

MALIGNANT EYELID TUMOURS

Dr.Ahmed Nour Kotb, MD

Lecturer & Consultant Of Oculoplasty, Zagazig Faculty of Medicine

Fellow of ICO, UK

Fellow of Sankara Nethralaya, India

- In general, the majority of malignant tumors affecting the eyelids and periorcular area are slowly enlarging, **destructive** lesions that **destroy** eyelid anatomy.
- It is extremely difficult to make the correct diagnosis of an eyelid lesion without **a biopsy**.
- Some malignant lesions may appear relatively innocuous , Conversely some benign lesions may appear extremely sinister.
- Early diagnosis can significantly reduce morbidity and mortality associated with malignant eyelid tumors.

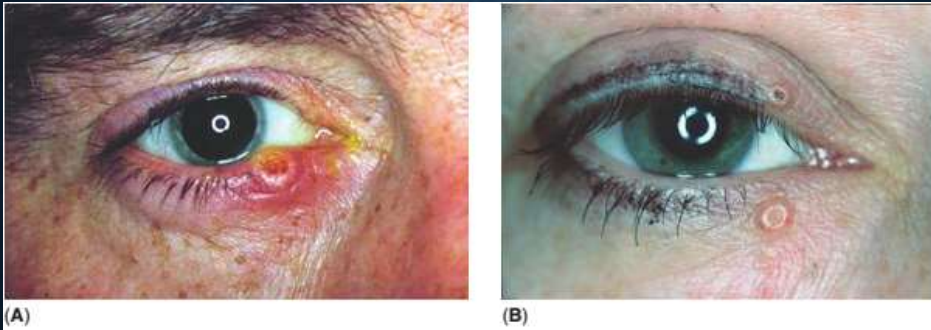
SIGNS OF MALIGNANCY

History:

- Progressive growth which may be slow or rapid.
- Irritation, intermittent drainage, bleeding, crusting, and changes in pigmentation.
- Malignant lesions frequently are not painful or tender.

Examination:

- **Irregular** shape, **rolled "pearly" borders**, and associated induration.
- **Telangiectasias**, or fine new vessels,
- Alterations of normal architecture including obliteration of epithelial folds and lines,
- **Loss of lashes**.
- **Absence of meibomian gland orifices** is particularly characteristic;
- Malignant lesions often have a "hardened" feel on palpation when compared to the surrounding skin.
- **Erosion** is common and **ulceration** leading to hemorrhage, exudation, and crust formation.
- **A new enlarging pigmented** lesion.
- **A scirrhous retracted** area.



(A) A lower eyelid lesion referred to as a suspected molluscum contagiosum. A incisional biopsy proved this lesion to be a squamous cell carcinoma.

(B) Typical molluscum contagiosum lesions of the eyelid.



(A) An early lower eyelid margin basal cell carcinoma demonstrating a typical localized loss of eyelashes, and pearly telangiectatic changes.

Another important warning signs:

- **Fixation to deeper tissues or bone.** This often suggests infiltration.
- **Regional lymphadenopathy** can be seen with infectious lesions, but should also raise suspicion for squamous cell, and especially sebaceous cell carcinoma.
- **Restriction of ocular motility** and **proptosis** suggest deep orbital extension and requires evaluated by means of CT or MRI scanning.
- If malignancy is suspected, except for basal cell carcinoma, **systemic evaluation for metastases** should be undertaken.

Features of benign lesions:

- Slow growth over months to years
- Well-demarcated borders
- Intact epithelium
- Even pigmentation when present



Rolled pearly borders
suggestive of Malignancy



Telangiectasia are fine dilated
b.v. seen within a lesion



Loss of lashes and telangiectasia

All eyelid lesions that are removed should be submitted for histopathological examination and the patient should be informed of the result.

It is not acceptable to reconstruct an eyelid or periocular tissue defect following the removal of a malignant tumor (except by simple direct closure) before first obtaining histological confirmation that the tumor margins are clear.

