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Case Study

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A CASE REPORT ON BASAL CELL CARCINOMA OVER THE LATERAL BORDER OF THE EYE

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ABSRACT

Basal cell carcinoma (BCC) is the most common skin cancer, mainly affecting fair-skinned individuals and commonly occurring on sun-exposed areas of the head and neck. About 10% of cases involve the eyelids, most often the lower eyelid. Risk factors include prolonged UV exposure, fair skin, genetic syndromes, immunosuppression, radiation exposure, and tumor suppressor gene mutations. BCC usually presents as a slow-growing, painless lesion, leading to delayed diagnosis. We report a case of BCC at the lateral border of the eye treated with wide local excision and reconstruction using a mastoid flap. Histopathology confirmed complete tumor removal, and recovery was uneventful. Although BCC rarely metastasizes, eyelid involvement requires careful management due to functional and cosmetic concerns. This report highlights the clinical presentation, management, and surgical reconstruction of eyelid BCC, along with a review of current concepts in pathogenesis and treatment strategies.

KEYWORDS: BCC (Basel cell carcinoma), canthus, tumor, Hedgehog pathway inhibitors (HPI).

INTRODUCTION

Basal cell carcinoma (BCC) is the most common type of skin cancer worldwide. It is the most prevalent cancer type among white-skinned populations (industrialized Western societies).[1] or Caucasians but rare among dark skinned peoples. The BCC usually a slowly enlarging tumour and symptoms are rare. 90% of cases occur in head and neck and about 10% of these involve the eyelids. Accounting for 90% of all cases, most frequently arises from lower eyelid followed by medial canthus, upper eyelid and lateral canthus.[2] In people with outdoor occupations like miners, quarry men, railway engine drivers and firemen, the frequency of BCC is high.[1] Distant metastasis is rare. Increased risk of suffering from BCC is associated with exposure to ultraviolet (UV)-B, hereditary diseases [e.g., Gorlin-Goltz syndrome and Xeroderma pigmentosum (XP)], ionizing radiation and long-term immunosuppression, particularly to tumor suppressor genes such as TP53 and PTCH1, contributes significantly to BCC pathogenesis. fair skin phenotype and among others.[3,4] The average age of the patients is over 40- 60 years, which is in accordance with the rapidly increasing incidence in an aging society.[1,4] BCC develops as epithelial-basaloid neoplasia and is accompanied by mostly infiltrating and destructive growth.[4] Reviewing the patient's history, checking symptoms, and performing a careful examination (including inspection, palpation, and slit-lamp examination) usually help in making a preliminary diagnosis. However, basal cell carcinoma has many clinical subtypes, and the diagnosis must be confirmed by histopathological examination to identify the exact type.[5] Basal cell carcinoma (BCC) subtypes such as nodular, infiltrative, and morpheaform are commonly seen around the eye. These subtypes differ in how they grow and in their risk of coming back after treatment. Morpheaform and infiltrative BCC are especially difficult to treat because their borders are unclear and they grow deep into the tissues, often requiring more advanced surgical methods.[3] However, Basal cell carcinomas (BCCs) are often overlooked because they grow slowly and usually do not cause pain. Patients

typically seek medical attention only when the tumor becomes large, starts bleeding, gets repeatedly infected, or affects nearby structures. In eyelid BCCs, this may lead to symptoms such as excessive tearing, restricted eye movement, or displacement of the eyeball. Although most BCCs can be successfully treated with local surgical removal, recurrence occurs in up to 20% of eyelid cases. Recurrent eyelid BCCs Generally has a worse prognosis than primary tumors. In addition, advanced cases such as those involving invasion into the orbit or brain, or spread to distant sites are difficult to manage and usually require care from multiple medical specialties. Therefore, this review summarizes the understanding of BCC pathogenesis, clinical features, and treatment options.[4]

VARIOUS SUB TYPES OF BCCS[5]

The main histopathological types of basal cell carcinoma (BCC) are nodular, superficial, and sclerosing (morpheaform).

Nodular BCC is the most common type and may develop a central ulcer as it grows, known as a rodent ulcer.

Superficial BCC consists of small groups of cancer cells located in the upper layer of the skin and connected to the epidermis. These tumors are surrounded by supportive tissue and inflammatory cells and may also contain nodular, micronodular, or infiltrative areas.

Sclerosing (morpheaform) BCC is harder to see and distinguish from normal skin and often spreads deeper than it appears. Because it grows aggressively and has poorly defined borders, it is difficult to remove completely and has a higher chance of recurrence compared to nodular BCC.[5]

Table 1: Histological subtypes of periocular BCC: Clinical behavior and recurrence risk

Subtype	Estimated Frequency	Growth Pattern	Aggressiveness	Recurrence Risk
Nodular	60–70%	Well-demarcated nests	Low	Low
Infiltrative	10–15%	Strands infiltrating stroma	High	Moderate to High
Morpheaform	5–10%	Thin cords in dense stroma	High	High
Micronodular	<5%	Small deep tumor islands	High	High
Superficial	<5% (periocular)	Horizontal, epidermal nests	Low	Moderate
Pigmented	Variable (by race)	Pigmented basaloid nests	Variable	Variable

MOLECULAR PATHOGENESIS[4]

Multi-step UV-induced carcinogenesis model[4]

Photocarcinogenesis is the process by which skin cancer develops due to long-term exposure to light from the sun. It happens in several stages and involves activation of cancer-causing genes [TP53 and PTCH1] and loss of genes that normally prevent cancer. This process depends on how much light a person is exposed to, how long the exposure lasts, and the type of light.Sunlight belongs to the non-ionizing electromagnetic spectrum and includes ultraviolet (UV) light, visible light and infrared radiation**.** Among these, UV radiation is the main cause of skin cancers such as basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)**.**

BCCs contain a very high number of UV-induced gene mutations, which damage important cell signaling pathways. Studies using modern genetic techniques have shown that about 75% of mutations in BCC are caused by UV exposure**.** DNA absorbs UV radiation, especially UVB rays**,** which directly damage DNA. This damage creates abnormal structures in DNA called photoproducts**,** which distort the DNA and block normal cell processes like replication and transcription.

