Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Clinical and Experimental Ophthalmology

Journal homepage: www.ijceo.org

Case Series

Predisposing factors in conjunctival melanoma in a south Indian population and its management - A retrospective interventional case series

Chinmayee J Thrishulamurthy[1], H Shafeeq Ahmed[1,*], Shwetha BV[1], Vidya Eswaran[1], Dayananda S Biligi[2]

[1]*Dept. of Ophthalmology, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India*
[2]*Dept. of Pathology, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India*

ARTICLE INFO

Article history:
Received 19-07-2023
Accepted 21-08-2023
Available online 29-09-2023

Keywords:
Conjunctival
Melanoma
Xeroderma pigmentosa

ABSTRACT

Background: Conjunctival melanoma is an uncommon malignancy particularly in the pigmented races. We report an interesting association of risk factors involved in this rare tumour in a South Indian population.
Results: A retrospective, interventional case series of three patients diagnosed with conjunctival melanoma on the basis of clinical and histopathological evaluations between the year 2017 and 2022. Among the three patients, one patient had Xeroderma pigmentosa, one patient had carcinoma of the ovary and one patient had a pre-existing nevus.
Conclusions: Conjunctival melanoma is a rare tumour in pigmented races and Xeroderma pigmentosa, pre-existing nevus and another malignancy predispose to a conjunctival melanoma.

1. Introduction

Although uveal melanoma is the most common intraocular tumour, Conjunctival melanoma is a very rare tumour of the conjunctiva with a very low reported incidence of 0.03 – 0.08. Conjunctival melanoma represents 1.6% of non-cutaneous melanomas.[1] It can arise anywhere on the conjunctiva – bulbar or non-bulbar- tarsal, forniceal conjunctiva or arising from the caruncle. The tumour is potentially life threatening with metastases are seen in 26% of cases and death occurs in about 13% at 10 years as reported by shields group in a series of 150 cases.[2] It is important to recognise the changes in the pigmented nevi of the conjunctiva early and treat them if there is any suspicion of a malignant change.

Conjunctival melanoma is diagnosed by clinical examination and confirmed by a histopathological examination. In this case series we look at the clinical profile of three patients diagnosed with conjunctival melanoma.

2. Methods

Retrospective chart review of three patients with histopathologically proven conjunctival melanoma between the year 2017 and 2022 was performed.

3. Case 1

A 17-year-old girl who was previously diagnosed as Xeroderma pigmentosum came with complaints of a swelling in the left eyelid seen since six months. She had skin lesions in the sun exposed areas of the face, neck and arms suggestive of Xeroderma pigmentosa. She had nodulo-ulcerative basal cell carcinoma over the ala of the right nose for which she was treated in the plastic surgery department. Best corrected visual acuity was 6/18 in both eyes. Right

* *Corresponding author*.
E-mail address: shafeeqahmed2002@gmail.com (H. S. Ahmed).

https://doi.org/10.18231/j.ijceo.2023.086

eyelid was normal, conjunctiva showed melanosis, cornea was hazy. Pupils were reactive in both eyes. In the left eye, a fullness was noted in the upper lid along with mechanical ptosis. On everting the upper lid, there was a large irregular multinodular lesion of 4 cm * 3 cm*1 cm in size arising from the tarsal conjunctiva and filling the upper fornix. The lesion was pale pink in colour, with areas of brownish pigmentation, firm in consistency and fixed to the underlying tarsal plate. It was difficult to reposit the lesion back into the fornix. There was no palpable regional lymph nodes. Incisional biopsy was done and histopathology was suggestive of amelanotic melanoma. Complete excision of the mass with 4 mm margin clearance was done and specimen sent for histopathological examination. She then underwent eyelid reconstruction by cutler beard technique. Flap was divided after one month. At third year follow up there was no recurrence of lesion or systemic metastases.