Classification of Malignant Eyelid Tumors

Epithelial

- Basal cell carcinoma
- Sebaceous gland carcinoma
- Squamous cell carcinoma
- Keratoacanthoma

Non-epithelial

- Merkel cell tumor
- Melanoma
- Kaposi's sarcoma
- Lymphoma—mycosis fungoides
- Metastatic tumors
- Angiosarcoma
- Microcystic adnexal carcinoma
- Primary mucinous carcinoma

Basal Cell Carcinoma, BCC

- It is a malignant tumor derived from cells of **the basal layer** of the epidermis. As these cells do **not produce keratin**, BCCs are not associated with hyperkeratosis in contrast to squamous cell carcinomas.
- Represents the most common malignant tumor of the eyelids, comprising **90%** of all malignant epithelial eyelid tumors. It is **40 times** more common than SCC.
- The etiology is linked to **excessive ultraviolet light exposure** in fair-skinned individuals. Over 99% of basal cell carcinomas occur in **Caucasians**.
- They are seen typically in **middle aged** and **elderly** adults, but are more frequently being seen in younger adults, and several cases have been reported in children without pre-existing genetic syndrome or a history of radiotherapy.
- While **metastases** are rare (0.028–0.55%), **local invasion** is common and can be very destructive.

Predisposing factors

- 1- Ionizing radiation.
- 2- Arsenic exposure.
- 3- Pre-existing scars.
- 4- Having had one BCC is risk for the development of additional lesions.

- **Basal cell nevus syndrome** (Gorlin-Goltz syndrome) or (nevoid BCC syndrome) is an AD disorder associated with multiple BCC affecting the face, trunk, and extremities with a high rate of recurrence.

*** In descending order of frequency,** BCCs involve the following locations:

- Lower eyelid (50–60%)
- Medial canthus (25–30%)
- Upper eyelid (15%)
- Lateral canthus (5%)

Clinical presentation:

- The typical presentation is of a **chronic, indurated, non-tender, raised, pearly, telangiectatic, well-circumscribed** lesion with an **elevated surround** and **depressed crater-like centre**.
- As the tumor grows in size a **central ulceration** may occur surrounded by a rolled border (also known as a “rodent ulcer”).

Clinical Varieties:

1 • Nodular :

the most common form and has the classic appearance of a pink or pearly papule or nodule with overlying telangiectatic vessels. may assume various clinical presentations such as papilloma (secondary to increased keratin production), a nevus (secondary to pigmentation), and a cyst (due to central tumor necrosis). The variety of clinical presentations of BCC accounts for the high incidence of misdiagnosis.



A typical lower eyelid nodulo-ulcerative BCC.

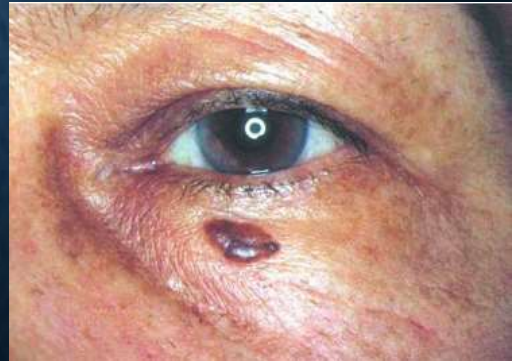
2•Ulcerative

3•Cystic

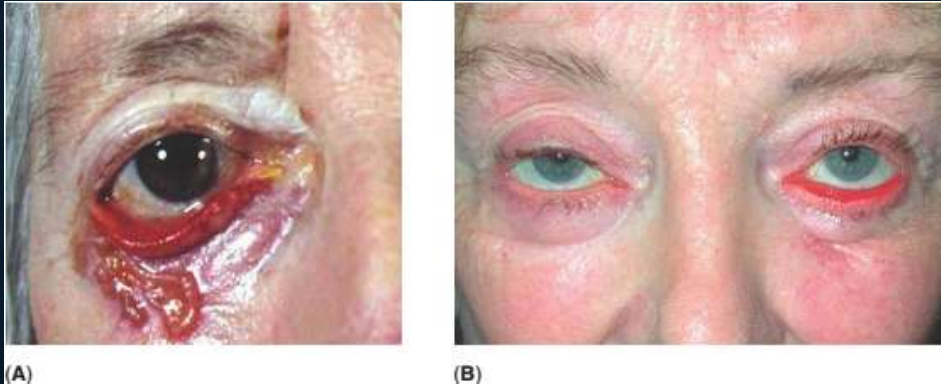
4•Pigmented with brown or black pigmentation. These lesions represent the most common pigmented malignancy on the eyelids, and may resemble malignant melanoma.