If this DNA damage is not repaired before the cell divides, it can cause permanent mutations, especially changes from C to T in the DNA sequence. Normally, the body repairs this damage through a system called nucleotide excision repair**.** When this repair system does not work properly, as in a rare genetic condition called xeroderma pigmentosum (XP)**,** UV damage builds up quickly. As a result, children with XP develop BCC and other UV-related skin cancers at a very young age, often around 8 years old.[4]

GENETIC PREDISPOSITION[4]

Most basal cell carcinomas (BCCs) do not develop because of an inherited genetic condition. However, several important genes are involved in their development. These include genes from the Sonic Hedgehog signaling pathway**,** such as PTCH1 (affected in about 73% of cases) and SMO (about 20%), as well as the TP53 tumor suppressor gene (about 61%) and genes from the RAS family. Around 85% of BCCs have activating mutations in the Hedgehog signaling pathway**,** which normally controls cell growth during early development. When this pathway is abnormally activated, it becomes the main driver of cancer formation in BCC. In addition to this, mutations are also found in other important cell signaling pathways involved in cancer development. One such pathway is the Hippo-YAP pathway**,** which helps control tissue growth and programmed cell death (apoptosis). Genetic studies using next-generation sequencing (NGS) have found mutations in Hippo-YAP pathway genes such as **LATS1 (16%)**, **LATS2 (12%)**, and **PTPN14 (23%)**. Other genes commonly mutated in BCC include **MYCN, PPP6C, STK19, RB1, FBXW7, and ERBB2**, all of which

contribute to abnormal cell growth and cancer development.

EPIGENETIC CHANGES[4]

Epigenetics refers to changes in gene activity that can be passed on to cells without changing the DNA sequence itself**.** These changes mainly include DNA methylation**,** histone modification**, and** regulation by microRNAs (miRNAs)**.**

DNA methylation is an important way the body controls whether genes are turned on or off. Some studies found abnormal methylation in genes related to BCC. For example, the **PTCH** gene promoter was found to be overly methylated in a few cases, suggesting it may play only a small role in BCC development. Other studies found reduced methylation in genes such as **FHIT** and **MYCL2**, especially in more aggressive or metastatic BCCs.

Histone modifications, especially methylation and acetylation, also affect gene expression. The enzyme **EZH2**, which adds methyl groups to histones, is increased in aggressive BCCs. In contrast, certain histone markers (**H3K27me3 and 5hmC**) are more common in less aggressive BCCs. These differences may help distinguish BCC from non-cancerous skin conditions.

MicroRNAs (miRNAs) are small molecules that control gene activity by blocking or reducing protein production. Several miRNAs are found at higher levels in BCC, such as **miR-223-3p** and **miR-197-3p**. **miR-203**, which is normally active in the epidermis, helps control cell growth by blocking the **c-JUN pathway**. This miRNA is found at lower levels in BCC, and research suggests it may have potential as a future treatment target.

SELECTED THERAPY OPTIONS FOR BCC-POSSIBILITIES AND LIMITATIONS

There are several treatment options available for basal cell carcinoma (BCC). The choice of treatment depends on how large the tumor is, whether it has come back, the need to preserve normal tissue, cosmetic concerns, and the patient's preference. The main goal of BCC treatment is to completely remove the tumor while maintaining good function and appearance of the affected area.[5]

1) SURGERY[5]

- The most common first-line treatment for periocular basal cell carcinoma (BCC) **is** surgical removal of the tumor**.** This can be done in two main ways.

(1) wide surgical excision followed by laboratory examination of the margins, or

(2) Mohs micrographic surgery**,** which checks the tumor margins during the operation.

- Complete removal of the tumor with clear margins (R0 excision), confirmed by histopathological examination, is still the gold standard treatment. Choosing a safe surgical margin around the eye is difficult because even a small amount of healthy tissue is important for proper function and appearance after reconstruction.
- For this reason, intraoperative margin control is used to check the tumor borders before reconstruction. Mohs surgery is the least invasive surgical option and involves removing the tumor in thin layers. Each layer is immediately examined under a microscope to see if cancer cells are still present. This process is repeated until no tumor remains.
- Mohs surgery provides very high cure rates—about 96–98% for primary BCC and 90–94% for recurrent BCC. Although it is time-consuming and costly, it is especially useful for tumors in cosmetically important areas such as the periocular region, and for morpheaform, infiltrative, or recurrent BCCs**.**
- Histopathological examination is essential to confirm the diagnosis, check whether the tumor was completely removed, and identify aggressive subtypes. This information helps guide follow-up care and predict prognosis.
- After surgery, the yearly recurrence rate is about 1–5%**.** However, large, recurrent, infiltrative tumors**,** tumors involving the orbit or brain**, or** metastatic BCCs often require other treatments. These may include **radiation therapy, chemotherapy, targeted therapy, or a combination of non-surgical treatments.**[5]

2) OCULOPLASTIC RECONSTRUCTION[4]

After complete tumor removal with clear margins (pR0 resection), patients may need different oculoplastic reconstruction methods. The choice of reconstruction depends on the size and location of the eyelid defect**,** whether the eyelid margin is involved, the age of the patient**,** the amount of available tissue (such as extra skin), the patient's preference**,** and especially the surgeon's experience**.** Because of this, oculoplastic surgeons must be familiar with many reconstruction techniques to properly restore the eyelid's structure.

The eyelid has two layers: the anterior lamella (skin and muscle) and the posterior lamella (tarsus and conjunctiva). When the defect involves the full thickness of the eyelid, both layers must be reconstructed**.**

A general rule in eyelid reconstruction is that only one flap should be used to repair the anterior lamella, and only one free graft should be used for the posterior lamella. If a free graft is used for the posterior layer, the anterior layer must be reconstructed with a flap, not another graft. Graft tissue can be taken from the same eyelid, the opposite eyelid, other body sites**,** or sometimes artificial support material**.**

Small full-thickness eyelid defects (≤25%) can usually be closed directly by stitching the tarsus and skin in two layers. A horizontal mattress stitch is used at the eyelid margin to help proper healing and prevent notching. Defects involving 25–50% of the eyelid width can be repaired by releasing the outer corner of the eyelid (lateral canthotomy and cantholysis) and pulling the

eyelid toward the center. A periosteal flap from the outer orbital rim may be added to strengthen the posterior layer in larger defects.

Medium-sized defects (about 33–66%, up to 75%) of the upper or lower eyelid can be repaired using a Tenzel semicircular rotation flap**,** which reconstructs the anterior lamella. Large defects**,** including those affecting up to the entire lower eyelid**,** may require more complex procedures such as a Hughes tarsoconjunctival flap**,** a midface lift**,** or free grafts to rebuild one or both eyelid layers.

