.034% of the Asian population and rarely found in Caucasians. It was found that 90% of Nevus of Ota occured unilaterally.² The exact pathophysiology of nevus of Ota is unknown, but some theories mentioned that it formed primarily from melanocytes that have not migrated completely from the neural crest to epidermis in embryogenic stage. The histology of nevus of Ota described with the presence of dendritic melanocytes, multiple uniform brown granules, surrounded by fibrous sheaths in the papillary and upper reticular dermis and normal overlying epidermis.²

Malignant transformation has been reported in nevus of Ota and oculodermal melanosis. In more than half of the patients, ocular melanocytosis involves conjungtival, scleral, and uveal tissues. Among ocular malignant complications, conjunctival and uveal melanoma have been reported while orbital involvement remains rarity (0.5%). We report malignant

orbital melanoma without ocular involvement with Ota nevus in a Malay male.

CASE REPORT

A 52-year-old man presented with redness mass in the left eye (LE) for 6 months. Examination revealed black spots on the left upper cheek [Fig 1], the white part of the left eye, and the left hard palate since born [Fig 2]. The patient also complained of impaired visual acuity, painless protrusion, and ocular displacement to superior of the left eye for 1,5 years. There was no history of trauma of the eyes or the head. He had history of ischaemic stroke vears earlier. hemiparesis of the right extremities, and impaired left 7th cranial nerve.

Visual acuity of LE was no light perception. Intraocular pressure unremarkable upon palpation, ocular motility was restricted to all directions. Mass was palpated in the inferior, lateral, and superolateral region. The mass was firm, immobile, and had distinct edge. Black patch lesion can be found in the inferior palpebral extending to upper half of the cheek. Conjunctival chemosis was found in the inferior and lateral region, the conjunctiva was black pigmented, and the cornea was slightly oedematous. Further examination showed a flat anterior chamber in the inferior region, anterior synechia at the inferior region, the pupil was oval and retracted to the inferior part. The lens was hazy and subluxated downwards, posterior lens capsule was hazy. Vitreous and posterior segment cannot be evaluated (fig 1 and 2).



Figure 1 and 2. Patient at initial presentation. Note the edematous cornea and conjunctival chemosis in the inferior and lateral area with palpable mass underneath. There were black patches on the left conjunctiva, sclera, eyelids, cheek, and mucosal surface of the hard palate.

Ultrasound of the left orbit showed mild echogenic haziness with posterior vitreous detachment. There was no mass or abnormal lesion seen in the choroid, and the retina and optic nerve head were unremarkable (Fig. 3). Orbital CT scan showed a homogenous and distinct mass occupying more than half of the anterior orbit and compressing the globe pushing it to the superior and after three cycle of chemotheraphy, orbital CT scan showed an improvement of the mass [Fig. 4]. There was no sign of intracranial extension or bone destruction.

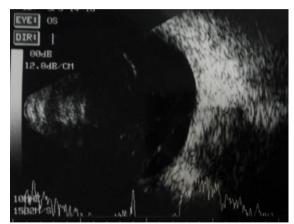


Figure 3. USG examination of the left eye

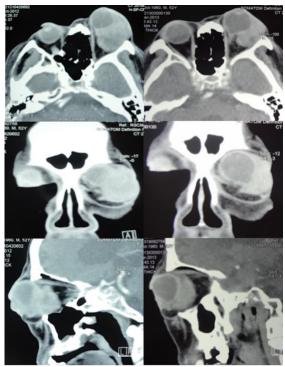


Figure 4. (**Left**) Orbital CT Scan of the left eye at the initial visit. (**Right**) Orbital CT Scan after three cycle of chemotheraphy confirmed around 33% of the mass size was reduced in comparation from the initial imaging.

Incisional biopsy was done and histopathology examination concluded the lesion as malignant melanoma [Fig. 5]. The immunohistochemical examination showed HMB45 strong diffuse staining, S100 strong diffuse staining, no specific finding of AE1/3, no finding of AE1/3, and no finding of CD15 [Fig. 6]. The result of the sample is negative for cytokeratin and EMA (epithelial membrane antigen).

