Dissertation on

A CLINICOPATHOLOGICAL STUDY TO ANALYSE THE IMPORTANCE OF HISTOPATHOLOGICAL EXAMINATION IN DIAGNOSIS OF EXCISED CONJUNCTIVAL LESIONS OF BULBAR CONJUNCTIVA

THE TAMILNADU

Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI

2018

CERTIFICATE

This is to certify that this dissertation entitled **"A CLINICOPATHOLOGICAL STUDY TO ANALYSE THE IMPORTANCE OF HISTOPATHOLOGICAL EXAMINATION IN DIAGNOSIS OF EXCISED CONJUNCTIVAL LESIONS OF BULBAR CONJUNCTIVA"** is a bonafide record of research work done by **Dr.N.SUDHA PRIYADHARSINI,** Post Graduate Resident in Department of Ophthalmology, Madurai Medical College, Madurai.

She has submitted this in partial fulfillment of the regulations laid down by The Tamil Nadu Dr. M.G.R. Medical University, for the award of Master of Surgery Degree Branch III (Ophthalmology), under our guidance and supervision during the academic years 2015-2018.

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This is to certify that this dissertation entitled **"A CLINICOPATHOLOGICAL STUDY TO ANALYSE THE IMPORTANCE OF HISTOPATHOLOGICAL EXAMINATION IN DIAGNOSIS OF EXCISED CONJUNCTIVAL LESIONS OF BULBAR CONJUNCTIVA"** is a bonafide record of research work done by **Dr.N.SUDHA PRIYADHARSINI,** Post Graduate Resident in Department of Ophthalmology, Madurai Medical College, Madurai.

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DECLARATION

I, **Dr.N.SUDHA PRIYADHARSINI** hereby solemnly declare that, this dissertation titled **"A CLINICOPATHOLOGICAL STUDY TO ANALYSE THE IMPORTANCE OF HISTOPATHOLOGICAL EXAMINATION IN DIAGNOSIS OF EXCISED CONJUNCTIVAL LESIONS OF BULBAR CONJUNCTIVA"** was done by me.

I also declare that this bonafide work / a part of this work was not submitted by me / anyone else, for any award, for Degree / Diploma to any other University / Board either in India / abroad. This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfilment of the rules and regulations for the award of Master of Surgery degree Branch -III (Ophthalmology) to be held in April 2018.

Place: Madurai (Dr.N.Sudha Priyadharsini)

Date:

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A CLINICOPATHOLOGICAL STUDY TO ANALYSE THE IMPORTANCE OF HISTOPATHOLOGICAL EXAMINATION IN DIAGNOSIS OF EXCISED CONJUNCTIVAL LESIONS OF BULBAR CONJUNCTIVA

INTRODUCTION

The conjunctiva is readily visible and so the tumors and other lesions in the conjunctiva are generally recognized at an early stage. Clinical diagnosis can often be made by ocular examination and slit- lamp bio microscopy, if features are characteristics. A biopsy is not necessary in cases of smaller tumors that appear benign. Small tumours can be better removed completely in one setting (excisional biopsy). Larger lesions, remove a portion of the tumor (incisional biopsy) to get a histopathologic diagnosis prior to more extensive therapy.It is rarely needed to do exfoliative cytology or fine- needle aspiration biopsy, as incisional biopsy is readily available. Slit- lamp examination of the cornea is needed in patients with suspected conjunctival tumors. Rule out any corneal involvement in squamous cell carcinoma and melanoma of conjunctiva before planning for surgery.

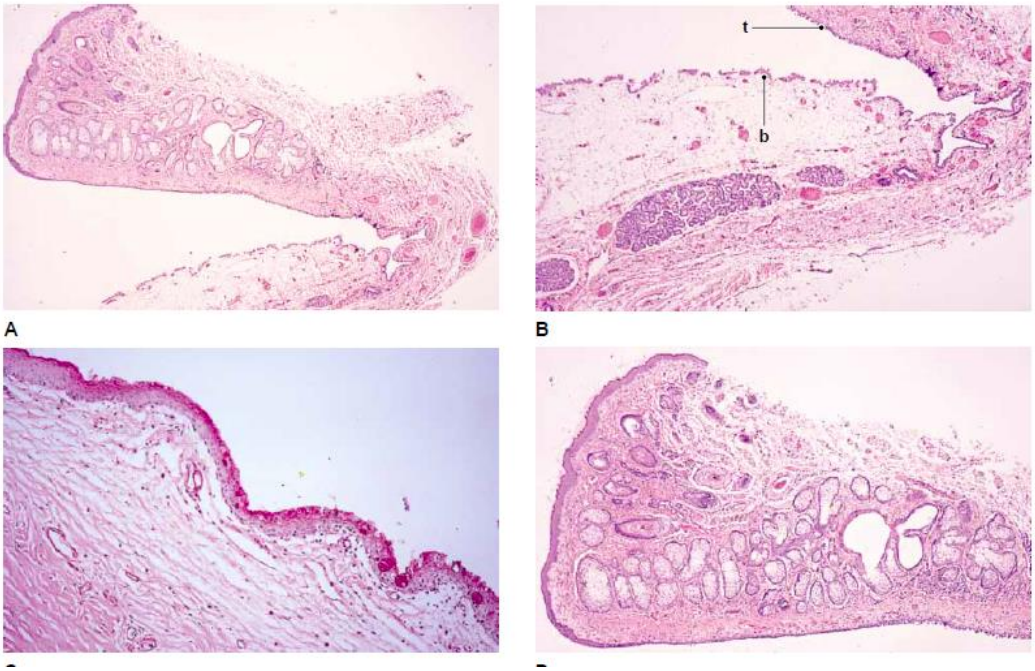
ANATOMY OF CONJUNCTIVA:

The conjunctiva has 3 geographic zones: palpebral, forniceal, bulbar. The palpebral conjunctiva starts from the mucocutaneous junction of lid and covers the inner surface of lid and attached firmly to the tarsus. The tissue is freely movable in the fornices, in the upper lid it is enmeshed with fibrous elements of the levator aponeurosis and Muller muscle. In the lower lid, fibrous expansions from the inferior rectus muscle join with the inferior tarsal muscle. The bulbar conjunctiva is freely mobile.It fuses with the Tenon capsule and gets inserted into the limbus. Blood supply to the bulbar conjunctiva is by anterior ciliary arteries and to the tarsal conjunctiva is by branches of the marginal arcades of lids. The proximal

arcade, along the upper border of the lid, gives branches proximally to the forniceal and the bulbar conjunctiva via the posterior conjunctival arteries. The ciliary arteries via the anterior conjunctival arteries gives the limbal blood supply. The innervation of the conjunctiva is from the ophthalmic division of trigerminal nerve.

The conjunctiva is a mucous membrane made of non-keratinizing squamous epithelium with lot of goblet cells and richly vascularized substantia propria having lymphatic vessels, plasma cells, macrophages, mast cells. A lymphoid layer is presents from the bulbar conjunctiva to sub tarsal folds.Specialized aggregations of conjunctiva-associated lymphoid tissue (CALT) correspond to mucosa associated lymphoid tissue (MALT) and have collections of T and B lymphocytes under the epithelium. They help in antigen processing. The conjunctival epithelium is 2 to 5 cells thick. The basal cells are cuboidal in shape and become flattened polyhedral cells at the surface. The goblet cells (mucous glands) are found in the inferior and medial part of the conjunctiva more in the region of the caruncle and plica semilunaris. They are sparsely found in the remainder of the conjunctiva and absent in the limba1 area.

FIGURE 1: HISTOLOGY OF CONJUNCTIVA



MANAGEMENT

Management of a conjunctival tumor may be

- serial observation
- incisional biopsy
- excisional biopsy
- cryotherapy
- chemotherapy
- radiotherapy
- modified enucleation
- orbital exenteration or
- Various combinations of the above.

  If large conjunctival defect present-mucous membrane grafts of the other eye conjunctiva, buccal mucosa, amniotic membrane graft may be done.

Observation

Most benign lesions like pingueculum, dermolipoma, and nevus are just observed. Anterior segment slit lamp photos are taken for photographic evidence for follow up every 1 year to look for any growth, malignant transformation, or compression on normal surrounding tissues.

Incisional Biopsy

For suspicious lesion like squamous cell carcinoma, PAM, melanoma, and conjunctival spread of sebaceous gland carcinoma if these tumours occupy >4 clock hours in conjunctiva. For larger lesions incisional wedge biopsy or punch biopsy done. Treatment planned based on biopsy reports.

Excisional Biopsy

In Intermediate and small tumors that are symptomatic or suspected to be malignant, excisional biopsy is preferred over incisional biopsy to avoid inadvertent tumor seeding. Excision biopsy needed in limbal dermoid, epibulbar osseous choristoma, steroid- resistant pyogenic granuloma, squamous cell carcinoma, and melanoma.in lesions of conjunctival fornix it is totally excised and the conjunctiva reconstructed with absorbable sutures , fornix deepening sutures, symblephron ring used. If defect is large mucous membrane graft used. Most malignant tumours are limbal in location. Limbal neoplasms invades the corneal epithelium, sclera, anterior chamber and the soft tissues of the orbit. If sclera is involved thin sclera biopsy taken to achieve tumour clearance. Friable tumors may cause seeding of tumour and so “no touch technique” followed.