TENZEL SEMICIRCULAR MYOCUTANEOUS ROTATION FLAP[4]

This technique is used to repair full-thickness defects of the upper or lower eyelid that are too large to close directly but involve less than 75% of the eyelid width**.** It is also an option for patients who do not want their eye to be temporarily closed for 3–4 weeks, as required with the Hughes procedure. The Tenzel flap is a semicircular skin-and-muscle flap. A curved incision is made at the outer corner of the eye, and the skin and orbicularis muscle are separated. A complete lateral cantholysis is performed to allow enough movement of the flap. The flap is then moved toward the center to cover the eyelid defect, and the defect is closed in the same way as a wedge resection. Finally, the outer wound created by the flap is closed with interrupted stitches.[4]

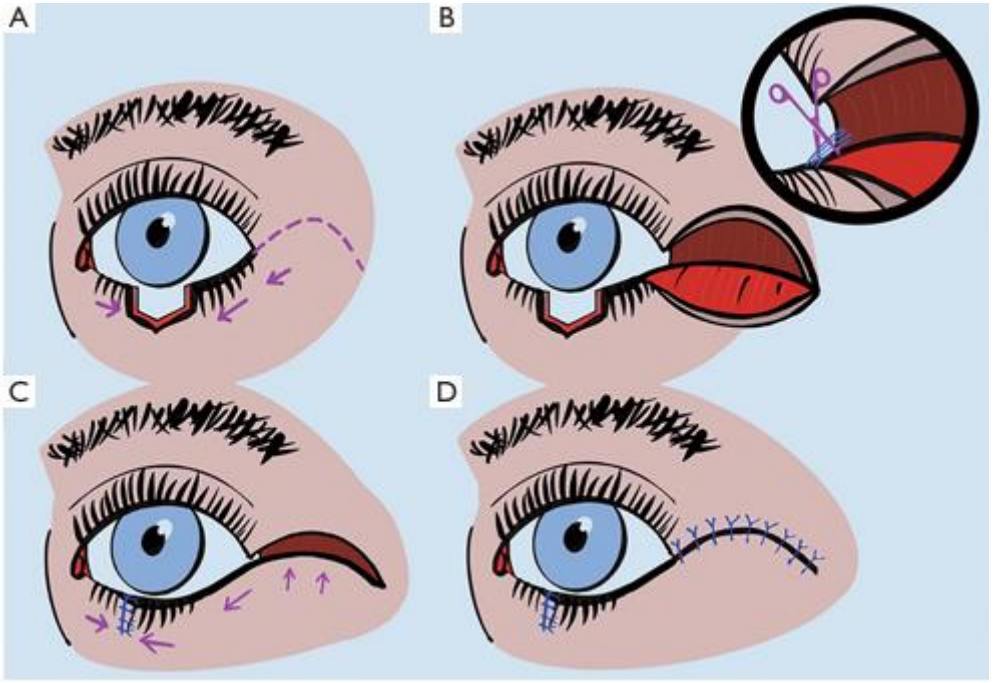


Figure 1: Schematic representation of an eyelid reconstruction with a Tenzel semicircular myocutaneous rotation flap. (A) The lower eyelid tumor has been removed, and the semicircular incision is marked on the skin; (B) after a lateral canthotomy with cantholysis and a skin incision proceeding superiorly past the lateral canthus in a semicircular shape, the myocutaneous flap is prepared; (C) the eyelid defect is now closed with a direct suture; (D) the lateral canthus is reconstructed, and the muscle skin flap is fixed in its new position by several sutures.[4]

2) CUTLER-BEARD BRIDGE FLAP[4]

The Cutler–Beard bridge flap is an important surgical method used to repair very large upper eyelid defects**,** usually involving more than 75% of the eyelid. Although the Tenzel flap can be used for some large defects, the Cutler–Beard technique is preferred for total or near-total upper eyelid loss**.**

This is a **two-stage procedure** in which tissue from the lower eyelid is used to rebuild the upper eyelid.

First stage: A rectangular, full-thickness flap is created from the lower eyelid by making a horizontal cut 4–5 mm below the lashes and a vertical cut down to the lower fornix. This flap, which includes skin, muscle, and conjunctiva, is then moved upward under a bridge of the lower eyelid and stitched into the upper eyelid defect.

Care is taken to keep part of the lower eyelid intact, including its blood supply, to reduce complications such as lower eyelid tissue death. The flap does not include tarsal plate**,** which can make the new eyelid margin unstable and may cause inward turning of the eyelid (entropion), especially in very large defects. To improve eyelid stability, **a** posterior lamellar graft may be added. This graft can come from donor sclera, ear cartilage, or the tarsus of the opposite eyelid**.**

Second stage

After 4–6 weeks, once healing has occurred, the flap is divided about 2 mm below the desired upper eyelid margin to allow for tissue shrinkage. The eyelid edge is then carefully reshaped and reattached. If needed, the conjunctiva is stitched to the skin at the new eyelid edge.

Although the reconstructed eyelid does not have eyelashes, this technique usually gives good function and appearance. This procedure should not be used if the affected eye is the patient's only orbetter-seeing eye, or if the patient does not want a second surgery.

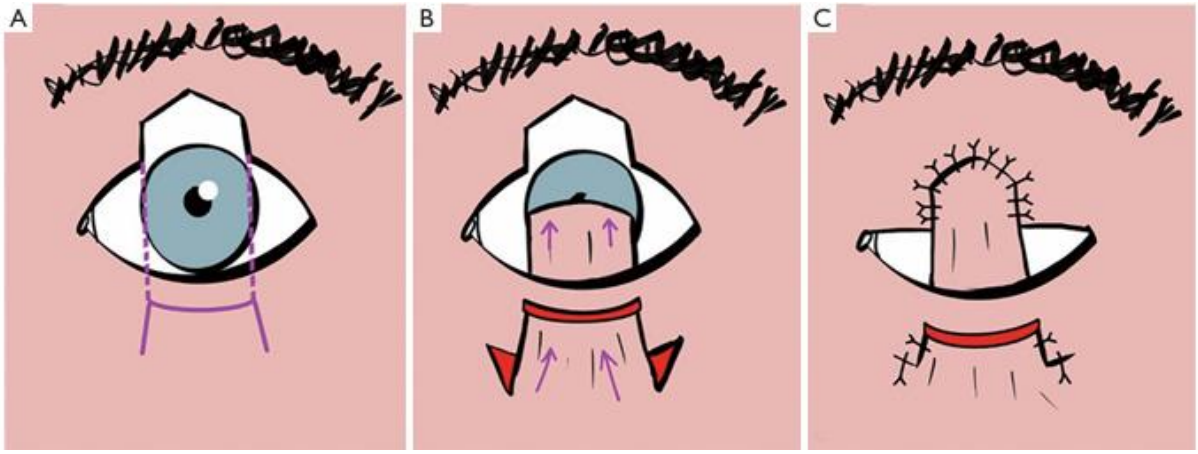


Figure 2: Diagram illustrating the basic steps of the Cutler-Beard bridge flap. (A) The extensive upper eyelid defect and the skin incision of a Cutler-Beard bridge flap; (B) a myocutaneous conjunctival sliding flap is prepared from the ipsilateral lower eyelid. Care should be taken to maintain an intact lower eyelid bridge with an intact eyelid edge and tarsus as well as intact medial and lateral palpebral arteries. This myocutaneous conjunctival advancement flap from the lower eyelid is then pulled cranially posterior to the lower eyelid bridge; (C) all three layers are sewn individually into the defect area of the upper eyelid. A posterior lamellar graft between the conjunctiva and orbicularis muscle may be attached to the levator aponeurosis to approximate the tarsus. The flap is cut and re-fixed to the marginal bridge of the lower eyelid in the correct layer 4 to 6 weeks later.

