Case study

RECURRENT MALIGNANT MELANOMA EYELID A CASE REPORT AND REVIEW OF LITERATURE

ABSTRACT:

Melanoma of the eyelid skin arises from the malignant proliferation of melanocytes. Eyelid melanoma (EM) is a rare condition that accounts for < 1% of all cutaneous melanomas. They are usually a result of DNA damage from exposure to UVB (290-320). Other common risk factors include Fair skin, red/blond hair, high-density freckling, light eyes (green/ hazel/blue), family history of melanoma or dysplastic nevi, immunosuppression (congenital or acquired), UVA (tanning beds, PUVA therapy). The most common location of eyelid melanomas is the lower eyelid, where it is approximately 2.6 times more likely to occur than the upper eyelid. Here we present a rare case of recurrent eyelid melanoma in a 62-year-old lady.

KEYWORDS: Nevi, Malignant melanoma, Metastasis, Upper eyelid, Radiotherapy.

BACKGROUND:

Ocular melanoma refers to malignant melanocytic proliferation involving any structure of the eye, orbit, or ocular adnexa. It is far less encountered than cutaneous melanoma. Ocular Melanoma of different tissue origins, such as the uvea, conjunctiva, eyelid, orbit, and lacrimal sac, is distinct in terms of patient characteristics, manifestations, and disease prognosis [1]. The most common histologic subtype of eyelid is ‘‘lentigo maligna melanoma.’’ The lower eyelid is more often involved, due to its more direct exposure to sunlight. Treatment for eyelid melanoma (EM) is basically surgical and reconstruction techniques include direct closure, full thickness skin graft, and local/regional or free flaps [2,3]. The most utilized globe-preserving treatment is radiation therapy, comprising Brachytherapy, proton beam therapy, stereotactic radiosurgery, and stereotactic radiotherapy [4]. All types of radiotherapy, if used as indicated, achieve good local tumour control and eye preservation rates [5,6]. Eyelid Melanomas are at highest risk for recurrence. Risk factors for treatment failure were older age, greater tumour thickness, greater basal dimension of the tumour, and proximity of the tumour to the foveal avascular zone [7,8]. Most recurrences occur at the posterior margin of the tumour [9]. The majority of recurrences are found in the first 2 years, and recurrences after 5 years are relatively rare [10]. Recurrence has also been associated with the development of metastatic disease [11]. Herein we describe a rare case of recurrent eyelid melanoma in a 62-year-old lady.

CASE REPORT:

A 62-year-old female patient a known case of Malignant Melanoma presented to our department with complaints of a multiple nodules under the upper eyelid with history of decreased vision and continuous watering in right eye. On examination, a nodule measuring 1x1cm noted near the inner canthus of right eye in the upper eyelid, hard in consistency, mobile, eye movements being restricted. Two sub centimetric nodules noted in upper eyelid, mobile, non-tender. Irregularity in right bulbar conjunctiva noted. **(Fig-1).** Enlarged lymph node in right pre auricular region measuring 1x1cm, hard in consistency, fixed, tender.

She had a past history of pigmented growth in the lower bulbar conjunctiva **(Fig-2)** 2 years ago, was evaluated outside and underwent excision for the same. Histopathological examination showed melanoma. Patient presented with swelling in the right lower eyelid**,**3 weeks after the excision. Map biopsy was done and was started on injection mitomycin C 0.04% as adjuvant therapy. She was lost to follow up.

Present PET CT showed FDG avid nodular enhancing lesion in right upper eyelid, extending for a length of about 2.8cms with maximum thickness of 1cm, SUV:7.1. FDG avid enlarged enhancing right intraparotid node is seen measuring 1.3 x 1cm with SUV: 11.5. She underwent right orbital exenteration with superficial parotidectomy and type III modified radical neck dissection with split skin grafting under general anaesthesia. Post operative histopathological examination revealed as malignant melanoma, epithelioid cell type. Intraparotid lymph node positive for metastatic deposit with Extranodal extension. 1 lymph node out of 18 was positive for metastatic deposit. Pathological staging PT4aN2M0 (Stage IIIC). She was planned for adjuvant radiation therapy and she received 60 Gy in 30 fractions to primary, 66 Gy in 30 fractions to the right parotid bed and 54 Gy in 30 fractions to ipsilateral neck nodes from level I to level V. **(Fig-3)** She completed the treatment uneventfully and on regular follow up.