SURGICAL TECHNIQUE OF EXCISION BIOPSY:

Done under microscope

The operative field should be left dry

Avoid wetting the field with balanced salt solution to prevent seeding of cells. Retrobulbar anesthesia used

The corneal epithelial component is approached first and the conjunctival component is dissected next so that the whole specimen resected in one piece. Absolute alcohol in an applicator is gently applied to the entire corneal component. Epithelial cellular devitalization and easy release of the tumor cells from Bowman’s.

The malignancy outlined with beaver blade using a delicate epithelial incision or epitheliorhexis technique 2 mm outside the corneal component.

With the beaver blade the corneal epithelium is sweeped from centre to limbus. A pentagonal or circular conjunctival limbal based incision is made outside the tumor margin.

The incision is carried through the underlying Tenon's fascia until the sclera is seen and full thickness conjunctiva and Tenon's fascia is included into the excisional biopsy. Cautery done to control bleeding. A second incision outlined by a superficial scleral groove approximately 0.2 mm in depth and 2.0 mm outside the base of the overlying adherent conjunctival mass. This groove is continued anteriorly up to the limbus. This area outlined by the scleral groove is cut by flat dissection of about 0.2-mm thickness within the sclera in an attempt to remove a superficial lamella of sclera, overlying Tenon's fascia and conjunctiva with tumor- free margins is removed in one piece without touching the tumor itself (no- touch technique). The removed specimen is held flatly on a piece of cardboard from the surgical tray and kept in fixative and given for histopathologic studies. This prevents the specimen from folding and so helps in better assessment of the tumor margins .Now new set of instruments used, to avoid contamination of healthy tissue with possible tumor cells. After excision of the specimen, cryotherapy is applied to the margins of the remaining bulbar conjunctiva. This is performed by freezing the surrounding bulbar conjunctiva by lifting it away from the sclera using the cryoprobe. When the ice ball reaches a size of 4 to 5 mm, it is allowed to thaw and the cycle repeated once. The cryoprobe is then moved to an adjacent area of the conjunctiva and the cycle is repeated until all of the margins have been treated by this method. Corneal margins need not be treated with cryoapplication. The tumor bed treated with absolute alcohol wash on cotton- tip applicator and bipolar cautery, to avoid direct cryotherapy to the sclera. Using clean instruments, the conjunctiva is then mobilized for closing the defect by making the intermuscular septum loose with Steven's scissors spreading and creating Trans positional conjunctival flaps. Closure is done with interrupted absorbable 6–0 or 7–0 sutures. An area of bare sclera can be left close to the limbus, but complete closure is better as this

promotes better healing and helps in further surgery in case the patient develop recurrence. The patient is given topical antibiotics and corticosteroids for 2 weeks and followed up at 3- to 6-month intervals.

Cryotherapy

In the management of conjunctival tumors, cryotherapy can be used as a supplemental treatment. It can eliminate microscopic tumor cells and prevent recurrence of malignant tumors. It can also be used as a mainstay of treatment for primary acquired melanosis and pagetoid invasion of sebaceous gland carcinoma. If cryotherapy can devitalize the malignant or potentially malignant cells, radical surgery like orbital exenteration can be avoided.

Chemotherapy

Topical eyedrops composed of mitomycin C, 5-fluorouracil, interferon, or cidofovir are effective in treating epithelial malignancies such as squamous cell carcinoma, primary acquired melanosis, and pagetoid invasion of sebaceous gland carcinoma.

Mitomycin C or 5-fluorouracil are employed most successfully for squamous cell carcinoma, especially after tumor recurrence following previous surgery. This medication is prescribed topically four times daily for a 1-week period followed by a 1-week hiatus to allow the ocular surface to recover. This cycle is repeated once again so that most patients receive a total of 2 weeks of the chemotherapy topically. Both mitomycin C and 5-fluorouracil are most effective for squamous cell carcinoma and less for primary acquired melanosis and pagetoid invasion of sebaceous gland carcinoma. Toxicities include most commonly dry- eye findings, superficial punctate epitheliopathy, and punctal stenosis. Corneal, scleral melt, and cataract can develop if these agents are used with open conjunctival wounds or used more. Topical interferon can be effective for squamous epithelial malignancies and is less toxic to the surface epithelium, but this medication may require many months of use to effect a result.

Other topical antiviral medications including cidofovir can be employed with little toxicity for squamous epithelial tumors.

Radiotherapy

Two forms of radiotherapy are employed for conjunctival tumors, namely external beam radiotherapy and custom designed plaque radiotherapy. External beam radiotherapy to a total dose of 3000 to 4000 cGy is used to treat conjunctival lymphoma and metastatic carcinoma if lesions are too large or diffuse to excise locally. Side effects are dry eye, punctate epithelial abnormalities, and cataract. Custom- designed plaque radiotherapy to a dose of 3,000 to 4,000 cGy can be used to treat conjunctival lymphoma or metastasis. A higher dose of 6,000 to 8,000 cGy can be employed to treat the more radiation- resistant melanoma and squamous cell carcinoma. The two designs for conjunctival custom plaque radiotherapy include a conformer plaque technique with six fractionated treatment sessions or a reverse plaque technique with the device sutured onto the episclera. Plaque radiotherapy to a low dose of 2,000 cGy is employed for benign conditions such as steroid resistant pyogenic granuloma that show recurrence after surgical resection.

Modified Enucleation

Modified enucleation is a treatment modality for primary malignant tumors of the conjunctiva that have invaded through the limbal tissues into the globe, causing secondary glaucoma. The mucoepidermoid variant of squamous cell carcinoma of the conjunctiva has a greater tendency for such invasion. At the time of enucleation, it is necessary to remove the involved conjunctiva intact to avoid spreading tumor cells. Thus, the initial peritomy should begin at the limbus, but when the tumor is approached, the incision should proceed posteriorly from the limbus to surround the tumor- affected tissue by at least 3 to 4 mm. The tumor will remain adherent to the globe at the limbus. Sometimes a suture is employed through the

surrounding conjunctiva into the episclera to secure the tumor to the globe. The remaining steps of enucleation are gently performed .The globe is removed with tumor adherent after cutting the optic nerve from the nasal side. The margins of the remaining, unaffected conjunctiva are treated with double freeze thaw cryotherapy.Residual conjucnctiva present for closure. A mucous membrane graft or amniotic membrane graft may be necessary for adequate closure and to provide fornices for a prosthesis. A simple horizontal inferior forniceal conjunctival incision from canthus to canthus may suffice, as long as the conformer is constantly worn as a template so the new conjunctival fornix grows deep and around this structure.

Orbital Exenteration

Orbital exenteration is the treatment of choice for primary malignant conjunctival tumors with orbital involvement. Either an eyelid- removing or eyelid- sparing exenteration is done, depending on the extent of eyelid involvement. The eyelid- sparing technique is done due to better cosmetic appearance and they heal within 2 or 3 weeks.If the anterior lamella of the eyelid is uninvolved with tumor, an eyelid- sparing (eyelid- splitting) exenteration may be accomplished .

Mucous Membrane Graft

Mucous membrane grafts are occasionally necessary to replace vital conjunctival tissue after removal of extensive conjunctival tumors. The best donor sites include the forniceal conjunctiva (ipsilateral or contralateral eye) and buccal mucosa from the posterior aspect of the lower lip or lateral aspect of the mouth. Such grafts are removed by a freehand technique, fashioned to fit the defect, and fit into place with cardinal and running absorbable 6–0 or 7–0 sutures. The tissue is delivered frozen and must be defrosted for 20 minutes. The fine, transparent material is carefully peeled off its cardboard surface, laid basement membrane

side up, and sutured into place with absorbable sutures. Topical antibiotic and steroid ointments are applied following all conjunctival grafting procedures. For graft harvest and placement, the surgeon should always use clean, sterile instruments at both the donor and the recipient sites. Free tumor cells can rest on instrument tips and later implant and grow in previously uninvolved areas if such precautions are not taken.

I.CONGENITAL LESIONS

A variety of tumors and related conditions may be present at birth and become clinically apparent shortly after birth. Most of the lesions are choristomas, consisting of tissue elements that are not normally present at the involved site.