3) HUGHES FLAP[4]: The tarsoconjunctival advancement flap (Hughes flap) is a surgical technique that uses tissue from the upper eyelid (tarsus and conjunctiva) to reconstruct large, full-thickness defects of the lower eyelid, even when the entire lower eyelid is missing. It is especially useful for central lower eyelid defects when some tarsus remains on both sides. Because it gives very good cosmetic and functional results, it is a key procedure in oculoplastic surgery.

In the classic Hughes procedure, the incision starts at the grey line of the upper eyelid. The eyelid is split through the full height of the tarsus, keeping the levator and Müller's muscles attached to the tarsus. The flap is then sutured to the lower eyelid defect to rebuild the posterior layer, while the anterior layer is reconstructed using either a skin graft or a skin-muscle flap. The flap is usually divided 2–8 weeks later.

However, complications at the donor site such as entropion, trichiasis, eyelash damage, and upper eyelid retraction have been linked to this technique. Many surgeons now fully separate the levator and Müller's muscles from the tarsus, but this leaves the flap with only a thin conjunctival blood supply, which can increase the risk of flap necrosis.

To address this, we use a modified Hughes procedure. In this method.

- 4 mm of marginal tarsus is preserved
- The levator muscle is completely separated
- Most of Müller's muscle fibers are left attached to the upper edge of the tarsus

This modified technique is effective for repairing up to 100% of the lower eyelid width. Keeping Müller's muscle attached makes the flap thicker and stronger, which appears to reduce the risk of early flap separation without increasing the risk of upper eyelid retraction.

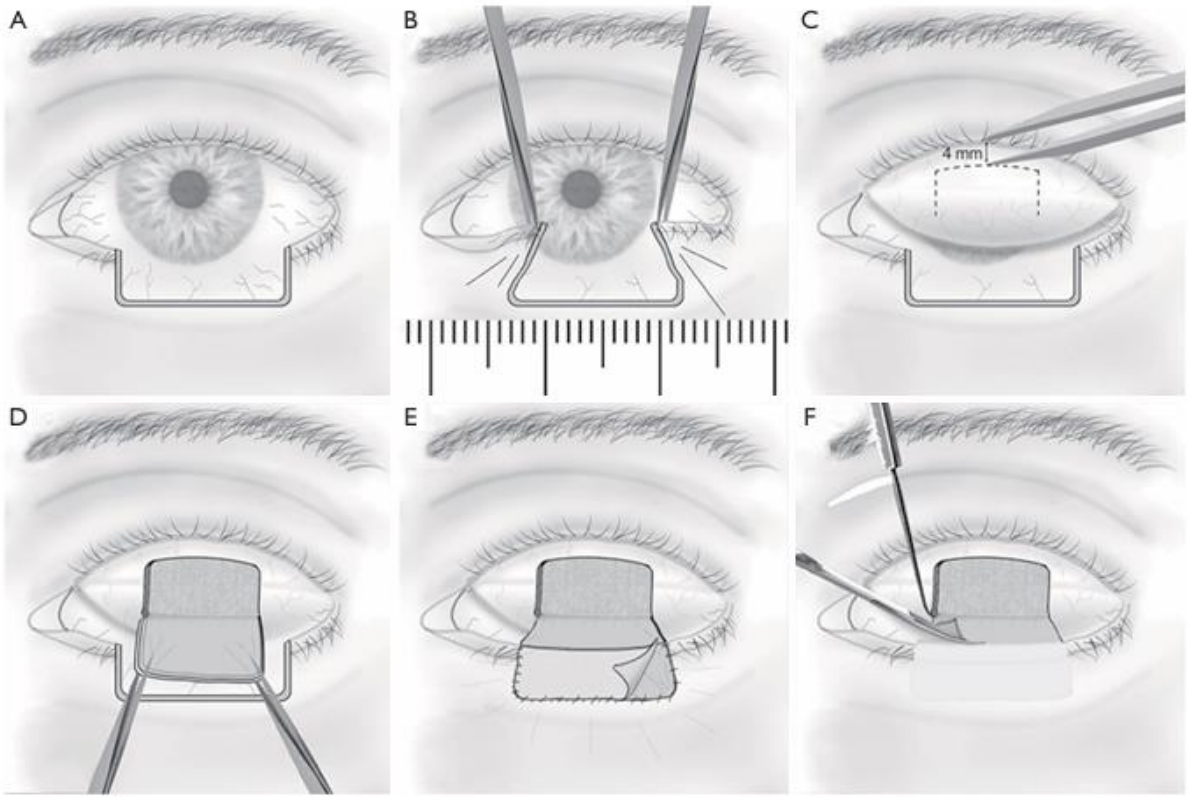


Figure 3: Schematic representation of the lower eyelid reconstruction with a modified Hughes procedure. (A) A full-thickness lower eyelid marginal defect >50% of the horizontal left eyelid width; (B) evaluation of the lateral and medial wound margins with two pairs of forceps to assess the horizontal width of the Hughes flap; (C) the upper eyelid is everted to present the conjunctiva, and 4 mm of the marginal tarsus is preserved; (D) tarsoconjunctival flap is prepared by separating the entire levator from the tarsus, but leaving most of Müller's muscle fibers attached to the superior tarsal margin; (E) the Hughes flap (posterior lamella) is sutured tarsus to tarsus into the defect. A free skin graft from the contralateral upper eyelid (anterior lamella) or a skin-muscle advancement flap is then fixed on the flap to reconstruct the anterior lamella of the lower eyelid; (F) the pedicle is cut 0.5 mm above the lower lid margin, after 6 weeks of Hughes flap fixation.[4]

4) ALTERNATIVE THERAPIES[4]

Surgical removal with histological margin control is the gold standard treatment for basal cell carcinoma (BCC). However, alternative treatments are also available and are included in the current German S2k guidelines and the European interdisciplinary guidelines.

These alternative treatments can be grouped into three main categories.

1. Radiation and systemic therapies

Radiation therapy and newer systemic treatments—such as Hedgehog pathway inhibitors, immune checkpoint inhibitors, and electrochemotherapy are used for advanced BCC. This includes tumors that are locally aggressive or metastatic, especially those that grow deeply and cannot be safely removed by surgery. Alternative treatments may also be chosen when a patient refuses surgery. In the updated guidelines, radiation therapy is no longer strictly a second-line option, allowing a multidisciplinary tumor board to choose the best treatment for each patient. For advanced BCC, either radiation or systemic therapy may be recommended after tumor board discussion.

2. Topical and minimally invasive therapies

Topical treatments can be used for small, low-risk BCCs (generally ≤2 mm thick). Tumors with a higher risk of recurrence are not suitable for these treatments. Risk factors include.