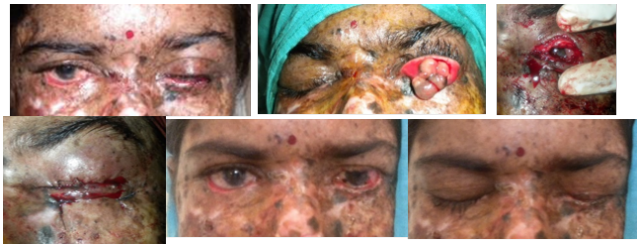

Fig. 1: Preoperative – eyelid mechanical ptosis, mass seen on upper tarsal conjunctiva after lid eversion, wide excision done. Reconstruction by cutler beard procedure and post-operative results with good anatomical and functional results

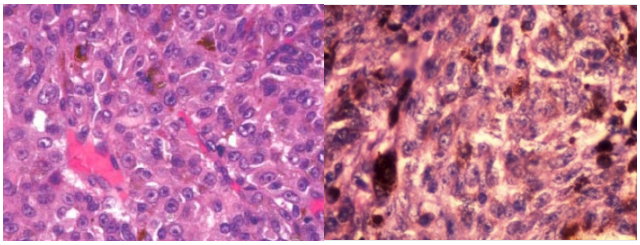

Fig. 2: Histopathology of lesion of showing bizarre polygonal epithelioid cells with large atypical nuclei, also seen are spindle cells.

4. Case 2

The second case was a 45-year-old male who presented with a growth in the nevus in the left eye since birth. Over the last one year he had seen a growth in the lesion. On examination, he had a large lesion on the lateral conjunctiva extending from the lateral canthus to the limbus. The lesion was heavily pigmented and measured 11 mm* 10mm with variable thickness with a maximum height of approximately 4 mm in the lateral part involving the temporal conjunctiva. The surface was irregular and the lesion was freely mobile over the conjunctiva. Visual acuity, anterior segment, fundus was normal. UBM and B scan showed no involvement of the sclera or intraocular structures. There were no palpable lymph nodes or other pigmented lesions elsewhere in the body. Systemic evaluation was normal. There were no other primary melanoma or metastases. Whole body PET scan was normal.

A diagnosis of conjunctival malignant melanoma was made and the lesion was excised with 4 mm margins. Cryotherapy was done to the edges and the base of the lesion.

Fig. 3: Pre-operative picture with surface ulceration and post-operative pictures of case 2

Patient was started on 3 cycles of mitomycin C 0.02% eye drops – four times a day for one week and a gap of one week and the cycle was repeated for 3 cycles. Conjunctiva epithelised in 3 weeks with a mild limitation of lateral movement. Patient is on follow up for any recurrence. At 2 year follow up patient is doing well with no recurrences.

5. Case 3

A 60-year-old lady came with the complaints of a painless swelling seen in the left eye noticed since one month. She had been operated for papillary carcinoma of the ovary and has completed chemotherapy and radiotherapy treatment in another oncology centre and had no recurrence or metastases. On examination she had a fullness in the left eyelid. On palpating the mass a pigmented tumour popped out of the eyelids. On everting the eyelid a multinodular irregular, 1 cm * 2 cm, pedunculated dark brown pigmented lesion with one area of whitish necrotic area seeming to arise from the conjunctiva near the upper tarsal border was seen. The lesion was mobile and not fixed to the underlying tarsal plate. It was firm in consistency, not associated with any inflammation and could be moved freely. Systemic evaluation for other swellings or metastases was normal. Lesion was excised with a 4 mm of normal conjunctiva and sent for histopathological examination. After margin clearance she was started on 3 cycles of mitomycin C 0.02% eye drops. Patient is doing well at third year follow up with no recurrences or metastases.

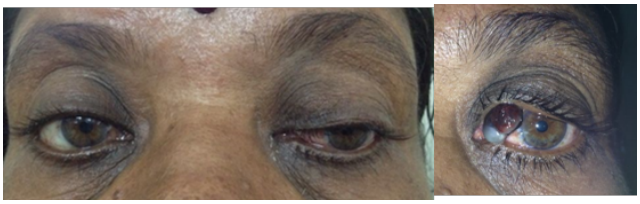

Fig. 4: Preoperative pictures of case 3 with surface ulceration

6. Results

Age range of our patients was from 17 years – 70 years, two cases were females and one patient was male. All cases in our series had some predisposing feature – Xeroderma pigmentosa, pre-existing nevus and non-ocular cancer.