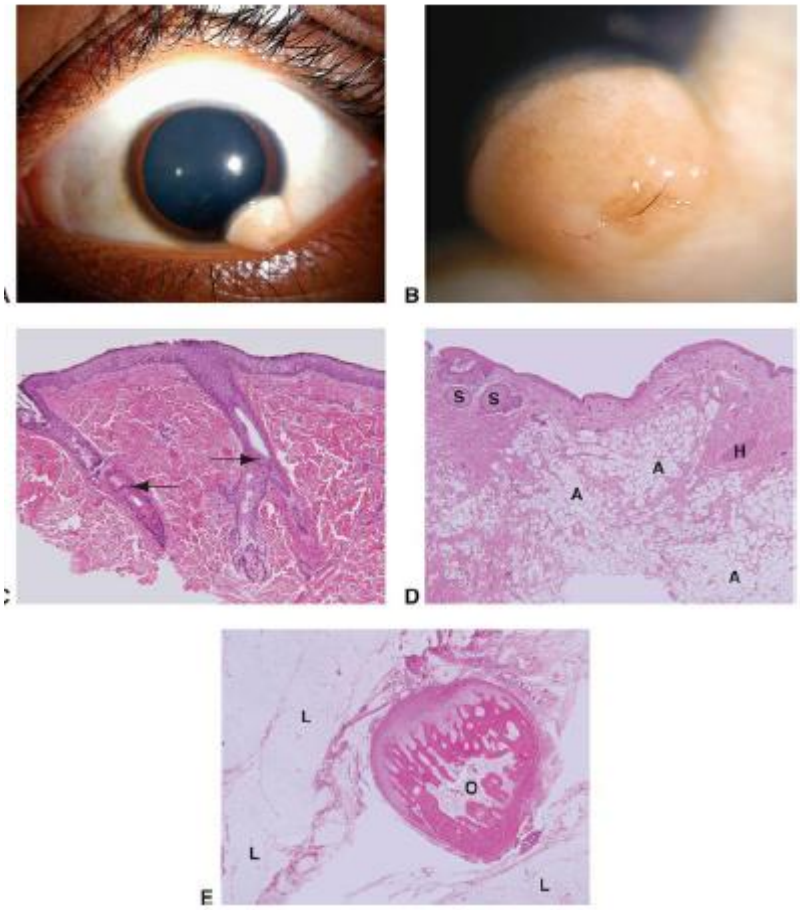
DERMOID

Conjunctival dermoid is a congenital well- circumscribed yellow- white solid mass that involves the bulbar conjunctiva or at the corneoscleral limbus. It occurs near the limbus inferotemporally, and often this tumor has fine hairs, best seen with slit- lamp biomicroscopy. It may extend to the central cornea or be located in other quadrants on the bulbar surface. It may be an isolated lesion or can be associated with Goldenhar's syndrome. The patient should be evaluated for ipsilateral or bilateral preauricular skin appendages, hearing loss, eyelid coloboma, and orbitoconjunctival dermolipoma, and cervical vertebral anomalies that comprise this uninheritable syndrome.

Histopathologically, the conjunctival dermoid is a choristomatous malformation that is made up of dense fibrous tissue lined by conjunctival epithelium with dermal elements like hair follicles and sebaceous glands. The management of dermoid includes observation if the lesion is small and visually non symptomatic. We can excise the lesion for cosmetic reasons, but the remaining corneal scar may be cosmetically unacceptable. Larger and symptomatic dermoids can cause visual loss from astigmatism. These can be managed by lamellar

keratosclerectomy and primary closure of overlying tissue if the defect is superficial or closure with corneal graft if the defect is deep or full thickness. The cosmetic appearance may improve, but the refractive and astigmatic error and visual acuity may not change .When the lesion is in the central cornea, a lamellar or penetrating keratoplasty may be needed and long-term amblyopia may be a problem. Rarely, extensive dermoids involve the lateral canthus, and planned excision with lateral canthal repair is necessary.

FIGURE 2: DERMOID – GROSS AND HISTOPATHOLOGICAL APPERANACE



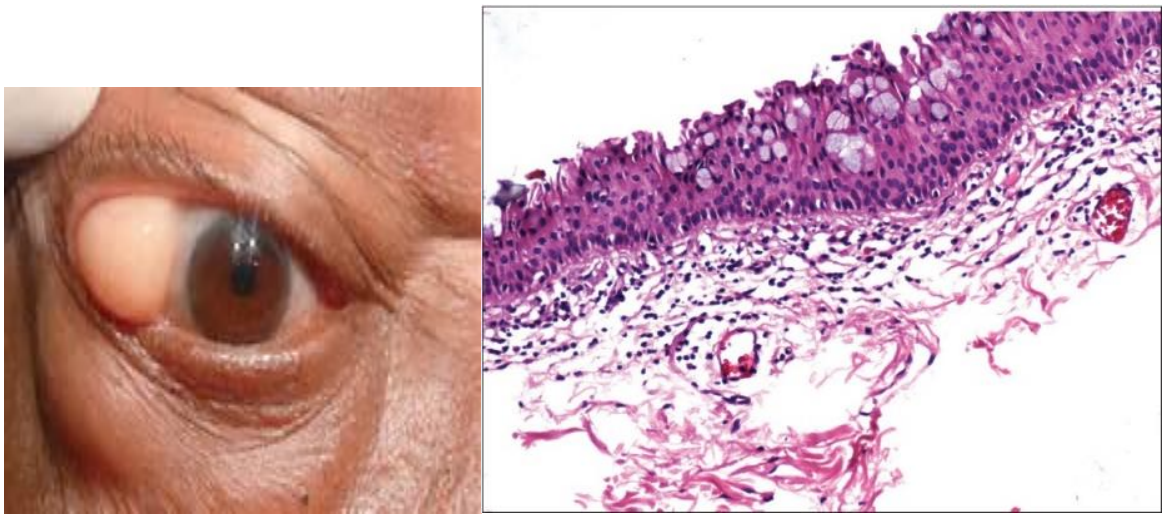
DERMOLIPOMA

Dermolipoma is congenital and present at birth, but it remains asymptomatic and may not be detected till adulthood, till it protrudes from the orbit from the conjunctival fornix

superotemporally. It appears as a pale yellow, soft, fluctuant, fusiform mass from the palpebral lobe of the lacrimal gland, best visualized with the eye in inferonasal gaze.

It extends for a variable distance into the orbital fat and on the bulbar conjunctiva, and occasionally it can extend anteriorly till the limbus. Unlike herniated orbital fat, dermolipoma can contain fine white hairs on its surface and it could not be reduced with digital pressure into the orbit. In computed tomography (CT) or magnetic resonance imaging (MRI), dermolipoma is similar to orbital fat. Histopathologically, it is lined by conjunctival epithelium on the surface and the subepithelial tissue has collagenous connective tissue. Most of dermolipomas need no treatment, but larger symptomatic ones and cosmetically unappealing can be managed by excision of the whole orbitoconjunctival lesion through a conjunctival forniceal approach or simply removing the anterior part of lesion similar to removal of prolapsed orbital fat.

FIGURE 3: DERMOLIPOMA – GROSS AND HISTOPATHOLOGICAL APPEARANCE



EPIBULBAR OSSEOUS CHORISTOMA

Epibulbar osseous choristoma is a rigid deposit of bone generally seen in the bulbar conjunctiva superotemporal quadrant. It is congenital and typically remains undetected till personally palpated by the patient. It is clinically rock- hard consistency on palpation, though fibrous tissue tumors can be similar. The diagnosis can be made with USG or CT to illustrate the calcium component. This tumor is managed by periodic observation. Sometimes patients have a foreign- body sensation, and such lesions can be excised with a circumtumoral conjunctival incision followed by dissection to bare sclera and full- thickness conjunctival resection done. For tumors that are adherent to the sclera, a superficial sclerectomy might be needed.

LACRIMAL GLAND CHORISTOMA

Lacrimal gland choristoma is a congenital lesion in young children as an asymptomatic pink stromal mass, mostly in the inferior bulbar or forniceal conjunctiva. It is found that this lesion presents in this location due to the pathway the lacrimal gland takes during embryogenesis from the inferior to superotemporal region. The lacrimal gland choristoma can mimic a focus of inflammation because of its pink color.A cystic appearance comes from this secretory mass if there is no attachment to the conjunctival surface. Excisional biopsy is usually done to confirm the diagnosis.

RESPIRATORY CHORISTOMA

Rarely a cystic choristoma, appearing as congenital sclerocorneal ectasia, is noted

COMPLEX CHORISTOMA

The conjunctival dermoid and epibulbar osseous choristoma are simple choristomas as they have one tissue type, such as skin or bone. A complex choristoma has a variety of tissue, such

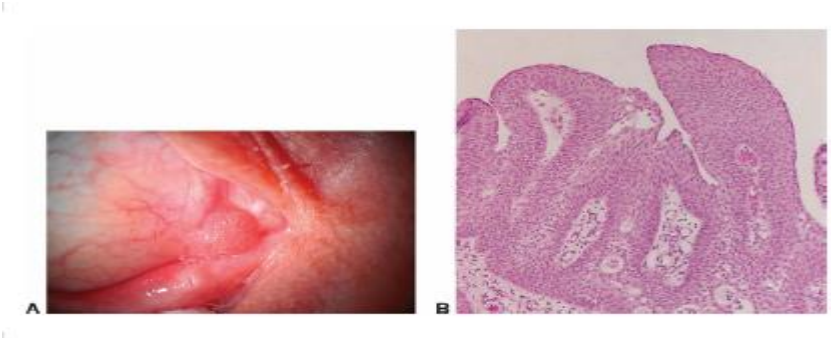
as dermal appendages, lacrimal gland tissue, cartilage and bone. It has variable in its clinical appearance and may cover epibulbar surface or form a circumferential growth pattern around the limbus. The complex choristoma has association with the linear nevus sebaceous of Jadassohn which has the cutaneous features such as sebaceous nevus in the facial region and neurologic features such as seizures, mental retardation, arachnoid cyst, and cerebral atrophy. The ophthalmic features of this syndrome are epibulbar complex choristoma and posterior scleral cartilage. The management of the complex choristoma is dependent on the extent of lesion. Observation and wide local excision with mucous membrane graft reconstruction may be done. In extensive lesion, where the lesion causes dense amblyopia and no hope for visual acuity, modified enucleation and ocular surface reconstruction may be done.