- Tumor size >6 mm near the eye
- Poorly defined borders
- Recurrent tumors
- Aggressive histological subtypes
- Tumors in previously irradiated skin
- Perineural invasion

For low-risk BCC, treatment options include.

- **Imiquimod**
- **5-fluorouracil (5-FU)**
- **Photodynamic therapy (5-ALA or MAL)**
- **Cryotherapy**
- **Laser therapy**
- **Curettage or shallow excision**
- Some topical treatments, such as ingenol mebutate and diclofenac, are not recommended because there is not enough scientific evidence supporting their effectiveness.

A major disadvantage of topical therapies is that complete tumor removal cannot be confirmed, unlike surgery. Therefore, especially in the peri-ocular (eye) area, surgery is usually recommended whenever possible.

3. Preventive (prophylactic) treatments

Some treatments may help reduce the risk of future BCCs.

- Nicotinamide can be used in patients with a history of BCC
- Retinoids are not effective in preventing BCC recurrence and may cause side effects such as headache, muscle pain, and serious birth defects
- There is no strong evidence that COX-2 inhibitors prevent BCC recurrence[4]

5) RADIATION THERAPY[4,5]

Radiation therapy (RT) is not used only after surgery. It may also be chosen as the primary treatment when a patient prefers it or when surgery is not possible. However, this decision should be made carefully because studies show that more than half of BCC patients develop acute or late side effects after RT. RT has shown relatively low recurrence rates**.**

- 7.4% for primary BCC
- 9.5% for recurrent BCC
- An overall 5-year recurrence rate of 15.8%

Recurrence after RT depends strongly on the histological subtype**:**

- **Nodular BCC:** 8.2% recurrence
- **Superficial BCC:** 26.1% recurrence
- **Sclerosing (morpheaform) BCC:** 27.7% recurrence

The sclerosing subtype is more aggressive and is associated with higher recurrence after RT. It is characterized by **high p53** and **low Bcl-2 expression**, and it occurs more often in patients who have received radiation. Choosing the best treatment for BCC depends on the clinical appearance**,** histological subtype, and tumor biology**.** If left untreated, BCC can grow and cause severe local destruction**,** affecting soft tissue, cartilage, and bone. In such advanced cases, surgery may no longer be possible**,** and radiation therapy may also be ineffective. Until recently, treatment options for locally advanced, infiltrative, or metastatic BCC were limited. Although metastatic BCC is very rare (about 0.003%–0.1%), it is usually linked to more aggressive tumor types and has a worse prognosis**.**

In jan 30, 2012, the FDA approved vismodegib, a drug that blocks the Hedgehog signaling pathway**,** for treating locally advanced or metastatic BCC. This approval was based on a phase II clinical trial (ERIVANCE), which showed.

- 43% response in locally advanced BCC
- 30% response in metastatic BCC
- **A** median response duration of 7.6 months

This targeted therapy provides an important alternative for patients with advanced BCC when surgery and radiation are no longer effective options.[4,5]

SYSTEMIC THERAPY

6) HEDGEHOG INHIBITORS[4,5]

The Hedgehog signaling pathway plays a key role in the development of basal cell carcinoma (BCC)**.** It is normally controlled by the **PTCH1 gene**, which is located on **chromosome 9q22**. PTCH1 produces a protein that blocks the activity of Smoothened **(SMO)**, an important protein in the Hedgehog pathway.

When a Hedgehog ligand such **as** sonic Hedgehog (SHH) binds to PTCH1, this block is removed. SMO then moves into the primary cilium**,** a small cell structure required for Hedgehog signaling. This activates Gli transcription factors**,** which turn on genes that control cell growth, movement, and new blood vessel formation. Cancer cells use these processes to grow and spread. Because of this, mutations in the Hedgehog pathway are central to the development of BCC**.**

Blocking the Hedgehog pathway is therefore an important treatment option for difficult or advanced BCCs**.** Currentl, two drugs are used for this purpose.

- **Vismodegib**
- **Sonidegib**

Both drugs block SMO, although they differ in how they are processed in the body. These medications are increasingly used as adjuvant or alternative therapies**.** Common side effects include hair loss, muscle cramps, tiredness, taste changes, and weight loss**.** Sonidegib tends to cause more frequent and more severe side effects**,** especially elevated creatine kinase levels**.** Because of these side effects, many patients stop treatment even at lower doses.

Another major problem with Hedgehog inhibitors is the development of drug resistance**,** which can cause the tumor to stop responding and start growing again. For example, some advanced periocular BCCs shrink within a few months of vismodegib treatment but later recur due to resistance**,** sometimes requiring extensive surgery such as orbital exenteration**.**

Studies show that tumor regrowth occurs in about 20–25% of patients with advanced BCC after around one year of treatment. One clinical trial found that sonidegib was less effective than vismodegib in advanced BCC.

Resistance is often caused by mutations in the SMO protein**.**

- Primary resistance (no initial response) occurs in about **50%** of patients
- Secondary resistance (loss of response after initial improvement) occurs in about **20%** of patients

Certain mutations, such as SMO G497W, prevent vismodegib from binding properly to SMO, leading to primary resistance. Other mutations, including PTCH1 mutations and SMO D473Y, cause secondary resistance after treatment by changing the structure of the protein and blocking drug entry.

In some cases, tumors bypass SMO completely by increasing Gli gene activity, allowing cancer growth through the Ras/MAPK pathway instead of the Hedgehog pathway. Research has shown that primary cilia help regulate this pathway switch, opening new possibilities for treating resistant advanced BCC.[4,5]

