Malignant tumors of the eyelid – To err is human, to learn divine

Errors, failures, they are just experiences that will obligate you to evolve. - Roberto Llamas

The annual age-adjusted incidence of eyelid malignancies in Asia ranges from 3.1 to 6.5 per million population.[1,2] There is no such data from India. Extrapolating the Asian data, we can roughly estimate the incidence of about 5000-6000 new cases of eyelid malignancies in India every year. An average ophthalmologist is likely to see one case of eyelid malignancy in three years or about 10 cases in an average practice life span. Evidently, eyelid malignancies are rare. However, since these patients generally present to an ophthalmologist first, we are in a privileged position to accurately diagnose them and guide their management as appropriate.

Misdiagnosis and Missed Diagnosis can Harm

Because of their vividly externally evident nature and relatively small size at presentation, eyelid malignancies present a unique opportunity for a prompt and accurate diagnosis and appropriate management, with optimal life, eye, and vision salvage. However, eyelid malignancies are often misdiagnosed and are inappropriately managed. A study published in this issue of the Indian Journal of Ophthalmology (IJO) reports an 18.7% rate of initial misdiagnosis among referred patients and inappropriate primary management before referral in 24%.[3]

Schiff *et al.* defined diagnostic error as "any mistake or failure in the diagnostic process leading to a misdiagnosis, a missed diagnosis, or a delayed diagnosis."[4] They divided the diagnostic process into seven stages – "access and presentation, clinical history taking, clinical examination, testing, assessment, referral, and follow-up".[4] There could be an omission (failure to do the right thing) or commission (doing something wrong) at any of these stages in the diagnosis and management of eyelid malignancies. The following circumstances in eye cancer management can constitute culpable negligence in care: "1. Failure to identify and investigate symptoms that an ophthalmologist with similar capabilities would have recognized and examined, 2. Failure to order appropriate tests for cancer corresponding with the medical state and symptoms of the patient, 3. Administer inappropriate or incorrect treatment, 4. Failure to provide standard follow-up care to evaluate the effectiveness of a prescribed treatment, 5. Failure to read or interpret cancer test results from the testing laboratory, 6. Intentionally not disclosing certain cancer-related symptoms to the patient, 7. Failure to execute further testing or treatment recommended by other medical professionals, or 8. Failure to refer the cancer patient to a specialist when they lack the required skillset and qualification to diagnose or treat the condition or symptoms of the patient".[5] Misdiagnosis is currently the leading cause (26%) of medicolegal claims in the United States.[6]

Do not Let Sinister Signs Slip by You

Accurate diagnosis requires background knowledge, targeted history, a keen eye for clinical signs, not an intuitive heuristic