II. BENIGN TUMORS OF SURFACE EPITHELIUM

PAPILLOMA

Squamous papilloma is a benign tumor that originates from human papillomavirus infection of conjunctiva. This tumor can occur in children and adults, and has a pink fibrovascular frond of tissue arranged in a sessile or pedunculated pattern. In children, the lesion is small, multiple, and found in the inferior fornix. In adults, it is solitary, more extensive, and extend to cover the full corneal surface resembling malignant squamous cell carcinoma.

FIGURE 4: PAPILLOMA – GROSS AND HISTOPATHOLOGICAL APPEARANCE



KERATOACATHOMA

The conjunctiva can produce benign reactive inflammatory lesions that resemble carcinoma such as pseudocarcinomatous hyperplasia and variant, keratoacanthoma. Sometimes a distinct nodule may be found. This lesion appears gelatinous or leukoplakic, similar to squamous cell carcinoma of conjunctiva, but its onset is more rapid. Acanthosis, hyperkeratosis, and parakeratosis are seen histopathologically.

HEREDITARY BENIGN INTRAEPITHELIAL DYSKERATOSIS

Hereditary benign intraepithelial dyskeratosis (HBID) is a condition seen in isolate of Caucasians, African Americans, and American Indians. It is an AD disorder and has bilateral elevated fleshy plaques on nasal or temporal perilimbal conjunctiva. Similar plaques can be seen on buccal mucosa. It can remain asymptomatic or can cause severe redness and foreign body sensation. Sometimes it can extend onto the cornea.

DACRYOADENOMA

Dacryoadenoma is a rare tumor, seen in children or young adults as a pink mass in inferior bulbar or palpebral region. It is uncertain if it is congenital or acquired. This benign tumour originates from the surface epithelium and proliferate to the stroma, forming glandular lobules.

KERATOTIC PLAQUE

Keratotic plaque is white limbal or bulbar conjunctival mass, seen in the interpalpebral region made of acanthosis and parakeratosis and keratinization of the epithelium. It is similar to squamous cell carcinoma with leukoplakia.

ACTINIC KERATOSIS

Actinic keratosis is a frothy, white lesion seen over a chronically inflamed pingueculum or pterygium. Histopathologically, it is made of a proliferation of surface epithelium with keratosis. Clinically, it is similar squamous cell carcinoma of the conjunctiva.

III. MELANOCYTIC TUMORS

Tumors arise from the melanocytes of the conjunctiva and episclera .Benign pigmented lesions include conjunctival nevus and racial melanosis. Ocular melanocytosis, a benign pigmentation of the sclera, is misdiagnosed as a pigmented lesion of the conjunctiva. Malignant or potentially malignant pigmented lesions include primary acquired melanosis and malignant melanoma

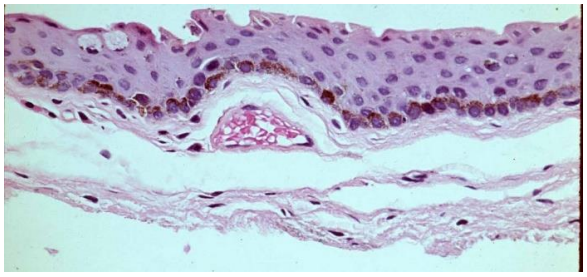
MELANOSIS

Epithelial Melanosis

Epithelial/ racial melanosis of the conjunctiva is a primary melanotic condition affecting blacks more than whites. Racial melanosis appears in early childhood and stabilizes in early adulthood. Flat patches of pigment are scattered in the conjunctival epithelium, mostly in the interpalpebral and perilimbal areas. Both eyes are affected, the amount of pigment may be asymmetric. The lesions fade near the fornices.Due to their intraepithelial location, these pigmented lesions are freely mobile over the globe. The pigmentation extend into the peripheral cornea and may be pronounced around the perforating branches of the anterior ciliary nerves. Histopathologic examination of epithelial melanosis shows an increased deposition of melanin granules in basal layer of the conjunctival epithelium. The conjunctival epithelium has normal morphology and maturation. The pigment does not extend than the basal epithelium and has no cellular atypia.

Epithelial melanosis is benign. Treatment is periodic observation. Care taken to distinguish racial melanosis and primary acquired melanosis, especially in dark pigmented patients, in whom distinction is difficult. Biopsies are useful to confirm the histopathologic diagnosis.

FIGURE 5: BENIGN MELANOSIS – HISTOPATHOLOGICAL APPEARANCE



SUBEPITHELIAL MELANOCYTOSIS

Clinical Presentation

Subepithelial (congenital) melanocytosis of the deep conjunctiva, episclera or superficial sclera is congenital condition that is common in African Americans, Asians, and Hispanics. The pigmented lesions appear bluish or slate-gray and usually unilateral. These lesions are deep and immobile. The overlying conjunctiva is unpigmented. The melanocytosis may affect the uvea, meninges, and soft tissues of orbit. Ipsilateral dermal melanocytosis in distribution of the ophthalmic and maxillary branches of trigeminal nerve is found in approximately 50% of patients with congenital melanocytosis. This is known to as oculodermal melanocytosis or nevus of Ota .

Histopathology

The classic histopathologic finding is focal proliferation of subepithelial melanocytes. These melanocytes are elongated and fusiform with prominent branching processes than the melanocytes in nevi.

FIGURE 6: SUBEPITHELIAL MELANOSIS – GROS AND HISTOPATHOLOGICAL APPEARANCE

Treatment and Prognosis

The prognosis is good.But white patients with lesion have more risk of developing uveal melanoma. Glaucoma with hyperpigmentation of the trabecular meshwork develops in about 10% of patients. Yearly ophthalmic review is needed.

CONJUNCTIVAL NEVI

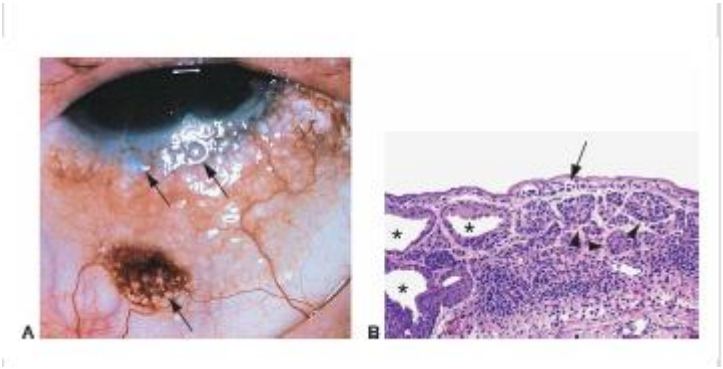
Classification and Clinical Presentation

Nevi are common lesions of conjunctiva. Their colour may be from tan to dark brown. 30%, however, may be light pigmented or nonpigmented. Pigmentation increases during puberty, and nonpigmented lesions can become pigmented, and seems as if the lesion has grown. Nevi can be congenital, but commonly arise during childhood or adulthood. Like skin nevi, conjunctival nevi are classified by layer in which they are seen into intraepithelial (junctional), compound, or subepithelial type of nevi. It is tough to distinguish layer involved on clinical examination alone. Nevi have little/ no malignant potential. Conjunctival nevi are solitary, well-circumscribed, flat/ raised, brown, pigmented, free mobile lesions most commonly found near the limbus.

Nevi can be focal or diffuse, but never multifocal. Many nevi have small cysts. Blue nevi are deeper, localized, have palpable thickness, and more cellular. They are gray or blue in colour

and appear early in childhood. Blue nevi are benign, but have malignant potential if they are hypercellular. Split nevus of the eyelid, may be found with malignant melanoma of the conjunctiva.

FIGURE 7: CONJUNCTIVAL NEVI – GROSS AND HISTOPATHOLOGICAL APPEARANCE



Histopathologic examination of conjunctival nevi has spindle-shaped or multipolar dendritic cells with fine melanin granules (nevus cells). The location of these cells detects if the nevus is junctional, subepithelial, or compound. In junctional, nests of nevus cells are present at the junction between the epithelial and subepithelial tissues. Junctional nevi may be tough to differentiate from PAM with atypia or melanomas histologically. Junctional nevi usually occur during childhood and pagetoid (intraepithelial) spread does not occur usually. Compound nevi of the conjunctiva show nevus cells within and beneath the epithelium. In subepithelial nevi, the cells are beneath the epithelium. Another variant, the combined nevus, is contains blue nevus and a junctional, compound, or subepithelial nevus. The blue nevus part of a combined nevi is smaller and deeper than other component.