Fig-1 showing nodules in upper eyelid and thickening in bulbar conjunctiva
Fig-2 showing pigmented growth in the lower bulbar conjunctiva

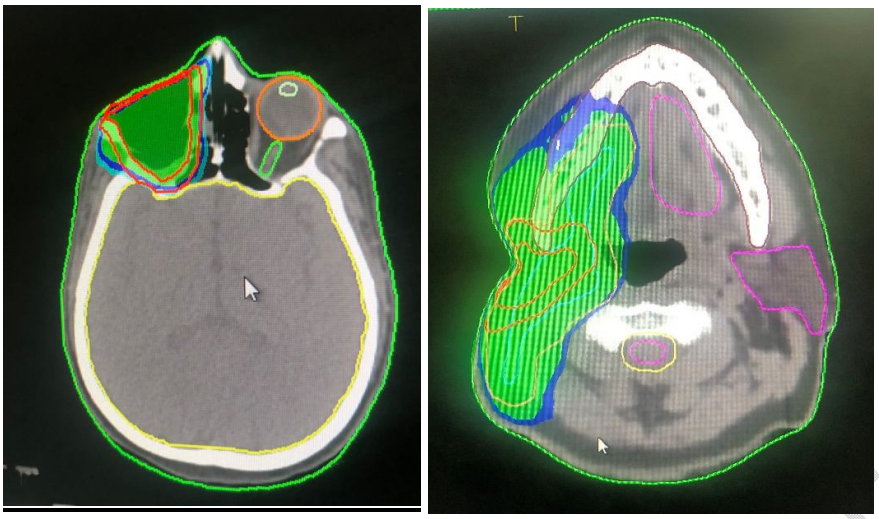

Fig-3 Showing the radiation target volumes and coverage

DISCUSSION:

Most common subtype of melanoma is superficial spreading, which makes up 70% of malignant melanoma cases [12]. These usually occur in trunk/extremities and are usually related to sun exposure. Nodular melanoma subtype makes up 15% to 30% of cases [12]. Lentigo maligna subtype commonly occurs in older patients in areas of skin with history of sun damage, commonly arises as macule, similar in appearance to freckle [13]. Least commonly occurring melanoma subtype is acral lentiginous melanoma, which makes up less than 5% of cases. It is most common type among patients of Asian origin and in those with dark skin; this subtype most commonly arises in palms of hand and soles of feet. Mucosal melanoma is rare, and makes up approximately 1% of all melanoma cases [14]. These most commonly occur in head and neck, anorectum, vagina, and vulva [15]. V600 or BRAF mutation status can help guide systemic therapy.

American Academy of Dermatology (AAD) recommends that those at high risk (strong family history of melanoma or personal history of multiple clinically atypical moles) undergo frequent self-examination with at least annual physician exam. In general, ABCDE system is important for screening—asymmetry, border irregularities, colour variation (different colours in same region), diameter >6 mm, enlargement or evolution of colour change, shape, or symptoms. Genetic counselling should be considered for those with strong family history [16].

Surgical excision is primary treatment for melanoma. Wide local excision is recommended, with margin requirement based on thickness of tumour. Sentinel lymph node status is the most important prognostic factor for recurrence in patients with melanoma. SLNB is recommended for patients with ≥0.75 mm or those with <0.75mm thickness with any high-risk feature (ulceration, LVSI, or mitotic rate greater than or equal to 1/mm2). Completion lymphadenectomy is recommended for patients with positive SLNB as ~18% of those with +SLN will have additional regional lymph nodes [17,18].