5•Morpheaform or sclerosing type appears as a flat, indurated yellow to pink plaque with ill-defined borders. It may simulate blepharitis or dermatitis.

This form of basal cell carcinoma is aggressive and can invade the dermis deeply. It characteristically occurs in the medial canthal region and can invade into the paranasal sinuses, lacrimal system, and orbit.



A pigmented lower lid BCC.



A lower lid ectropion secondary to a BCC adherent to the inferior orbital margin.

The most difficult BCCs to manage are as follows:

- A • Morpheaform BCCs.
- B • BCCs that are fixed to bone.
- C • Medial canthal BCCs.



(A)



(B)



(C)

D • BCCs with orbital invasion

E • Recurrent BCCs, especially following radiotherapy (E).

F • BCCs in patients with basal cell nevus syndrome (BCNS).



(F)



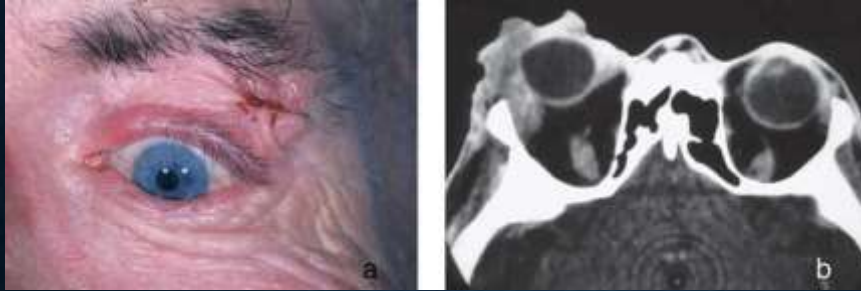
(D)



(E)

(F) (BCNS) with prosthetic nose showing facial disfigurement following multiple surgical procedures over the course of 40 y.

- Recurrent tumors tend to be more aggressive and infiltrative and show a lower rate of cure than with primary lesions
- Although BCCs “never” metastasize, approximately 130 cases of metastases have been described in the literature.

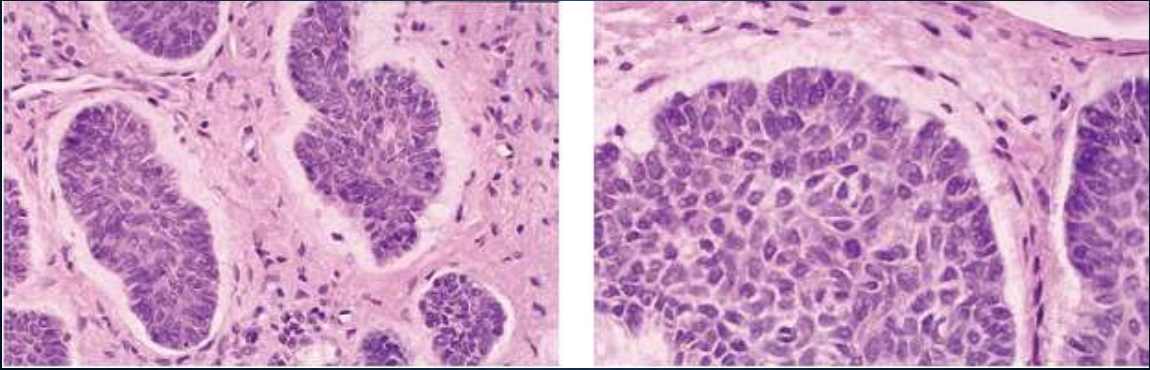


Basal cell carcinoma with extension into the anterior orbit.
 a. Lesion of the left brow;
 b. corresponding CT scan.