Treatment and Prognosis

Nevi are benign and most do not need treatment or surgical excision. Sometimes nevi may be inflamed and exhibit times of rapid growth causing the clinical suspicion of malignancy. The

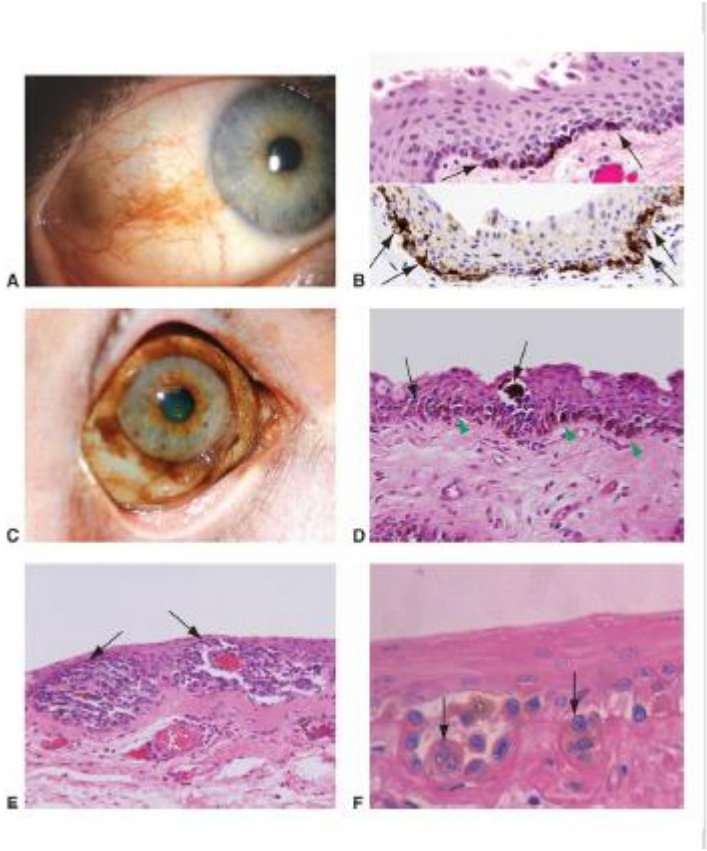
rapid growth occurs around puberty and most commonly found in compound nevi near the limbus. Patients with allergies can be prone. Histopathology shows the benign, inflammatory nature of nevi. Nevi of the palpebral conjunctiva, fornix, caruncle, and cornea should be suspicious of being malignant and an excisional biopsy needed.

PRIMARY ACQUIRED MELANOSIS

Clinical Presentation

PAM of the conjunctiva made of unilateral, multiple, flat, indistinct areas of golden to dark brown colour with irregular margins. The size and colour of PAM lesions changes over time. The lesions are freely mobile and involve any part of the conjunctiva. Slit-lamp biomicroscopy, includes lid eversion with careful inspection of the palpebral conjunctiva. Double eversion of the upper lid is needed to see the entire upper fornix. The lacrimal gland and lacrimal sac may be involved rarely by PAM. PAM is common in middle-aged /elderly whites and is rare in blacks of all ages. The prevalence of PAM in the general population ranges from 10% to 36%. The melanosis in PAM is due to an increase in melanin production (with or without melanocytosis). Malignant transformation of PAM lesions occurs when histologic atypia is present. 50% of patients with PAM with atypia may transform to melanoma. This rate is 90% for lesions that have epithelioid cells or a pagetoid growth. Malignant transformation is suspected in enlarging, highly vascularized lesions, and lesions more than 7.5 to 10 mm, or in lesions having patchy pigmentation. Development of nodules in a previously flat lesion is an ominous sign.

FIGURE 8: PAM – GROSS AND HISTOPATHOLOGICAL APPEARANCE



Histopathology

Clinical features cannot distinguish precancerous PAM (with histologic atypia) and benign PAM without atypia. Suspicious lesions, should undergo an excisional biopsy, because this is the only way to find the presence or absence of atypia. Lesions without histologic atypia never become malignant. Histologically, PAM lesions without atypia may have increased melanin production with or without melanocytosis. The melanocytosis is restricted to the basilar regions of conjunctival epithelium. Nuclear hyperchromasia is absent and nucleoli are not prominent. Patients with PAM without atypia tend are younger than patients with PAM and atypia. PAM without atypia become PAM with atypia. PAM with atypia has an increased chance of malignant transformation. Five patterns of atypical cells have been described with different rates of progression to melanoma. These are small polyhedral cells, spindle cells,

large dendritiform melanocytes, epithelioid, or polymorphous (mixture). The atypia degree increases with size of the nucleus and prominence of nucleoli. Lesions composed of epithelioid cells or showing pagetoid spread have highest rate of malignant transformation. Immunohistostaining with the monoclonal antibodies MIB-1 and PC-10 staining for the proliferation markers Ki-67 and the proliferating cell nuclear antigen (PCNA), may help differentiate between PAM with / without atypia.

Treatment and Prognosis

Complete excision of all lesions with atypia is goal of treatment, obtaining tumor-free margins. In diffuse PAM, excision of any nodular areas is important. Multiple map biopsies of the conjunctiva, and areas where there is no pigment, is needed in assessing the extent of the disease. Cryotherapy, radiotherapy, or topical mitomycin C are useful adjunctives. Topical mitomycin C is useful in patients with diffuse disease, with the entire ocular surface. Extensive cryotherapy of the limbus can affect the stem cell population. Cryotherapy causes necrosis of anterior segment. Six weekly cycles of topical mitomycin C 0.04% has good response,] but cytologic changes in the conjunctiva mimicking malignancy after giving topical 0.02% to 0.04% mitomycin C drops is also noted. These changes localized to the superficial layers of the conjunctival epithelium and include enlarged nucleus, chromatin smudging-hyperchromasia, cytoplasmic eosinophilia, single cell necrosis, and subepithelial inflammation. Primary acquired melanosis can recur after excision, and new lesions develop elsewhere on the conjunctiva. Due to risk of malignant transformation and the possibility of recurrences after excision, patients with PAM should have careful ocular examination and documentation and cervical LN status.

IV. VASCULAR TUMORS

PYOGENIC GRANULOMA

Pyogenic granuloma is proliferative fibrovascular response to tissue insult by either inflammation, surgery, or any nonsurgical trauma. It is classified as a polypoid form of acquired capillary hemangioma. It appears as an elevated red mass, often with a good blood supply. Microscopically, it is composed of “granulation tissue” with chronic inflammatory cells and small calibre blood vessels. As the lesion is neither pyogenic nor granulomatous, the name pyogenic granuloma is a misnomer. Pyogenic granuloma responds to topical corticosteroids, but most cases ultimately require surgical excision. In recurrence, low- dose plaque radiotherapy can be applied.

FIGURE 9a: PYOGENIC GRANULOMA – GROSS AND HISTOPATHOLOGICAL APPEARANCE

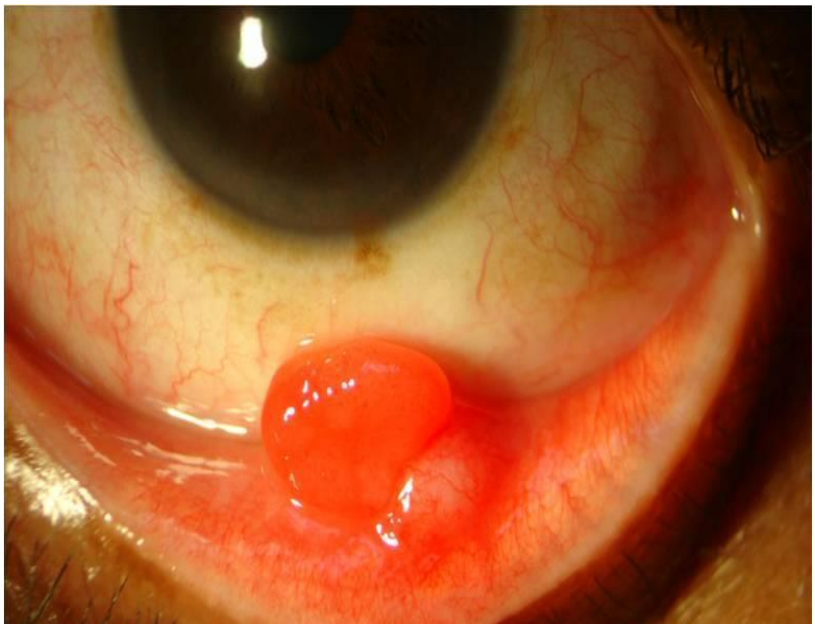
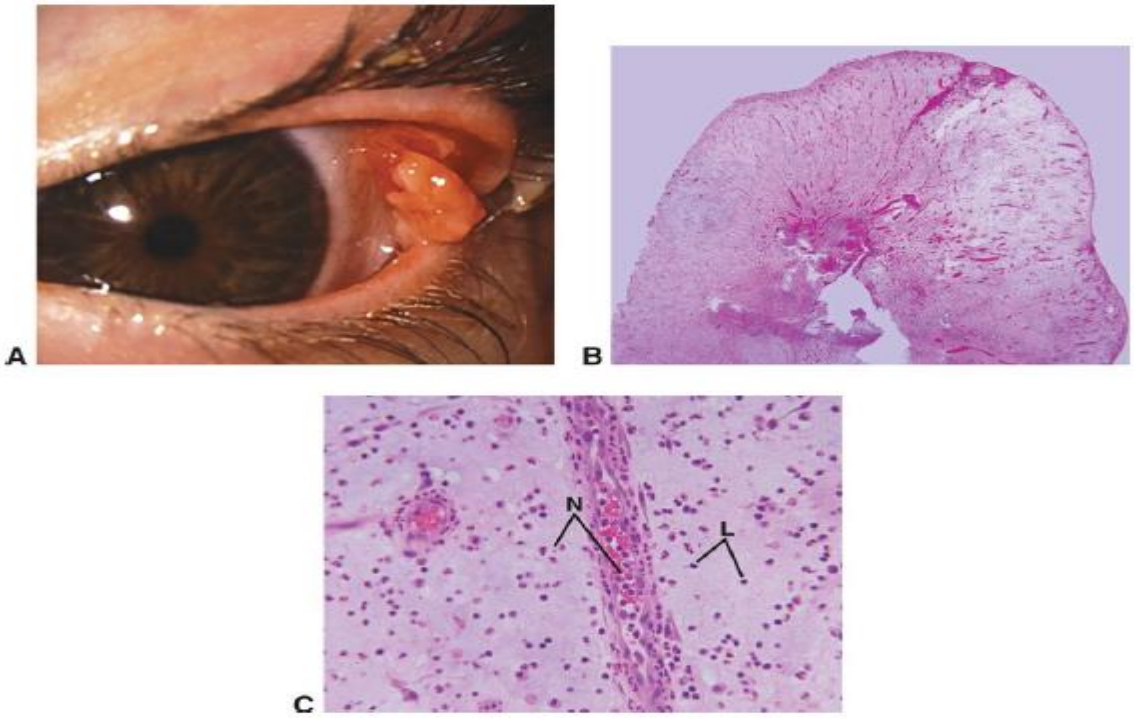