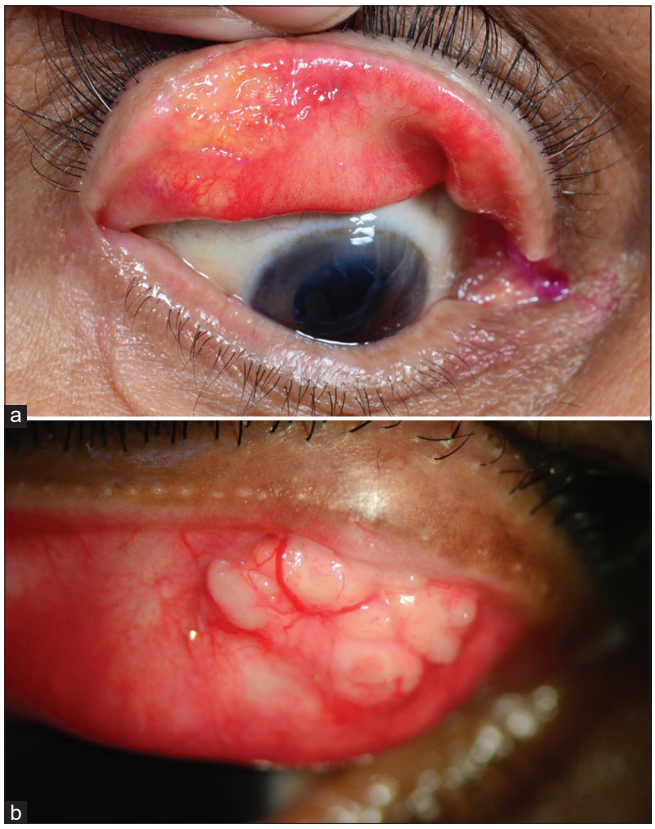

Figure 1: Unilateral blepharoconjunctivitis with a placoid mass involving the tarsal and palpebral conjunctiva – a case of sebaceous gland carcinoma with Pagetoid invasion (a); A nodular variant of sebaceous gland carcinoma simulating a chalazion but the everted eyelid shows a multilobulated lesion involving the tarsus (b)

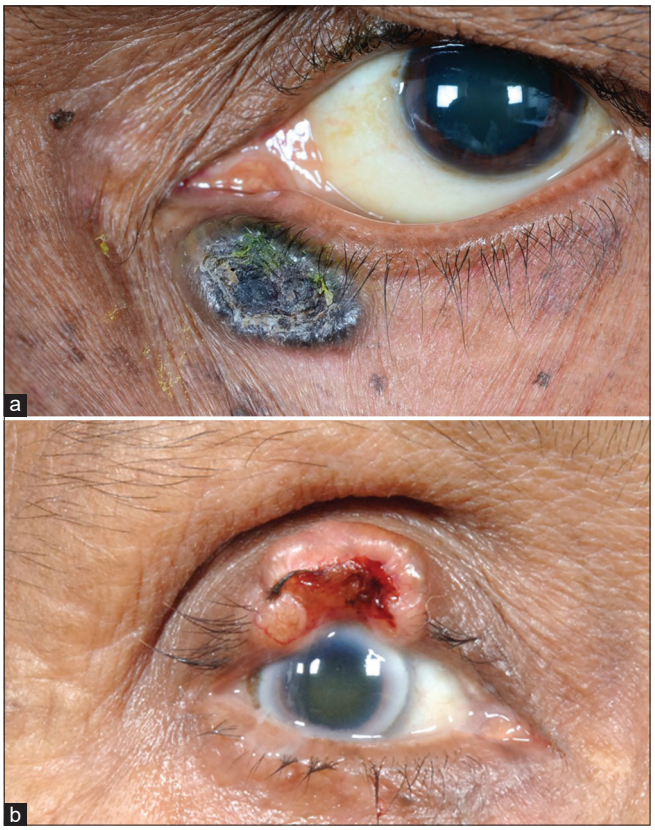

Figure 2: Basal cell carcinoma manifesting as a chronic pigmented placoid mass in the lower eyelid with a surface crust. It does not generally involve the eyelid margin and is more commonly found in the lower eyelid. (a); A noduloulcerative type of squamous cell carcinoma of the upper eyelid with skin, eyelid margin, and tarsal involvement (b)

approach as clinicians are programmed to, but a method-based, nothing-missed clinical evaluation, integration of clinical findings with appropriate investigations, and finally logical, evidence-based, and experience-tempered conclusions. The three most common eyelid malignancies in India are sebaceous gland carcinoma (SGC), basal cell carcinoma (BCC), and squamous cell carcinoma (SCC).[7]