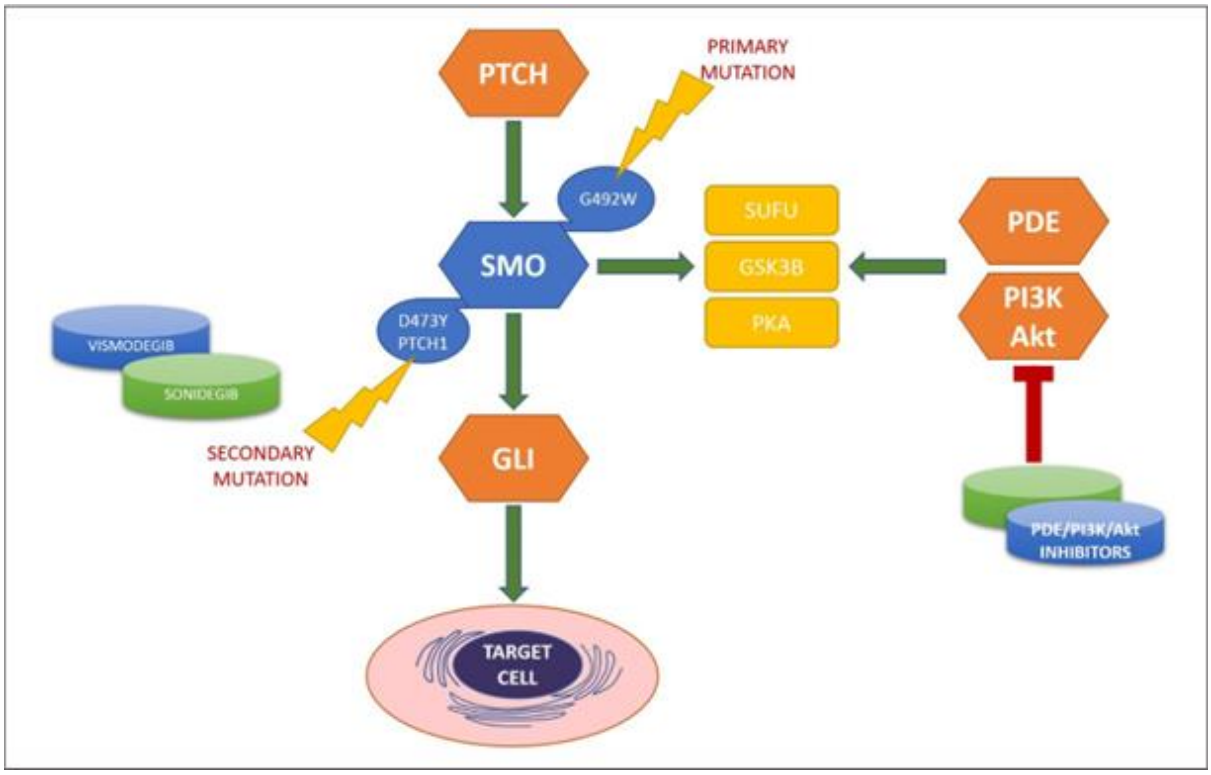


FIGURE 4: Hedgehog pathway inhibitors (HPI), such as Vismodegib and Sonidegib, are used in surgically advanced tumors as neoadjuvant therapy, prior to Mohs micrographic surgery or radiotherapy, allowing the tumor to decrease in size. Site of action and inhibition of different HPI. Patched, PTCH. PTCH1, a member of the patched gene family and the receptor for sonic Hedgehog (SHH). The PTCH1 gene product, is a transmembrane protein that suppresses the release of smoothened protein (SMO). When SHH binds PTCH1, SMO is released and signals cell proliferation. SUFU — suppressor of the fused protein; GSK3B — glycogen synthetase kinase 3B; PKA — protein kinase A; GLI — transcription factor GLI; PDE — cyclin nucleotide phosphodiesterase; PI3K/Akt — phosphoinositide 3 kinase.[5]

7) IMMUNE CHECKPOINT INHIBITORS[4]

Immune checkpoint inhibitors, especially PD-1 antibodies, have greatly changed cancer treatment in recent years. They were first shown to be effective in lung cancer and later achieved major success in skin melanoma.

The importance of this discovery was recognized with the Nobel Prize in Medicine in 2018. Normally, immune checkpoints act like “brakes” that stop the immune system from attacking the body’s own cells. Cancer cells use these checkpoints to hide from the immune system.PD-1 inhibitors remove these brakes, allowing immune cells such as T-lymphocytes to recognize and destroy cancer cells. This treatment works especially well in cancers with many genetic mutations, such as basal cell carcinoma (BCC).

Several case reports have shown promising results using PD-1 antibodies in patients with locally advanced or metastatic BCC, suggesting that this therapy may be a useful option when other treatments fail.[4]

8) COMBINATION OF DIFFERENT SYSTEMATIC THERAPIES[4]

New studies and case reports on combined treatment using Hedgehog pathway inhibitors and immune checkpoint inhibitors are eagerly awaited. It is important to see whether combining these therapies improves treatment success and whether the side effects remain acceptable for patients**.**

9) TOPICAL THERAPY[4]

Topical treatments for BCC are commonly used in dermatology, but they are rarely used in ophthalmology. For BCC around the eye, surgical removal with histological control is usually the first treatment offered.

Topical therapies are considered only if the patient strongly refuses surgery, and even then, they should be used in collaboration with an experienced specialist.

10) IMIQUIMOD THERAPY[4]

Imiquimod is a medication that stimulates the immune system by activating toll-like receptor 7. It was first used to treat viral skin infections. For basal cell carcinoma (BCC), imiquimod is used as a 5% cream, applied 5 days a week for 6 weeks. In Europe, it is approved for treating BCCs smaller than 2 cm in diameter.Studies show that imiquimod is less effective than surgery in preventing recurrence, but it works better than 5-fluorouracil (5-FU) and photodynamic therapy with MAL. Common side effects include redness, swelling, skin peeling, blistering, and pain at the application site. Some patients may also experience flu-like symptoms and swollen nearby lymph nodes.

11) 5-FU[4]

5-FU is a mitosis inhibitor well known in ophthalmology and currently used after filtering glaucoma surgery. It is applied to the skin in a 5% concentration twice a day for 4 weeks (80). Side effects can also include redness, swelling, desquamation, blistering, and pain.

12) PHOTODYNAMIC THERAPY[4]

5-aminolevulinic acid (5-ALA) and its ester methyl-aminolevulinate (MAL) are topical treatments used for basal cell carcinoma (BCC). MAL is approved for BCC treatment only in Germany. These substances are applied to the skin and then activated using red light (635 nm). Inside the tumor, 5-ALA or mal is converted into PROTOPORPHYRIN IX, which becomes active when exposed to light. This produces singlet oxygen, which destroys the cancer cells. This treatment is less effective than surgery with histological margin control and also less effective than imiquimod in preventing recurrence. Common side effects include pain during treatment, skin redness, and later erosion and crust formation at the treated area.

13) CRYOTHERAPY[4]: Cryotherapy uses liquid nitrogen applied by contact or spray to freeze the tissue at –196 °C**.** Studies have shown that cryotherapy is less effective than radiation therapy. In addition, scarring is common after this treatment, which can sometimes hide a tumor recurrence in the early stages.

14) LASER THERAPY[4]

In the laser treatment for BCC, there are two types: ablative and non-ablative.

- Ablative lasers (CO_2 or Er:YAG) remove the tumor from the skin surface.
- Non-ablative lasers destroy the tumor's blood vessels without removing the tissue Because BCCs can grow deeper under the skin; patients need careful follow-up after treatment.

15) INGENOL MEBUTATE[4]

Ingenol mebutate, a compound from garden milkweed, helps kill cells and is mainly used for actinic keratosis. There is no phase III study yet to confirm its effectiveness in BCC, although phase II results were promising. Common side effects include redness, swelling, peeling, blisters, rashes and pain.