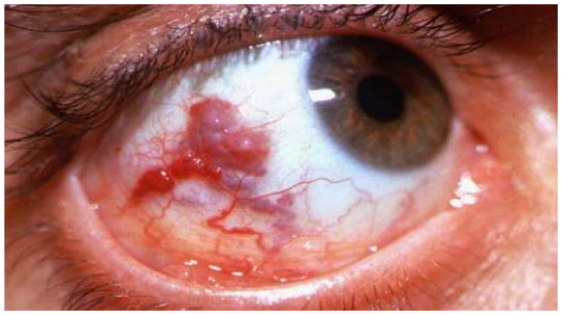
FIGURE 9b: PYOGENIC GRANULOMA – GROSS AND HISTOPATHOLOGICAL APPEARANCE



CAPILLARY HEMANGIOMA

Capillary hemangioma of conjunctiva generally occurs in infancy, or several weeks following birth, as red stromal mass, associated with cutaneous / orbital capillary hemangioma. The conjunctival mass may enlarge over several months and spontaneously involute. Management –observation, surgical resection /local /systemic prednisone can be given.

FIGURE 10 – CAPILLARY HEMANGIOMA – GROSS APPEARANCE



CAVERNOUS HEMANGIOMA

Cavernous hemangioma is rare. This benign tumor is a red or blue lesion in the deep stroma in young children. It is similar to the orbital cavernous hemangioma that is diagnosed in young adults.Managed by local resection.

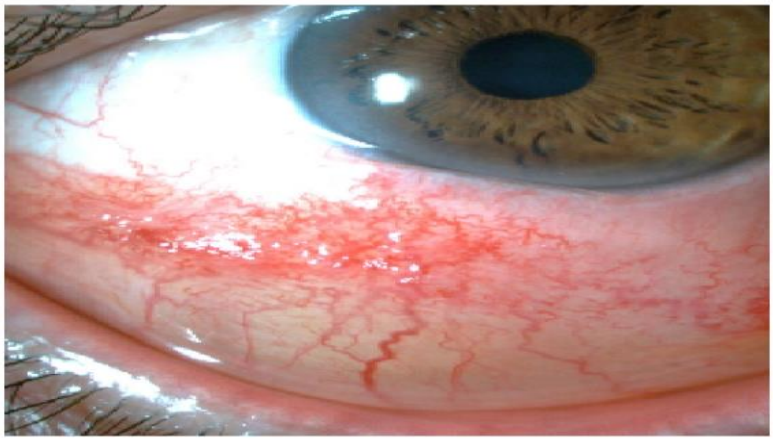
RACEMOSE HEMANGIOMA

Dilated arteriovenous communication without intervening capillary bed (racemose hemangioma) is found in conjunctiva. It remains stable for years and is monitored conservatively. Rule out Wyburn- Mason syndrome in these cases.

LYMPHANGIOMA

Conjunctival lymphangioma can occur as isolated conjunctival lesion or, is a superficial component of deeper diffuse orbital lymphangioma .It becomes clinically apparent in first decade and appears as multiloculated mass containing variable- sized clear dilated cystic channels .Blood is seen in most of the cystic space called “chocolate cysts.” The treatment of conjunctival lymphangioma is difficult because surgical resection or radiotherapy cannot eradicate the mass.

FIGURE 11 – GROSS APPEARANCE OF LYMPHANGIOMA



VARIX

Varix is a venous malformation found in orbit and the conjunctiva. It is a mass of dilated venous channels that enlarges with Valsalva manoeuvre. Treatment is cautious observation. If painful, cold compresses and aspirin may be used. Surgical resection should be cautious due to the risk for prolonged bleeding.

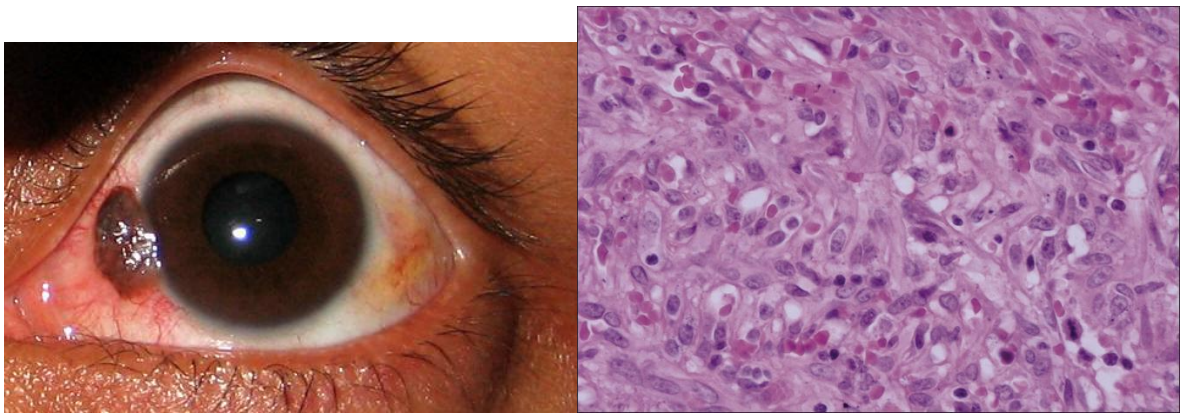
HEMANGIOPERICYTOMA

Hemangiopericytoma is made of pericytes that surround blood vessels. It shows both benign and malignant cytologic features. Appears as a red conjunctival mass originating from the stroma. Wide surgical resection with tumor- free margins is needed.

KAPOSI'S SARCOMA

Kaposi's sarcoma is a cutaneous malignancy that occurs in elderly /immunosuppressed patients.This tumor has become more common in AIDS and affects mucous membranes, such as conjunctiva. Clinically it appears as reddish vascular masses that resembles a hemorrhagic conjunctivitis. It is moderately responsive to chemotherapy and marked response to low- dose radiotherapy.

FIGURE 12: KAPOSI SARCOMA – GROSS AND HISTOPATHOLOGICAL APPEARANCE



V. FIBROUS TUMORS

FIBROMA

Fibroma is a rare conjunctival tumor which appears as a white stromal mass, unifocal or multifocal. Surgical resection is needed.

Fibrous Histiocytoma

It is a rare mass of the conjunctiva and made of fibroblasts and histiocytes. Clinically and histopathologically it is similar to many other amelanotic stromal tumors. In the conjunctiva it may be benign, locally invasive, or malignant. Wide excision with tumor- free margins is needed.

NODULAR FASCIITIS

It is a benign proliferation of connective tissue that commonly occurs in the skin and lesser in the eyelid, orbit, and conjunctiva. Clinically and histopathologically it resembles fibro sarcoma. The lesion is a solitary white mass in Tenon's fascia. Complete excision is needed as the lesion tend to recur.

VI. NEURAL TUMORS

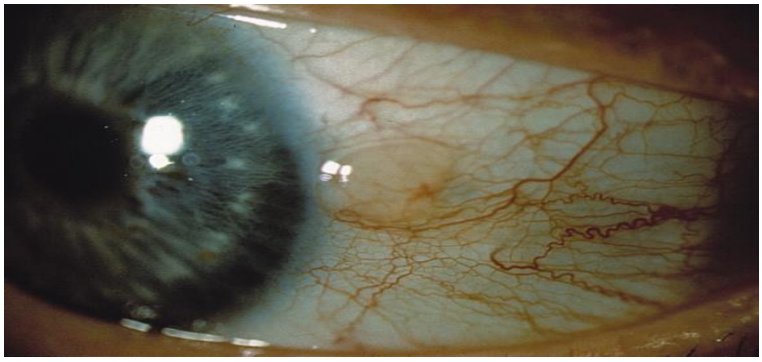
Neural tumors of the conjunctiva are rare. They manifest a more yellow appearance than fibrous tumors.