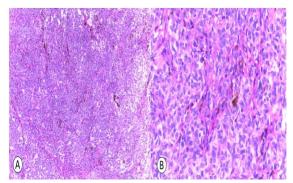


Figure 5. Histopathology examination shows round to spindle shape cell with pleomorphic and hyperchromatic nuclei and eosinophilic cytoplasm some containing brown pigment (H&E x40, x100)

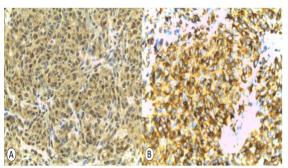


Figure. 6. Immunohistochemical Staining. (A) S100 positive, diffuse; (B) HMB45 Positive diffuse.

On further investigation for systemic involvement, liver metastases was confirmed. Six cycle of chemotherapy consisting of Cisplatin 30 mg, Vinblastin 2 mg, and Dacarbazin 1200 mg was administered [Fig. 7].



Figure 7. Patient after three cycle of chemotheraphy. Note that the bulky mass appearance at the left inferior temporal site has markedly reduced.

DISCUSSION

Orbital involvement of malignant melanoma can be the result of primary orbital melanoma or as an extension from pre-existing melanoma in the conjunctiva, eyelid, uveal, sinus, and oral mucosa. Malignant transformation has been reported in oculodermal melanosis. Among ocular complications, orbital melanoma is rarely found. The odds of developing uveal melanoma in a patient with nevus of Ota is 1 in 400 cases, with the most common being uveal melanoma. Orbital malignant melanoma is extremely rare.^{2,3}

Symptoms and signs of malignant melanoma are; black spots on the eyelid, conjunctiva, sclera, cheek, and oral

conjunctival mucosa, eye protrusion, chemosis, edematous cornea, hazy and subluxated lens, impaired visual acuity, no tenderness, and lower intraocular pressure.^{1,4} In this case, there was extensive bluish-black pigmentation on the left side of the patient's which is classified as type II Tanino of nevus of Ota and there was a local spread of the tumor in LE, involving the bone, orbital tissues, and optic nerve resulting in visual impairment [Table 1].8 According to studies, primary orbital melanoma is usually well-circumscribed, this is aligned with findings in our case as demonstrated in the CT Scan. 8,9,10

Table 1. Table 1. Tanino's classification⁸

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Type	Sub-type	Areas Involved
Type-I	IA	Mild orbital type- distribution over the upper and lower eyelids, periorbital, and temporal.
	IB	Mild zygomatic type- infrapalpebral fold, nasolabial fold and zygomatic regions are affected
	IC	Mild forehead type- only forehead is affected
	ID	Ala nasi alone is affected
Type-II		Moderate type- The lesions affect upper and lower eyelids, periocular, zygomatic, cheek and temple regions
Type III		The condition is distributed over the scalp, forehead, eyebrows, and nose
Type-IV		Bilateral type

Malignant melanoma can accurately diagnosed by ophthalmoscopy, fluorescein angiography, ultrasonography, CT Scan, and MRI.^{1,4} Our patient was presented with protrusion and ocular displacement towards superior region of the left eye. The histopathology analysis done by transconjunctival biopsy revealed that the mass was malignant melanoma. The risk of biopsy in malignant melanoma is extremely dangerous since the tumor may spread. However in our case, definitive diagnosis was needed to be able to determine chemotherapy regimen and further management. Moreover, metastasis was already observed and thus limit the treatment modality option.

The primary orbital tumor arises from orbital melanocytes of neural crest origin. ^{5,6} The abnormalities of neural crest migration lead to the development of these congenital dermal melanoses. Primary orbital melanoma tends to spread along the

nerves through the superior and inferior orbital fissures.^{5,7}

In this case, there was extensive bluishblack pigmentation on the left side of the patient's which is classified as type II Tanino of nevus of Ota and there was a local spread of the tumor in LE, involving the bone, orbital tissues, and optic nerve resulting in visual impairment. Primary melanoma is usually orbital circumscribed, as demonstrated in the CT Scan. 8,9,10 The management of Nevus of Ota ranges from camouflage, cryotherapy, microsurgery, and laser surgery which is the treatment of choice. 1,2 Orbital exenteration aims to control local tumor and to prevent distant organ metastasis (such as liver, bone, lymph nodes, and brain). Orbital exenteration with total tumor removal is the treatment of choice if no metastatic involvement is established. In the presence of systemic metastasis, such as in our patient, the indication for orbital exenteration is limited for cosmetic purposes. Wound healing after exenteration is another consideration in our case and chemotherapy immediate is beneficial.^{3,4} In our case, six cycles of chemotherapy were administered and after three cycles, orbital CT scan showed decreasing mass size.^{1,4} Unfortunately the patient passed away due to liver metastases complications before completing the whole cycle regiment.