Histopathology:

- **Basophilic tumor cells** with hyperchromatic nuclei form irregular lobules.
- Along the periphery of the tumor lobules, the cells often are arranged radially with their long axes parallel to each other, creating so-called “**peripheral palisading**”.
- Stroma surrounding the tumor is often mucinous and artifactually shrinks away from the tumor islands during histological processing, creating thin clefts.
- **Clefts and mucinous matrix** help to distinguish poorly differentiated BCC from poorly differentiated squamous cell carcinoma.

Tumor lobules may have **central necrosis**, a **prominent adenoid pattern**, or strands of basaloid cells in a **dense fibrous stroma** (morphea or sclerosing pattern).



DIFFERENTIAL DIAGNOSIS

- Malignant melanoma,
- Sebaceous cell carcinoma,
- Squamous cell carcinoma,
- Actinic keratosis,
- Radiation dermatitis,
- Keratoacanthoma,
- Cutaneous horns,
- Dermoid and sebaceous cysts,
- Eccrine and Apocrine cysts,
- Papillomatous lesions,
- Seborrheic keratosis,
- Blepharitis, chalazion,
- Eczema, psoriasis,
- Seborrheic dermatitis.

TREATMENT

1- Surgical Excision: The goal is the complete removal of tumor cells with preservation of uninvolved eyelid and periorbital tissues. If excision is done without histologic control, a **4 mm margin** will give adequate results in most cases.

- Even with residual tumor at the cut margin the recurrence rate is only 38%.

** Mohs' micrographic surgery with frozen section control has proven to yield the highest cure rate with the most effective preservation of normal tissue.

Recurrence rates with this technique are reported at 0.5–1%.

2- Radiation therapy in doses of 4,000–6,500 cGy has been reported to yield a 5-year tumor free control rate of 91%.

it may be more appropriate for the treatment of advanced invasive or recurrent tumors.

3- Cryotherapy:

often used to treat non-periorbital lesions but when used on the eyelid → notching of the lid margin, malpositions of the eyelid, symblepharon formation with fornix foreshortening, and pigmentary changes of the eyelid skin may be seen as complications.

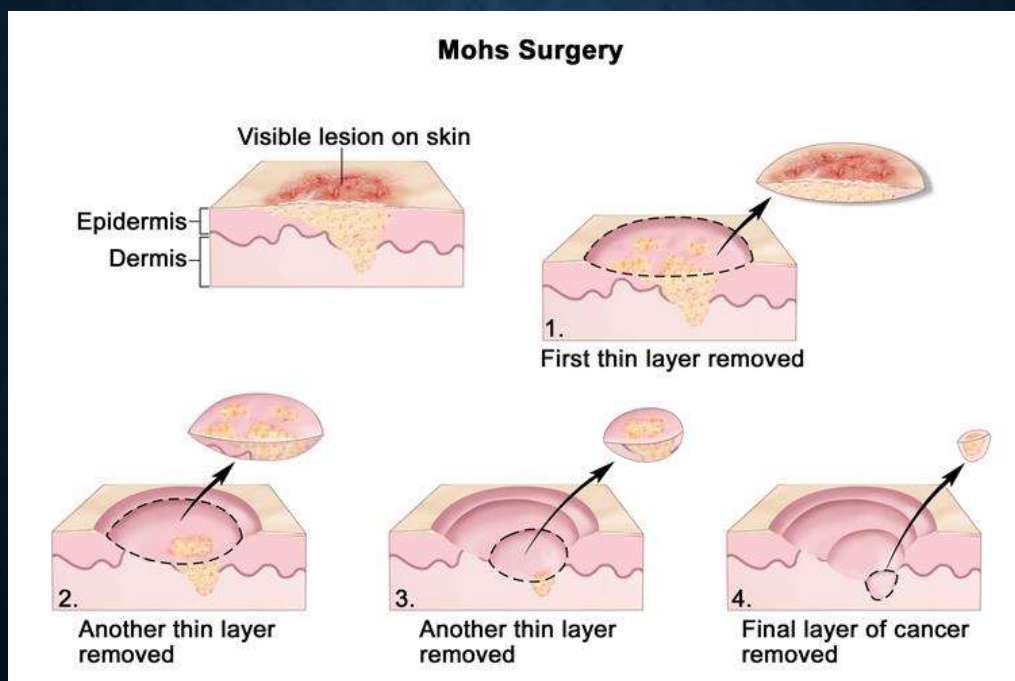
* It is also associated with a higher recurrence rate.