NEUROFIBROMA

It can occur in the conjunctiva as solitary /a diffuse / plexiform variety. The former is not associated with systemic conditions and the latter is a part of von Recklinghausen's neurofibromatosis. The solitary tumor is slowly enlarging raised stromal mass that is

managed by complete surgical resection. The plexiform type is difficult to surgically excise, and debulking procedures are necessary.

FIGURE 13: NEUROFIBROMA – GROSS APPEARANCE



NEURILEMOMA

Also known as schwannoma, is a benign proliferation of Schwann cells surrounding the peripheral nerves. This tumor commonly from the orbit, rare in the conjunctiva. Clinically, this lesion is yellowish- pink, nodular mass in conjunctival stroma. Complete excision is needed.

GRANULAR CELL TUMOR

It is a rare tumor it is of Schwann cell origin. This benign tumor and clinically appears smooth, vascular, and pink, and located in the stroma or within Tenon's fascia. Histopathologically, it is made of large round cells with granularity to the cytoplasm. Complete excision is needed.

VII. HISTIOCYTIC TUMORS

XANTHOMA

Xanthoma most common in the cutaneous dermis, near extensor surfaces and on the conjunctiva it is rare. Conjunctival xanthoma is a yellow subepithelial smooth mass affecting

epibulbar surfaces. Bilateral conjunctival involvement has been noted and is termed xanthoma disseminatum. Histopathologically, subepithelial infiltrate - lipidized histiocytes/, eosinophils, / Touton giant cells are noted.

JUVENILE XANTHOGRANULOMA

It is a relatively common cutaneous condition that is painless, pink skin papules with spontaneous resolution, in children under the age 2 years. Conjunctival, orbital, and intraocular involvement is seen. The conjunctival mass appears as an orange- pink stromal mass, typically in young adults. If the classic skin lesions are present, treatment with observation or topical steroid ointment is provided. Else, biopsy is needed, and recognition of the typical histopathologic features of histiocytes admixed with Touton's giant cells helps to confirm the diagnosis.

RETICULOHISTIOCYTOMA

It is a rare tumor, seen as part of a systemic multicentric reticulohistiocytosis. Clinically, the tumor is seen as a pink, vascular limbal mass in adult. Histopathologically, it is made of large histiocytes with granular cytoplasm.

VIII. **MYXOID TUMORS**

MYXOMA

Myxoma is a rare tumor that appears as orange- pink mass within stroma. This is associated with Carney complex, a syndrome of cardiac / systemic myxomas, cutaneous lentigines, and Sertoli cell tumor of testicles. Histopathology shows slender stellate and spindle cells interspersed in loose stroma.

IX. **LIPOMATOUS TUMORS**

LIPOMA

It is rare and generally is found in adults as yellowish- pink stromal mass.Most are the pleomorphic type having large lipid vacuoles surrounded by stellate cells.

FIGURE 14 – LIPOMA – GROSS APPEARANCE

HERNIATED ORBITAL FAT

Orbital fat presents in the conjunctiva as a herniation from superotemporal orbit. The condition is bilateral and represents deficiency in orbital connective tissue to maintain the proper location of orbital fat. Clinically, it is deep to Tenon's fascia and is prominent on inferonasal gaze. Digital reposition of the fat into the orbit is possible, but only temporary. Management is observation.If dry eye occurs resection of the herniated fat and resuspension of the orbit position of the fat is done. Histopathologically, the tissue is made of large lipid cells.

LIPOSARCOMA

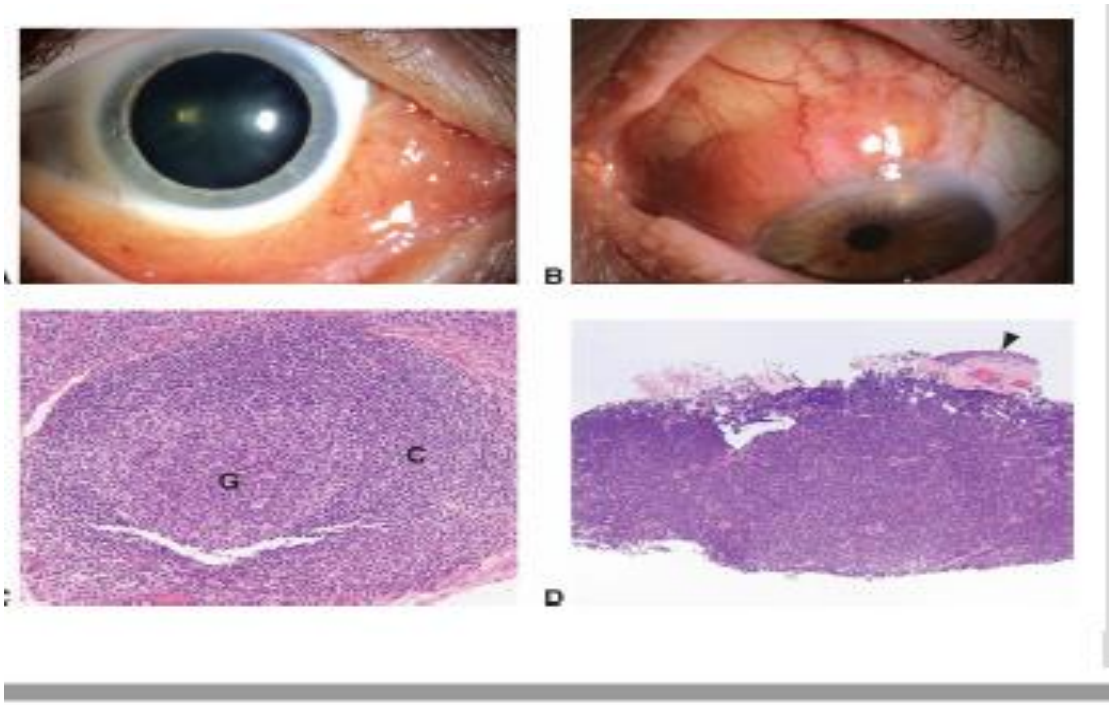
It has been rarely seen and shows features similar to lipoma. Histopathologically, neoplastic stellate lipid cells and "signet- ring" type cells have been seen.

X. **LYMPHOID TUMORS**

Lymphoid tumors can be isolated lesions or manifestation of systemic lymphoma.

Clinically, appears as a diffuse, slightly elevated pink mass in the stroma or deep to Tenon's fascia, most common in the forniceal region. This is similar to the smoked salmon; and so called the "salmon patch". It is tough to differentiate between a benign and malignant lymphoid tumor.So, biopsy is needed to establish the diagnosis, and systemic evaluation needed in all affected patients to exclude the possibility of systemic lymphoma. Histopathologically, "sheets of lymphocytes" are found & classified as reactive lymphoid hyperplasia or malignant lymphoma. Mostly they are B- cell lymphoma (non- Hodgkin's type). Rarely T- cell lymphoma is seen .Treatment of the conjunctival lesion includes chemotherapy if systemic lymphoma is present or external beam irradiation (2,000 to 4,000 cGy) if it is localized to the conjunctiva. Other options are excisional biopsy & cryotherapy, local interferon injections/ observation.

FIGURE 15: LYMPHOMA – GROSS AND HISTOPATHOLOGICAL APPEARANCE



XI. **LEUKEMIA**

Leukemia manifests in the ocular region as hemorrhages due to anemia and thrombocytopenia rather than leukemic infiltration.Leukemic infiltration can be found with CLL. The tumor appears as a pink smooth mass in the conjunctival stroma at the limbus/ the fornix, similar to a lymphoid tumor. Biopsy shows sheets of large leukemic cells. Treatment of the systemic condition is needed with secondary resolution of conjunctival infiltration.

XIII. **METASTATIC TUMORS**

These rarely occur in the conjunctiva, can be from breast carcinoma, cutaneous melanoma, and other primary tumors. Metastatic carcinoma is one or more fleshy pink vascularized conjunctival stromal masses. Metastatic melanoma to the conjunctiva is pigmented.

XIV**. SECONDARY CONJUNCTIVAL INVOLVEMENT FROM ADJACENT TUMORS**

The conjunctiva may be secondarily involved by adjacent structures tumours, by direct extension from tumors of eyelids. The most important tumor causing is sebaceous gland carcinoma of the eyelid. This shows pagetoid invasion & extends into the conjunctival epithelium & causes clinical picture similar to chronic unilateral blepharoconjunctivitis. Uveal melanoma in the ciliary body can go extrasclerally to the subconjunctival tissues, producing a primary conjunctival tumor. Rhabdomyosarcoma of orbit, a tumor found in children, presents first with conjunctival lesion before the orbital mass is discovered.

XV. **CARUNCULAR TUMORS AND CYSTS**

The caruncle is a unique that contains elements of conjunctiva and skin. The tumors in the caruncle are similar to those in mucous membranes and skin. By histopathologic, 95% caruncular tumors are benign and 5% are malignant. The most common lesions are papilloma

and nevus. Other lesions are pyogenic granuloma, inclusion cyst, and sebaceous hyperplasia, & sebaceous adenoma, oncocytoma. Malignant tumors like squamous cell carcinoma, melanoma, lymphoma, & sebaceous carcinoma are rare in the caruncle. The oncocytoma is benign tumor occurs more commonly in lacrimal / salivary glands. In caruncle it arises from accessory lacrimal gland tissue &often has a blue cystic appearance. The treatment of caruncular masses is observation / local resection

XVI. OTHER MISCELLANEOUS LESIONS THAT CAN SIMULATE CONJUNCTIVAL NEOPLASMS

A few nonneoplastic conditions can be similar to neoplasms. These include pinguecula, pterygium, foreign body, inflammatory granuloma, amyloidosis. In most cases, the history and clinical finding, and in some excision of the mass may help to exclude a neoplasm.