7. Discussion

Conjunctival melanoma is a rare tumour occurring at $1/40^{th}$ times than a choroidal melanoma and 500 times less common than a cutaneous melanoma with an incidence of 0.2 to 0.8 per million in the white population. Over the last three decades in the United States, though the uveal melanoma is stable, conjunctival melanoma is increasing in white men and over 60 years.·· The incidence in white men has increase 295% in the last 27 years.[3] Similar trend was observed in Sweden and Finland as well. Both conjunctival and cutaneous melanoma possibly suggests role of increased sun exposure.[4,5] In India few isolated cases have been reported.[6]

Conjunctival melanoma is generally seen in older population. Conjunctival melanoma is slightly higher in females with a 3:2 ratio.[7] It is a very rare tumour in India with very few reported cases.[6] The incidence decrease as we come south in Europe and America.

The tumour can arise de novo or from pre-existing nevus or from PAM – Primary Acquired Melanosis. Conjunctival nevi rarely undergo malignant transformation with a risk of less than 1%. (3 patients out of 410 patients with a mean of 7 year follow up).[2] About 60% of conjunctival malignant melanoma tumours arise from PAM. Around 16% of PAM with severe atypia undergo malignant transformation to malignant melanoma with greater areas of PAM having a higher risk of malignant transformation.[2] Lesions arising out of PAM have an increased tendency for recurrence sometimes even after eight years. Hence, it is important for long term surveillance.[8]

Location of tumour could be palpebral, tarsal, forniceal, bulbar, caruncular or limbal. Caruncular melanomas have a poorer prognosis compared to other locations. For a localised caruncular lesion without evidence of multimodality exenteration is not advocated as exenteration clears only 2mm on the nasal side, caruncle being a skin derivative, therefore caruncular melanomas fare worse than other conjunctival location. Also, once sub epithelial space is invaded exenteration rarely alters the prognosis[8] in tumours with medial extension external beam radiation can be combined with excision to prevent spread into lacrimal apparatus, nasal cavity and sinuses.[7]

Invasive melanomas with thickness under 1.5mm were associated with a favourable outcome irrespective of whether they were treated with local excision or exenteration. Larger lesions fare badly in terms of survival despite exenteration. In lesions greater than 2 mm exenteration did not improve the mortality rates. In a study by A D A Paridaens et al involving 95 cases of conjunctival melanoma who underwent exenteration mortality rates were 33 – 50% irrespective of exenteration in melanomas thicker than 1 mm.[8]

Treatment depends on presentation – age, site, thickness, primary or secondary. Therapeutic options include local excision, cryotherapy, β irradiation, chemotherapy, irradiation, exenteration or a combination of many treatments. Reese in 1964 coined the term precancerous melanosis and was the first to advocate exenteration at an early stage of disease for diffuse lesions. Complete local excision is the treatment of choice. Local excision with beta irradiation (Sr – 90 / Y - 90) or cryotherapy. Cryotherapy: was advocated by Jackobeic 1 in 1980 as an adjunct to local excision (1) Jackobeic advocated a high success rate of cryotherapy for PAM and unifocal lesions but a 45% risk of metastases for patients with multifocal disease.[2] Side effects of cryotherapy are symblepharon, ptosis, dry eye, motility disturbances, trichiasis, and loss of eyelashes, corneal abrasions, opacification and vascularisation, iritis, posterior synechiae, cataract.[2] Reese has advocated that enucleation is contraindicated as it leaves potentially dangerous areas of conjunctiva and hence increase risk of metastases. A combination of complete excision, cryotherapy, and β irradiation should be tried before considering exenteration as it is a severely disfiguring condition. Orbital exenteration must be reserved for advanced disease as palliate care and must not be done as an initial treatment. Exenteration in 95 patients either as a primary modality or as a secondary modality was found to be a good option in tumours less than 1 mm thickness. But a mortality of 33 – 50% was noted in tumours over 1 mm thickness. Orbital invasion in exenteration specimen implies increased regional lymphatic and distant blood metastases.[8]