High-dose IFNα continued for 1 year has historically been the standard of care for patients with resected node-positive melanoma (stage III) and should be considered for patients with

negative nodes and increased risk of recurrence (stage IIB and IIC). Role of immunotherapy in adjuvant setting is evolving. NCCN now has ipilimumab use as category 1 treatment option in adjuvant setting after resection of clinical stage III disease, based on results of EORTC 18071, which demonstrated Recurrence free survival benefit with use of adjuvant ipilimumab compared to placebo [19]. Ipilimumab—monoclonal antibody acts by blocking cytotoxic T-lymphocyte antigen-4 (CTLA-4) receptor present on T-lymphocytes. CTLA-4 downregulates T-cell activation and thus ipilimumab stimulates T-cell activity. Vemurafenib—specific inhibitor of V600 mutation of BRAF (seen in 40%–60% of advanced melanoma patients). Dabrafenib and trametinib (MEK inhibitor) are also approved for use in BRAF-mutated metastatic melanoma [20,21]. Pembrolizumab/Nivolumab are anti-PD-1 inhibitors with evolving use in melanoma.

Definitive radiation therapy is used when surgery would be disfiguring. RT alone is considered in patients with superficial lentigo maligna (confined to epidermis) and lentigo maligna melanoma (invasive into dermis). These patients are often elderly and can present with large superficial lesions on face. Nonsurgical options can offer better function and cosmesis [22]. No standard dose, but 50 Gy/20 fractions using appropriate energy electrons is reasonable [23]. For more deeply invasive tumours, data is sparse, though there have been reports of effective local control with much higher doses (100+ Gy) delivered with 60 Kvp x-rays. Indications for adjuvant radiation therapy for treating primary tumour bed includes melanomas with desmoplastic or neurotropic features, thick lesions (>4 mm) particularly if ulcerated or associated with satellitosis. Can also be used for positive margins, but re-resection preferred. Indications for radiation therapy are stronger if multiple risk factors are present. Potential indications for treating regional lymph nodes include: multiple positive lymph nodes, extracapsular extension, lymph node size ≥3 to 4 cm, sentinel lymph node involvement but without complete or inadequate lymph node dissection and recurrent disease [24]. Single-institution retrospective data from MDACC suggests that patients with stage I/II cutaneous melanoma who did not have Sentinel lymph node biopsy or Lymph node dissection who went on to have subsequent adjuvant treatment with hypofractionated regional nodal RT had good outcomes (89% 5- and 10-yr actuarial regional control and 10-yr symptomatic complication rate of 6%) [25]. NCCN suggests that patients who meet Burmeister criteria may be considered for adjuvant RT. Most common fractionation includes 48 Gy/20 fractions over 4 weeks (Burmeister) or 30 Gy/5 fractions over 2.5 weeks. Hypo fractionated RT (30 Gy/5 fractions) is safe and effective for adjuvant treatment of melanoma with excellent 10-year local control rate [26]. Adjuvant nodal RT reduces nodal recurrence in select patients with high-risk features after nodal dissection [26,27].

Desmoplastic melanoma is rare subtype of melanoma which tends to be locally aggressive with increased chance of Local recurrence rather than distant or lymph node metastasis. It tends to spread along path of large named nerves (neurotropic), especially in head and neck–region where wide surgical margins are difficult to achieve. Retrospective evidence from MDACC suggests that use of postoperative RT significantly reduces local recurrence in patients with desmoplastic melanoma [28]. Hence, we recommend to consider adjuvant radiotherapy to reduce the local recurrence in high-risk melanoma and recurrent melanoma of eyelids.

CONCLUSION:

Malignant melanoma of eyelid should be detected early, especially when growing on pre-existing nevus to prevent life threatening complications, which has been documented in high number of cases. We recommend radiation in adjuvant setting and in recurrent Eyelid Melanoma.

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