4- Topical 5% neomycin cream: Its use reported also Tumor regression.

Mohs surgery: developed in **1938** by **Frederic Mohs**, is microscopically controlled **surgery** to remove a visible lesion on the skin in several steps.

It is a refinement of frozen-section control of tumor margins that **allows a 3D** assessment of tumor margins rather than the 2D analysis provided by routine frozen section. In this technique, the surgical removal of the tumor is performed by a **dermatological surgeon** with specialized training in tumor excision and mapping of margins.

First, a thin layer of cancerous tissue is removed. Then, a **second** thin layer of tissue is removed and viewed under a microscope to check for cancer cells. More layers are removed one at a time until the tissue viewed under a microscope shows no remaining cancer. This type of surgery is used to remove as little normal tissue as possible.



Squamous Cell Carcinoma

- Most commonly affects elderly, fairskinned individuals.
- It arises from **keratinocytes** of the epidermis.
- SCC tends to arise in areas of skin damaged by chronic sun exposure, ionizing radiation, carcinogens (e.g., arsenic), (PUVA) therapy for psoriasis, and the human papilloma virus.
- **Intrinsic factors** include xeroderma pigmentosum, oculocutaneous albinism, and immunodeficiency. Chronic skin dermatoses, inflammation, ulceration, and contracted scars → the most common intrinsic factor leading to this tumor in **black** patients.
- Lymphatic spread and perineural invasion are possible.

CLINICAL PRESENTATION

- The most common site is the **lower lid**, like BCC.
- Initial changes look like a **chronic eczema-like** lesion. The tumor often originates in an actinic keratosis, but tends to be thicker, larger and have a more heaped-up keratinization.
- These lesions have a tendency to **ulcerate**, and growth may be **endophytic** or more **exophytic** with raised papillary verrucous borders.
- Occasionally it can take on the appearance of a **cutaneous horn**.
- Long-standing lesions become **friable** and **bleed easily**.
- **Necrosis** may follow with superimposed bacterial infection.
- **Orbital extension** and Palpable **regional LN** has been frequently reported.



SCC



TREATMENT

- Diagnosis requires a **biopsy** for histologic confirmation.
- **The goal** is complete removal of tumor cells with eyelid reconstruction.
- **Mohs' micrographic surgery** provides the highest cure rate.

- **Radiation therapy** is generally not recommended as the initial treatment, but it may be useful in the treatment of advanced or deeply invasive recurrent lesions.

- **Cryotherapy** is often used to treat non-periorbital lesions. when applied to the eyelids, complications such as marginal notching, ectropion, symblepharon formation, fornix foreshortening, and depigmentation of eyelid skin.
Cryotherapy is also associated with a higher recurrence rate.
- **Orbital exenteration** for deep orbital invasion.

Sebaceous Cell Carcinoma

- A **highly malignant** neoplasm that arises from sebaceous glands, meibomian glands, or glands of Zeis.
- Aggressive tumor with a **high recurrence rate**.
- propensity of SC to mimic benign conditions has been termed a “masquerade syndrome”
- It is the **third most common** eyelid malignancy, accounting for **1% to 5.5%** of all eyelid cancers.
- It affects **all races** and more common in **women** than in men.
- Usually presents in the **6th to 7th decades**, but cases in younger patients, even children, have been reported.
- A clear link between sebaceous gland carcinoma and **prior radiation therapy**, but **no** association with exposure to **UV light**