Folberg et al. in a series of 53 patients treated with exenteration reported lesser risk of metastases in patients without orbital invasion (15 (43%) of 35) versus patients with orbital invasion (16(89%) of 18) on histopathology of exenteration specimen. Prophylactic lymph node treatment: by irradiation or excision: while may prolong disease free interval does not increase survival rate.[9]

Prognosis depends on various factors like location, size, thickness and time interval between disease onset and

presentation. Locations like palpebral conjunctiva, fornices, caruncle, plica, lid margins are found to have a 2.2 times higher mortality than bulbar conjunctival melanoma.[7] Caruncular melanomas have a poorer prognosis compared to the other locations.[8] Size of more than 1 mm who underwent exenteration mortality rates were 33 – 50% irrespective of exenteration in melanomas thicker than 1 mm. A thickness more than 1.8 mm was found to be having a bad prognosis as done by silvers et al and was supported by a study by Folberg et al.[9] Extent of disease at presentation is the most important factor which determines prognosis. Long delay by patient or doctor may allow an intraepithelial melanoma to become invasive disease and increase mortality rate.[7] Incisional biopsy should be avoided and diagnosis to be based on clinical examination and excision biopsy results. Conjunctival cryotherapy and alcohol keratectomy helps to reduce recurrence by limiting subclinical disease.[9]

8. Conclusion

Conjunctival melanoma is a rare neoplasm in the pigmented races.in pigmented races it is important to screen patients for any systemic predisposing condition or primary tumour elsewhere. A high degree of suspicion, wide excision with margin clearance, histopathological examination and a good follow up is important in these tumours.

9. Source of Funding

None.

10. Conflict of Interest

No conflict of interest

References

1. Scotto J, Fraumeni JF, Lee JA. Melanomas of the eye and other noncutaneous sites: epidemiologic aspects. *J Natl Cancer Inst*. 1976;56(3):489–91.
2. Shields CL, Shields JA, Gündüz K, Cater J, Mercado GV, Gross N, et al. Conjunctival melanoma: risk factors for recurrence, exenteration, metastasis, and death in 150 consecutive patients. *Arch Ophthalmol*. 1960;118(11):1497–507.
3. Yu GP, Hu DN, Mccormick S, Finger PT. Conjunctival melanoma: is it increasing in the United States? *Am J Ophthalmol*. 2003;135(6):800–806.
4. Triay E, Bergman L, Nilsson B, All-Ericsson C, Seregard S. Time trends in the incidence of conjunctival melanoma in Sweden. *Br J Ophthalmol*. 2009;93(11):1524–8.
5. Tuomaala S, Eskelin S, Tarkkanen A, Kivelä T. Population-based assessment of clinical characteristics predicting outcome of conjunctival melanoma in whites. *Invest Ophthalmol Vis Sci*. 2002;43(11):3399–408.
6. Grover AK, Rastogi A, Chaturvedi KU, Sota LD, Gupta AK. Malignant melanoma of the conjunctiva. *Indian J Ophthalmol*. 1993;41(1):26–9.
7. Paridaens AD, Minassian DC, Mccartney AC, Hungerford JL. Prognostic factors in primary malignant melanoma of the conjunctiva: a clinicopathological study of 256 cases. *Br J Ophthalmol*. 1994;78(4):252–9.
8. Paridaens AD, Mccartney AC, Minassian DC, Hungerford JL. Orbital exenteration in 95 cases of primary conjunctival malignant melanoma. *Br J Ophthalmol*. 1994;78(7):520–8.
9. Folberg R, Mclean IW, Zimmerman LE. Malignant melanoma of the conjunctiva. *Hum Pathol*. 1985;16(2):136–43.

Author biography

Chinmayee J Thrishulamurthy, Associate Professor https://orcid.org/0000-0003-1671-8474

H Shafeeq Ahmed, MBBS Student https://orcid.org/0000-0003-1671-8474

Shwetha BV, Assistant Professor

Vidya Eswaran, Assistant Professor

Dayananda S Biligi, Professor and HOD

Cite this article: Thrishulamurthy CJ, Ahmed HS, Shwetha BV, Eswaran V, Biligi DS. Predisposing factors in conjunctival melanoma in a south Indian population and its management - A retrospective interventional case series. *Indian J Clin Exp Ophthalmol* 2023;9(3):449-452.