16) DICLOFENAC[4]

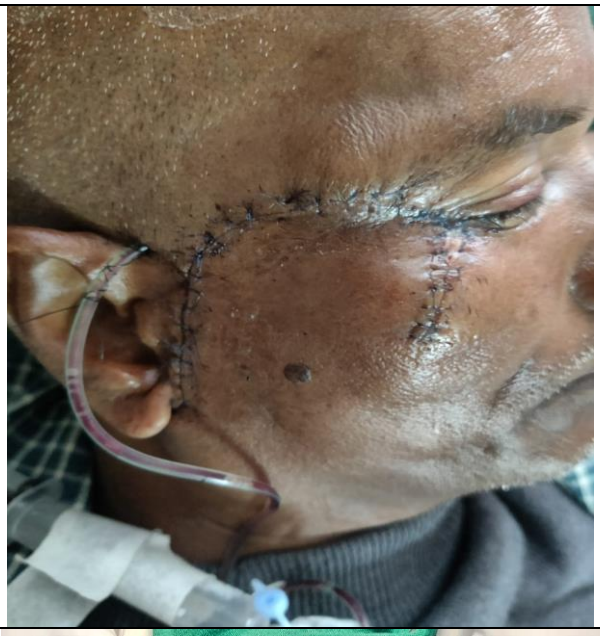
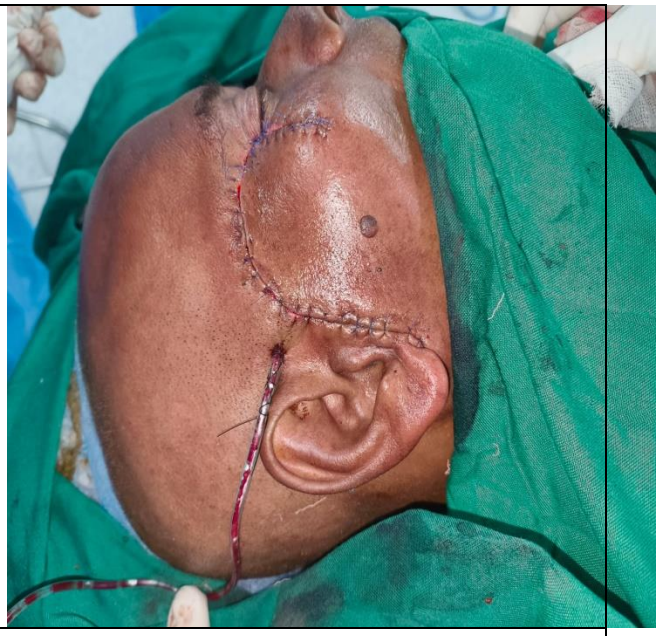
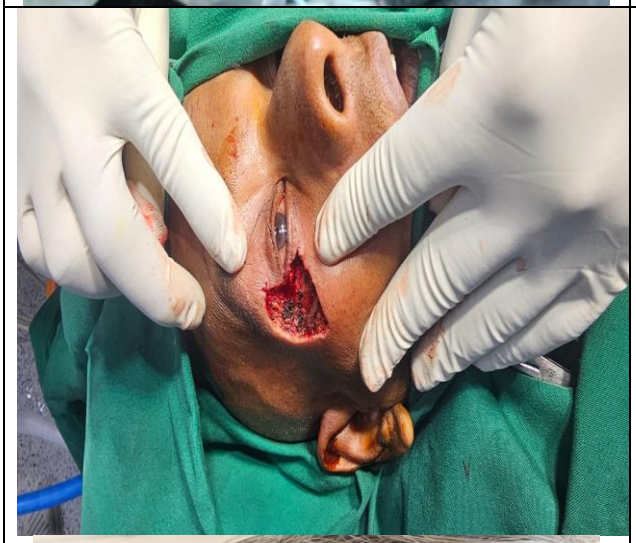
Because of the possible role of COX2 in the development of BCC, an approach with the COX2 inhibitor diclofenac was pursued. An inhibitory effect on superficial BCCs was seen in a phase II study, whereas no effect was seen in nodular BCCs (83). Therefore, treatment with a COX2 inhibitor cannot currently be recommended.

17) PROPHYLACTIC THERAPY[4]

Nicotinamide (vitamin B3) helps cells repair DNA damage caused by UV light. Studies like the Nurses' Health Study and Health Professionals Follow-Up Study looked at its effects. Taking 500mg of a nicotinamide twice daily reduced the risk of developing new BCCs by about 20% in patients who had at least 2 non-melanoma skin cancers in the past 5 years. However, it did not prevent BCCs in people without previous skin cancers. Unlike squamous cell carcinoma (SCC), retinoids do not seem to prevent BCC. Because nicotinamide can cause headache, muscle pain, dry eyes/mouth, joint pain, fatigue, depression, and birth defects, its routine use is not recommended.

CASE REPORT

A 47 years old man came to OP department of surgical oncology with chief complaints of hyperpigmentation patch or lesion over the right lateral border of the eye since 1 year. Initially small in size and gradually increased with not associated with any aggravating and reliving factor. And no past history of co-morbidity, weight gain, fever and nothing significant etc.


ON EXAMINATION:
BP: 120/80 mm of hg
PR: 82 bpm
RR; 18cpm, SPO2; 98%@RA
PICCLE: - negetive

ON SYSTEMIC EXAMINATION:

- CNS: conscious and oriented
- RS: B/L NVBS+ve added sounds
- CVS: S1,S2+ve no added sounds
- P/A: soft non tender no organomegaly

LOCAL EXAMINATION: A solitary hyperpigmentation patch of size 2x2cm present over the right lateral border of the eye and ruled out edge positive.

INVESTIGATIONS

ECG	Normal signs rhythm	
2D-echo	Normal valves and chamber, LV EF 60%	
HISTOPATHOLOGY	Where microbiology shows that nests and nodular pattern of arrangement of tumor cells with peripheral palisading the cells have scant cytoplasm and large oval granular nuclei seen. Foci of keratinisation present. Stroma is edematous with scattered inflammatory cells. Features are suggestive of basal cell carcinoma right lateral border of eye.	
SEROLOGY HIV 1 &11	NEGETIVE	
CBC	**RESULTS**	
HEMOGLOBIN	**12.5**	**REFERE- RANGE**
WBC	**10800**	**13- 18 gm%**
NEUTORPHILS/ LYMPHOCYTES	**79/16**	**4000-11000cells/ cumm**
RBC	**4.2**	**40/70-20/40%**
PLATELET	**2.69**	**5.5- 6.5mill/cumm**
PCV	**41.9**	**1.5-4.5 lakh/cumm**
MCV	**99.5**	**45- 55%**
RBS	**129**	**80- 100 fl**
T.PROTINE	**6.2**	**< 200mg/dl**
ALBUMIN	**3.2**	**6- 8.3 g/dl**
T.BILIRUBIN	**0.4**	**3.2- 5.4g/dl**
CON. BILIRUBIN	**0.2**	**0.2- 1.2 mg/dl**
UNCON. BILIRUBIN	**0.1**	**0.1- 0.4 mg/dl**
ALP	**95**	**0.2- 0.7 mg/dl**
ALT	**31**	**20- 140 U/L**
AST	**38**	**0- 45 U/L**
S.UREA	**25**	**0- 40 U/L**
CREATININE	**1.0**	**15- 45 mg/dl**
SODIUM	**137**	**0.7- 1.4 mg/dl**
POTASSIUM	**3.9**	**136- 145 mEq/L**
CHLORIDE	**103**	**3.4- 5 mEq/L**
HBS AG- RAPID	**POSITIVE**	**96- 106 mEq/L**
HIV	**NEGETIVE**	
HCV	**NEGETIVE**	
BLOOD GROUPING	**O +ve Rh +ve**	