Clinical Presentation

- In contrast to periocular BCC and SCC, the most common location for periocular SC is **the UL**, followed by the LL and caruncle.
- Patients usually complain of an eyelid mass, irritation, redness, or discharge. Less frequent presentations: ulceration and a pedunculated mass.
- The majority of cases present as a **painless yellow solitary nodule** or **diffuse erythema and thickening** of the eyelid margin (often associated with intraepithelial invasion (**pagetoid spread**)).
- Clinical high suspicion for SC are a **recurrent chalazion**, chronic unilateral blepharitis, and conjunctivitis and Madarosis.
- * **Local Spread** into the globe, the orbit, the sinuses, or the brain.
- * **Metastases** via **local lymphatics** to preauricular and submandibular LN.
- * **Hemotogenous spread** to distant sites.
- * Once metastases develop, the five-year survival rate is **only 30% to 50%**.



TREATMENT

*Any suspicious eyelid lesion or one that does not respond to medical therapy or recurs in the same location deserves a biopsy.

((A full-thickness eyelid biopsy or a punch biopsy of full-thickness tarsus))

* **Wide surgical excision with microscopic monitoring** of the margins is the treatment of choice.

* **Mohs' micrographic surgical excision** may be used, but it may **not** be as successful as in BCC or SCC due to the possibility of **multicentric skip** lesions and pagetoid spread.

* If the tumor is very large or recurrent with spread to the bulbar conjunctiva or to orbital tissues, a **subtotal or complete exenteration** may be necessary.

* If spread to regional LN, the patient need **LN or radical neck dissection**.

* **Radiation therapy** can be considered as an adjunct to local surgery. But irradiation alone is inadequate, and recurrence usually occurs within three years.

LYMPHOMA

- **B-cell lymphoma** is a systemic malignancy of lymphoid tissue.
- Lymphoma more typically involves the **orbit**, and eyelid involvement is usually due to forward extension of the tumor.
- Most orbital lymphomas are of the **non-Hodgkin's variety**, and most are low-grade proliferations of small, monoclonal lymphocytes.
- In many cases lymphoma may be confined to the periorbital region without systemic involvement. In some instances **both orbits** may be involved.
- The majority of these primary orbital adnexal lymphomas are believed to be **mucosal-associated lymphoid tissue (MALT)—type** tumors arising from extranodal mucosal tissues, and they may be associated with **(AIDS)**.

- About **5%** of patients with systemic lymphoma develop orbital or adnexal metastases.
- Seen primarily **in patients 50 to 70 years of age**. Individuals who initially have well-differentiated localized disease have a **15%** chance of developing systemic disease; whereas **50% to 60%** of those with less well differentiated disease may manifest systemically within five years.

Therefore, patients who present with isolated orbital disease should be re-examined at periodic intervals for systemic involvement.

Clinical Presentation:

- Onset is **gradual** and mostly **painless**.
- Lid involvement presents as swelling, mechanical ptosis, and a subcutaneous palpable mass.
- A **salmon-colored** lesion may extend beneath the conjunctiva.
- Orbital involvement: proptosis and often a downward displacement of the globe → lesions have a predilection for the superior orbit.
- Limitation of ocular motility and decreased vision are late signs.

- In **40%** of patients with orbital lymphoma there is evidence of systemic involvement at presentation.

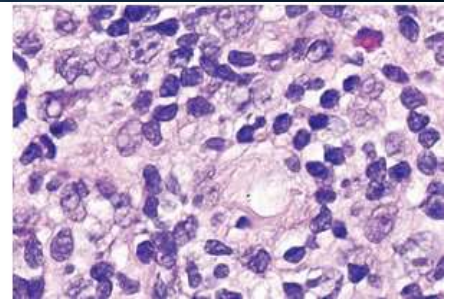
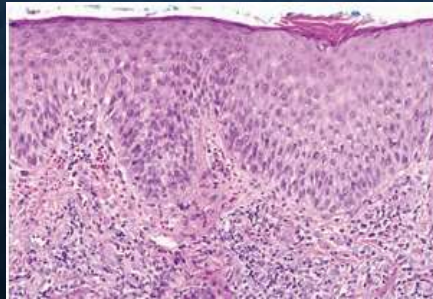


Histopathology

- Both **B-cell** and **T-cell lymphomas** may occur as primary cutaneous processes or spread secondarily to the eye, and the histopathology reflects the specific entity.
- The lymphomatous infiltrate in systemic lymphomas is typically in the dermis and subcutis, while primary cutaneous lymphomas may have both dermal and epidermal components.