While a large noduloulcerative lesion is hard to miss, a diagnostic dilemma may exist in over half of the patients who present with nodular SGC that simulates a chalazion or with intraepithelial SGC masquerading as unilateral blepharoconjunctivitis [Fig. 1a and b].[8] The nodular variant of SGC generally extends beyond the upper edge of the tarsus and often shows a full-thickness infiltration of the tarsal conjunctiva or a break-through nodule or an ulcer or a noduloulcerative lesion, which is evident only on eyelid eversion.[8] A meticulous evaluation using a slit-lamp will help pick-up additional features that support the clinical diagnosis of SGC versus a chalazion - relatively sparse eyelashes in the involved area, loss or obliteration of meibomian gland orifices, widening of the eyelid margin, abnormal vascularity of the eyelid margin, and alteration in the sharp anatomy of the posterior eyelid margin (rounding).[8] Intraepithelial SGC may or may not have an evident nodular or a noduloulcerative lesion. In addition to some of the eyelid margin and tarsal features seen in nodular SGC, intraepithelial SGC is characterized by diffuse congestion and thickening of the palpebral and bulbar conjunctiva, tumor pannus over the cornea, cicatrizing conjunctivitis, and thick ropy discharge.[8] Atypical age (>40 years) for a chalazion and recurrence following curettage, along with any of the accompanying features listed above, warrants an extremely high index of suspicion and referral to an expert for protocol-based management.[8] Any elderly patient with unilateral chronic blepharoconjunctivitis for which there is no evident cause and that does not respond to conventional treatment in a finite period also qualifies for an expert evaluation for possible map biopsy (biopsy from 17 predetermined conjunctival locations to diagnose and to meticulously determine the extent) and further management as appropriate.[8]

BCC is essentially a slow-growing, locally destructive skin cancer involving the eyelids and the periocular area [Fig. 2a]. Advanced tumors, however, may infiltrate the eyelid full-thickness and very rarely extend to the orbit. The classic manifestation is a smooth, translucent nodule with rolled pearly white edges with telangiectasia and often a central ulcer or a crust covering it. Relatively uncommon morpheaform, superficial, infiltrative, micronodular, and linear variants are prone to misdiagnosis. The morpheaform variant can manifest as lower eyelid cicatricial ectropion because of its desmoplastic nature. BCC can be pigmented in Asian Indians and can be misleading.

SCC is more aggressive than BCC and is difficult to miss because of its striking vascular nodular or noduloulcerative manifestation with keratin and crusting, with the involvement of the eyelid margin, a full thickness of the eyelid and orbit [Fig. 2b]. SGC and SCC have a relatively higher metastatic potential as compared to BCC, necessitating a careful evaluation of the regional lymph nodes.

Protocol-based Management Optimizes the Outcome

Gupta *et al.*, in this issue of IJO, report that about 5% had local tumor recurrence and about 10% had metastasis at a relatively short mean follow-up of about 21 months.[3] A strict protocol-based approach helps achieve excellent life, eye, and vision salvage.[8] In brief, an elaborate pre-operative mapping of the extent of the tumor, complete excision with intraoperative frozen section-guided margin control, map biopsy for SGC to rule out intraepithelial tumor and treatment as appropriate, careful evaluation of the regional lymph nodes clinically and by sentinel node biopsy or positron emission tomography scan if indicated, and close follow-up for at least 3 years are the keys to success. Recent advances such as neoadjuvant and adjuvant chemotherapy in SGC, topical chemotherapy and brachytherapy for intraepithelial SGC, biological target therapy for BCC and SCC, and adjuvant radiotherapy for residual tumor may further help improve the outcome.

Appropriate Referral is the Key to Success

Eyelid malignancies primarily present to an ophthalmologist and thus provide an opportunity for an early and accurate diagnosis and appropriate management. Comprehensive ophthalmologists may not be equipped to provide the standard of care the patients with eyelid cancers deserve. An incisional biopsy is not required before referral and may indeed complicate the primary management. Inappropriate omission or commission in cancers can affect life salvage and thus have ethical and medicolegal implications. Patients with eyelid cancers are best triaged to an oculoplastic expert with a background in ocular oncology or to an ocular oncologist for optimal management.

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Access this article online

Quick Response Code:

Website: www.ijo.in

DOI: 10.4103/0301-4738.299219

Cite this article as: Honavar SG. Malignant tumors of the eyelid – To err is human, to learn divine. Indian J Ophthalmol 2020;68:2333-4.