PRE- ANESTHESIA RECORD		**POST OP ORDERS:**
➢ Elective case ➢ Patient should be NBM ➢ Patient general fitness done for surgery ➢ Preop- Diagnosis: BCC OF RIGHT EYE ➢ Poposed procedure/ Surgery: under general anesthesia wide local excision with mastoid flap reconstruction. ➢ GPE; conscious and oriented ➢ O/E: Normal, S/E: normal ➢ Spine: normal ➢ FoNA: +ve ➢ BHT: 15sec ➢ ASA- PS: 1 ➢ IV fluid; 1pint RL @ 100ml/hr ➢ Inj-TT 0.5mg ➢ Inj- ondonsetron 4 mg given ➢ Inj- pantoprazole 40 mg given at 6am	Before and during surgery medication given: pre induction/ sedation/ analgesia/ others: ➢ Inj – glycopyrolate 0.2 mg ➢ Inj – midazolam 1mg ➢ Inj- pentazocin 30 mg ➢ Inj- Veccuronium 4mg for relaxant ➢ Inj- propofol 100mg for induction ➢ ET Tube size 8.5cm oral ➢ Mainteance: O2- N2o 40:60%, Cuffed- at 23cm, ➢ Parameters: FiO2:355, TV;430ml, RR:12, 1:E: 1:2, PEEP: 4	➢ NBM till further order ➢ Propped up position ➢ Inj – pipzo 4.5 mg IV TID ➢ Inj- dexona 8mg IV BD ➢ Inj- pantop 40mg IV OD ➢ Inj- ondonsetron 4mg IV BD ➢ Inj- Paracetamol 1gm IV TID ➢ Inj- Tramadol 1amp in 100ml NS SOS ➢ Tab- chymoral fort PO BD

➢ Inj ciplox 500mg given ➢ Informed and written consent taken ➢ Patient shifted to OT ➢ Surgical position is supine		

Figure 5: The image demonstrates the patient's postoperative improvement following surgical intervention.

DISCHARGE MEDICATIONS: paient was admitted with above mentioned complaints and after relevant investigation done, under general anaesthesia wide excision with mastoid flap done and managed with IV fluids, IV antibiotics, IV analgesics and IV pipzo and patient is now hemodynamically stable and tolerating orally and can be discharged with following advice.

SL.NO	NAME OF THE DRUG	FREQUENCY	ROUTE	DOSE
1.	REGULAR DIET			
2.	TAB- CEFEXIME	1-0-1	PO	200mg
3.	TAB- RANTAC	1-0-1	PO	150mg
4.	TAB- PARACETAMOL	1-0-1	PO	500mg
5.	TAB- B COMPLEX	0-1-0	PO	

DISCUSSION

Basal cell carcinoma (BCC) is the most common cutaneous malignancy worldwide and predominantly affects fair-skinned individuals, particularly in industrialized Western societies. It shows a strong predilection for sun-exposed areas, with nearly 90% of cases occurring in the head and neck region. Eyelid involvement accounts for approximately 10% of all BCCs, with the lower eyelid being the most commonly affected site, followed by the medial canthus, upper eyelid, and lateral canthus. Although less frequent, lateral periocular lesions are clinically significant due to their proximity to vital ocular structures and the potential for functional and cosmetic impairment.

BCC usually presents as a slowly enlarging, painless lesion, which often results in delayed diagnosis. In the present case, a 47-year-old male presented with a gradually enlarging hyperpigmented lesion over the right lateral border of the eye for one year, without pain or systemic symptoms. This presentation is consistent with the indolent nature of BCC. Chronic ultraviolet (UV-B) exposure is the most important etiological factor, especially in individuals with fair skin and those engaged in outdoor occupations. Other risk factors include ionizing radiation, hereditary syndromes such as Gorlin–Goltz syndrome and xeroderma pigmentosum, long-term immunosuppression, and genetic mutations involving tumor suppressor genes such as *TP53* and *PTCH1*.

Histopathological examination is essential for definitive diagnosis, as BCC exhibits multiple clinical and histological subtypes. In this case, histopathology revealed nests and nodular arrangements of basaloid tumor cells with peripheral palisading, scant cytoplasm, large oval nuclei, focal keratinization, and edematous stroma with scattered inflammatory cells. These features are characteristic of nodular BCC, the most common

subtype, which generally carries a favorable prognosis when completely excised. More aggressive subtypes, such as infiltrative and morpheaform BCC, are associated with poorly defined margins and higher recurrence rates.

Surgical excision with histologically clear margins remains the treatment of choice for periocular BCC. In the present case, wide local excision was performed under general anesthesia due to the lesion's size and location, ensuring adequate margin control. Reconstruction of eyelid defects poses a challenge because of the functional and cosmetic importance of the eyelids. The use of a mastoid flap in this patient provided reliable vascularity, adequate tissue coverage, and satisfactory functional and cosmetic outcomes. The postoperative course was uneventful, and histopathological examination confirmed complete tumor clearance.

Although BCC has a low metastatic potential, recurrence rates of up to 20% have been reported in eyelid tumors, particularly in aggressive histological subtypes or cases with incomplete excision. Recurrent tumors generally have a worse prognosis than primary lesions. Advanced cases with orbital or intracranial extension are difficult to manage and often require a multidisciplinary approach. Therefore, early diagnosis, complete surgical excision, appropriate reconstruction, and long-term follow-up are essential for optimal outcomes in patients with periocular basal cell carcinoma.

CONCLUSION

Basal cell carcinoma of the eyelid is a common yet potentially destructive malignancy that requires early recognition and prompt management to prevent functional and cosmetic morbidity. This case emphasizes the importance of thorough clinical evaluation and histopathological confirmation in establishing the diagnosis. Wide local excision with adequate margins remains the cornerstone of treatment, while appropriate reconstructive techniques, such as mastoid flap reconstruction, play a crucial role in restoring eyelid function and appearance. Early diagnosis, complete tumor excision, and careful long-term follow-up are essential to minimize recurrence and achieve optimal outcomes in patients with periocular basal cell carcinoma.

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