Differential Diagnosis

reactive lymphoid hyperplasia, plasmacytoma, lacrimal gland tumors, and chloroma.



TREATMENT

Biopsy is recommended to establish a diagnosis.

Once the diagnosis is confirmed, a general physical examination, -

- CBC,
- Bone marrow biopsy,
- Liver and spleen scan,
- Bone scan,
- Chest X ray,
- Serum immuno-protein electrophoresis,
- CT scanning of the thorax and abdomen, for the detection of mediastinal and retro peritoneal lymph node involvement

Treatment Varieties:

1- **Observation without treatment** for low-grade tumors with only local orbital involvement may be appropriate.

2- **Radiotherapy** at 2500 to 3000 cGy reported to achieve excellent control for isolated orbital lymphoma.

3- **Chemotherapy** for less well-differentiated tumors & systemic disease.

** For individuals with low-grade tumors that are confined to the eyelid and orbit, prognosis is excellent even without treatment. Overall, the five-year survival rate is **93%**.

Malignant Melanoma

- Cutaneous MM is an invasive proliferation of **malignant melanocytes**, and accounts for **1%** of all eyelid malignancies.

- The incidence increases with age.

- Classified into 4 types:

1- lentigo maligna melanoma (5%),

2- superficial spreading melanoma (70%),

3- nodular melanoma(16%),

4- acral lentiginous melanoma(9%).

- **Nodular melanoma** and **lentigo maligna melanomas** are the most common types affecting the eyelids.

In all types, initially, a noninvasive horizontal growth phase occurs, followed by an invasive vertical growth phase.

**Changes in outline and color are features that tend to distinguish melanoma from benign pigmented lesions.

Risk factors for the development of malignant melanoma:

- congenital and dysplastic nevi,
- changing cutaneous moles,
- excessive sun exposure and sun sensitivity,
- family history,
- age greater than 20 years,
- Caucasian race.
- Patients with the dysplastic nevus syndrome.

Prognosis:

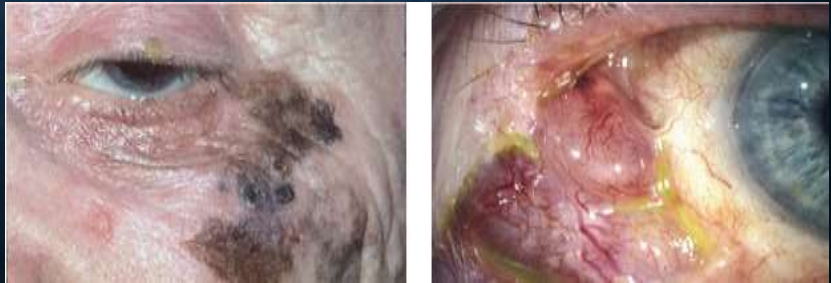
- Metastatic potential are linked to the **depth** of invasion and **thickness** of the tumor.
- Lesions **less than 0.75 mm** have a five-year survival rate of **98%**, while those **greater than 4 mm** have a **less than 50%** survival rate.
- MM involving the eyelid margin has a **poorer prognosis**.

Clinical Presentation:

- **Superficial spreading melanoma** presents as a small, pigmented lesion with mild elevation and irregular borders.
- **Nodular melanoma** may present as a markedly pigmented or amelanotic nodule that rapidly increases in size with associated ulceration and bleeding.

- Suspicion of MM:

- 1* Any lesion that develops hues of white, gray, blue, black, red, or pink
- 2* Variation in brown pigment especially if in an asymmetric fashion
- 3* Papule or nodule formation of a previously flat pigmented lesion, bleeding, ulceration, or loss of fine skin lines.



Differential Diagnosis:

Nonmalignant pigmented nevi, pigmented basal cell carcinoma, pigmented seborrheic keratosis, dysplastic nevi, Kaposi's sarcoma and hemangioma.