Therapy for the patients with malignant orbital melanoma is one of the most important things that determine the outcome. Lack of patient's awareness, advanced stage of the disease, therapeutic option will slightly worsen the prognosis of the disease.1 Koranyi et al. (2000) have reported better prognosis in a case with a short history and early treatment.¹¹ In contrast with a study reported John et al (2009), the patient have the skin lesions examined periodically, therefore when the lesions become malignant, aggressive measures can be taken immediately to prevent metastases.³

It is important to raise awareness of early detection in malignant melanoma in

patients with dermal melanocytes which clinically presents as patchy pigmentation in the ophthalmic and maxillary branches of the trigeminal nerve region. A skin biopsy should be performed if signs of malignant transformation is suspected. evaluation with ophthalmologist should be done to detect potential complications. Ophthalmological examination of visual acuity, intraocular lamp examination, pressures, slit gonioscopy, and fundus examination needs to be done to rule out any uveal melanomas, conjunctival melanomas, as well as orbital melanoma as reported in this study.¹² Physician should educate the patients that nevus of Ota are benign lesions that may present as unilateral pigmentation along the periocular area, despite malignancy periodic transformation is rare, evaluation is necessary to monitor the progression of the lesion. Immediate medical consultation is highly suggested if the lesion changes in regards of size and shape.

In conclusion, this was rare case of orbital malignant melanoma associated with nevus of Ota which required periodic re-evaluation. It is important for clinician to conduct comprehensive examination of the eve as there is possible malignant transformation that involves the orbit. Raising awareness in patients with Nevus of Ota along with screening and early provide detection various treatment modality alternatives that can yield better prognosis and outcome.

REFERENCES

- 1. Henry HL, Chan MB, Kono T. Nevus of Ota: Clinical aspects and management. Skin Med 2003;2:89-96.
- 2. Sharon S, Grigg JR, Billson FA. Bilateral naevus of Ota with choroidal melanoma and diffuse retinal pigmentation in a dark skinned person. Br J Ophthalmol 2005;89:1529.
- 3. John H, Britto JA. Nonchoroidal intraorbital malignant melanoma arising from naevus of Ota. Ophthal Plast Reconstr Surg 2010;63:387-9.
- 4. Radhadevi CV, Charles KS, Lathika VK. Orbital malignant melanoma associated with

- nevus of Ota. Indian J Ophthalmol 2013;61(6):306-10.
- Albert DM, Miller JW, Jakobiec FA. Albert & Jakobiec's Principles & Practice of Ophthalmology. 3rd ed., vol. 4. Philadelphia: WB Saunders & Co.; 2000. p. 3238-9.
- 6. Buntinx-Krieg T, Ouyang J, Cartwright M. An orbital malignant melanoma arising in cellular blue nevus in a patient with nevus of Ota. Cureus 2016;8(7).
- 7. Nitta K, Kashima T, Mayuzumi H, Akiyama H, Miyanaga T, Hirato J, Kishi S. Animaltype malignant melanoma associated with nevus of Ota in the orbit of a Japanese woman: a case report. Melanoma research 2014;24(3): 286.
- 8. Huang WH, Wang HW, Sun QN, Jin HZ, Liu YH, Zuo YG, Zhao YL. A new classification of nevus of Ota. Chinese medical journal 2013;126(20):3910-3914.
- 9. Figueira E, Rajak S, McKelvie P, Kalantzis, G, Ismail A, Gonzales M, Selva D. Primary orbital melanoma: a case series and literature review. Orbit 2018;37(5):352-357.
- Guledgud MV, Patil K, Srivathsa SH, Malleshi SN. Report of rare palatal expression of Nevus of Ota with amendment of Tanino's classification. Indian Journal of Dental Research 2011;22(6):850.
- 11. Koranyi K, Slowik F, Hajda M, Banfalvi T. Primary orbital melanoma associated with oculodermal melanocytosis. Orbit. 2000:19:21-30
- 12. Agarwal P, Patel BC. Nevus Of Ota And Ito. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020. Available from: https://www.ncbi.nlm.nih.gov/books/NBK5 60574/