TREATMENT

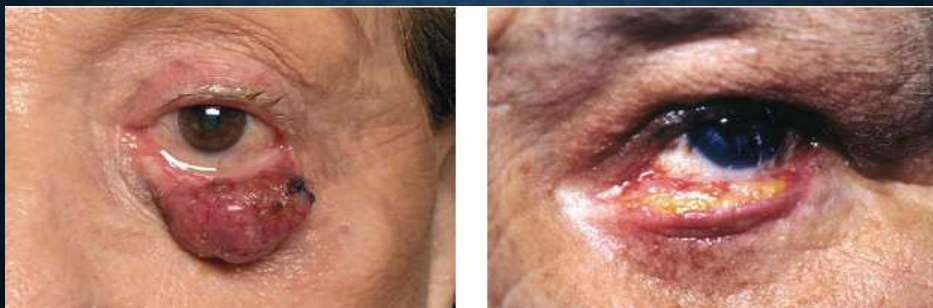
- * **Surgical excision with wide margins of 1 cm** confirmed by histologic monitoring is the best option.
- Mohs' micrographic surgery may be helpful.
- * **Regional lymph node dissection** should be performed for tumors greater than 1.5 mm depth and/or for tumors that show evidence of vascular or lymphatic spread.
- * **A metastatic evaluation** also is recommended for patients diagnosed with any malignant melanoma.

Merkel Cell Tumor

- It is a rare **aggressive** neuroendocrine neoplasm composed of **Merkel cells**, of neural crest origin.
- Merkel cell carcinoma accounts for **less than 1%** of cutaneous malignancies
- Role for **chronic sun exposure** has been proposed.
- It occurs most commonly in **very elderly Caucasian** patients
- Equal incidence among men and women.
- The tumor is seen on the head and neck in 50% of cases.
- **Metastases** occur initially to the regional lymph nodes.
- Overall 2-year mortality rate is **30% to 50%**.

Clinical Presentation:

- Presents as a **solitary, vascularized, nontender red or violaceous dome-shaped nodule** or **firm plaque**.
- The epidermal surface is usually shiny, with fine telangiectasia.
- Usually rapidly growing, hard and **painless**.
- The upper eyelid is the most common site and may lead to mechanical ptosis.



TREATMENT

1- Wide surgical excision with at least margins of 3 mm.

Mohs microsurgery with histologic control of margins is preferred, but this tumor may be discontiguous histologically making Mohs surgery less effective than for many other tumors.

2- Selective lymphadenectomy with sentinel node biopsy may be useful.

3- Prophylactic node dissection combined with local excision and adjuvant radiotherapy is reported to improve survival rates.

4- Chemotherapy remains unclear but so far it has not been shown to improve survival.

Local recurrence is expected in 30% to 40% of cases, sometimes with invasion of adjacent tissues.

Eye lid Metastatic Tumors

- Account for **less than 1%** of lid tumors.

- **primary sites** are breast, cutaneous melanoma, lung, colon, and prostate malignancies.

- **Females** are affected more than males in a ratio of **4:1** ((reflecting the fact that breast carcinoma represents more than a third of eyelid metastases)).

- In rare cases an eyelid tumor can be the presenting sign of an occult carcinoma.

CLINICAL PRESENTATION

1-**First pattern** (most common): diffuse, painless, noninflammatory, full-thickness, often leathery **induration** of the lid that may cause ptosis, lid lag, or epiphora.

These lesions usually represent scirrhous or desmoplastic metastases from breast carcinoma.

2- **The second pattern**: uninflamed, nontender subcutaneous **nodule**.

3- **The third pattern**: solitary **ulcerated** lesion.



TREATMENT:

* **Biopsy** is required for diagnosis.

* **Debulking** of large symptomatic tumors may be necessary to restore eyelid function with **systemic treatment for underlying primary disease**.

* If the metastatic eyelid lesion does not respond to chemotherapy, 3000 to 5000 cGy of **external beam irradiation** will often reduce the size of the tumor.