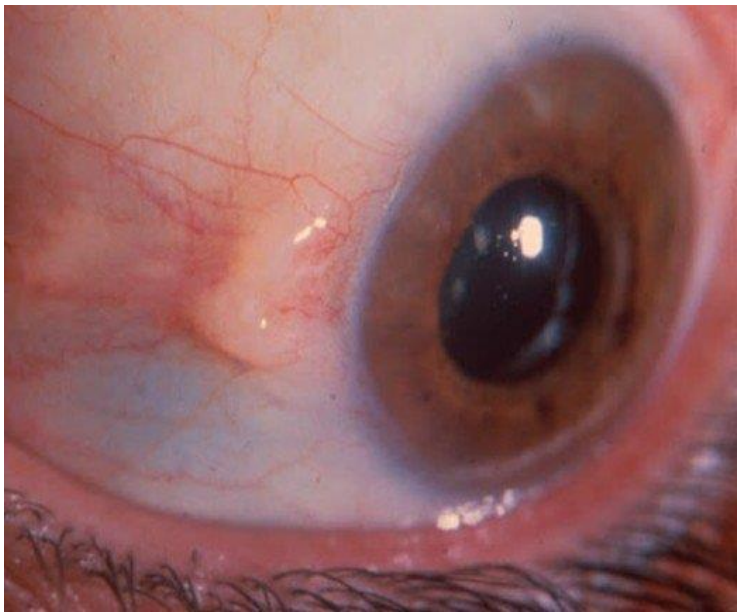
XVII. DEGENERATIONS

PINGUECULA AND PTERYGIUM

A pinguecula is small, yellowish nodule, bilateral and located at the nasal / temporal limbus. A manifestation of actinic damage “exposure to sunlight” or environmental factors, like dust and wind, ageing- this growth is more common. On histology, the stromal collagen has fragmentation and basophilic degeneration known as elastotic degeneration as the degenerated collagen stains positively when using histochemical stains for elastic fibre like the Verhoeff–van Gieson stain. A pterygium is like the pinguecula in etiology & location but differs in its invasion of the ‘superficial cornea’ as a vascular, wing-shaped growth. Histology shows elastotic degeneration; prominent blood vessels may be seen if vascularity seen clinically and variable amount of chronic inflammation. Recurrent pterygia may not have histologic feature of elastotic degeneration and are exuberant fibroconnective tissue response. In pingueculae and pterygia overlying epithelium may show mild squamous metaplasia.

Thus, with actinic damage to the skin, there is the possibility for future malignant transformation, though this occurs in rare cases with pingueculae and pterygia. If conjunctival squamous neoplasia occurs, it occurs over an area of preexisting elastotic degeneration. If epithelial hyperplasia, nuclear hyperchromasia and pleomorphism, & excess mitotic figures are seen in an excised pinguecula or pterygium, a diagnosis of OSSN should be assigned.

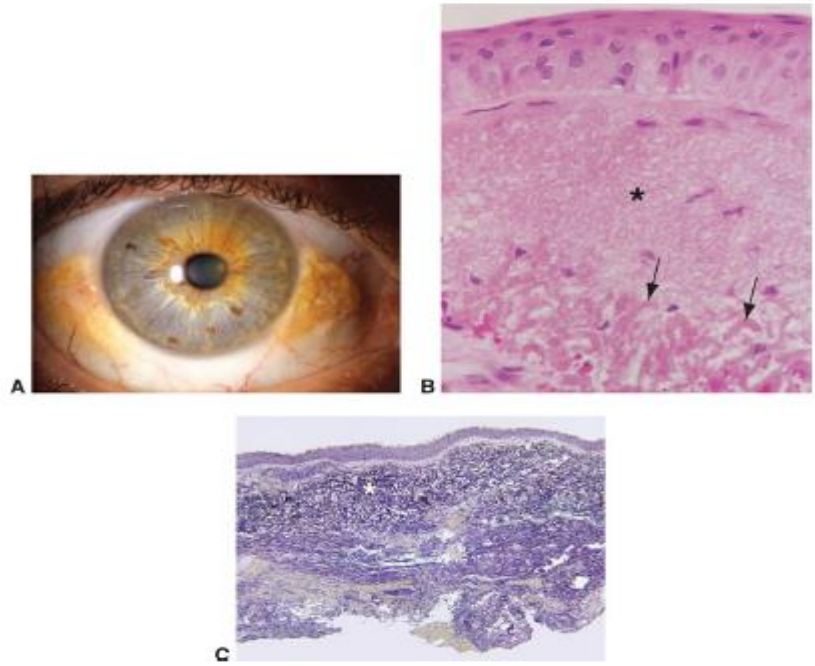
FIGURE 16: PINGECULA GROSS APPEARANCE



SENILE SCLERAL PLAQUES

These occur in the sclera rather than the cornea / conjunctiva. These lesions areYellow, gray, /black vertical bands anterior to insertion of the medial & lateral rectus muscles in elderly. They are more common after 60 years, like pinguecula and pterygium, may be due to UV exposure. Histologically, calcium deposits with reduced cellularity and hyalinization are seen. They do not need therapy

FIGURE 17: SENILE SCLERAL PLAQUE – GROSS AND HISTOPATHOLOGICAL APPEARANCE

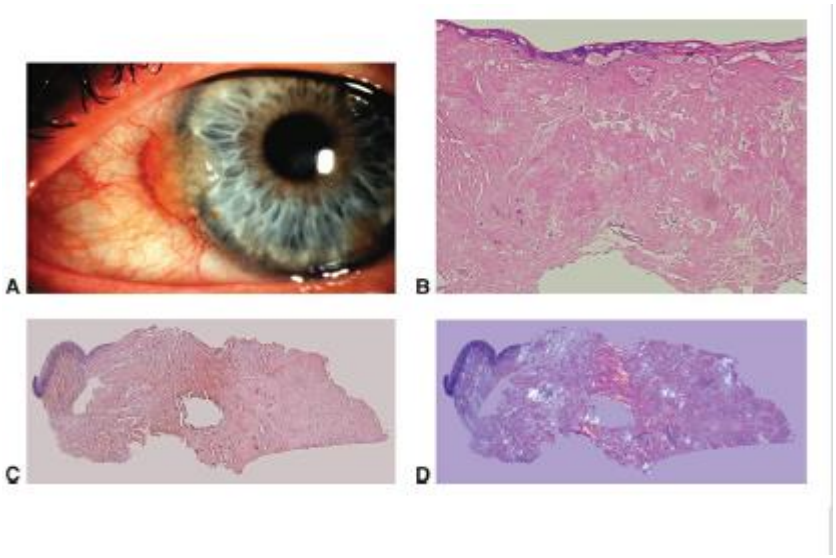


AMYLOID DEPOSITS

It is most commonly an idiopathic localized process in healthy young and middle-aged adults. They are typically made of monoclonal immunoglobulin “AL amyloid” produced by local clonal plasma cells. Conjunctival amyloidosis is due to long-standing inflammation, like with trachoma (AA amyloid). Conjunctival amyloidosis may occur in primary conjunctival lymphoma /plasmacytoma (or) secondary to systemic lymphoma / plasma cell myeloma. Clinically, conjunctival amyloidosis seen as a salmon-coloured nodule which is associated with hemorrhage. Histologically, appears as eosinophilic extracellular deposits in the stroma, in a perivascular distribution. On Congo red stain, under standard light, amyloid deposits are seen orange. When viewed with polarized light & rotating polarization filter, they exhibit birefringence. Other useful staining methods -crystal violet and the fluorescent stain

thioflavin. Electron microscopy shows fibrils. Immunohistochemical methods, sequencing & mass spectrometry–based proteomic analysis are used in amyloid subtyping.

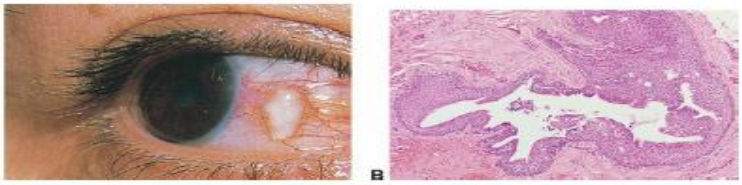
FIGURE 18: AMYLOID DEPOSITIS – GROSS AND HISTOPATHOLOGICAL APPEARANCE



EPITHELIAL INCLUSION CYST

This may form at a site of previous accidental / surgical trauma (like after strabismus surgery, retinal surgery, or enucleation). Clinically, it is a transparent, cystic elevation on the ocular surface with associated injection. Histologic examination shows cystic space lined by conjunctival epithelium in the stroma. The lumen may be empty / have inspissated proteinaceous material & cellular debris.

FIGURE 19: EPITHELIAL INCLUSION CYST – GROSS AND HISTOPATHOLOGICAL APPEARANCE



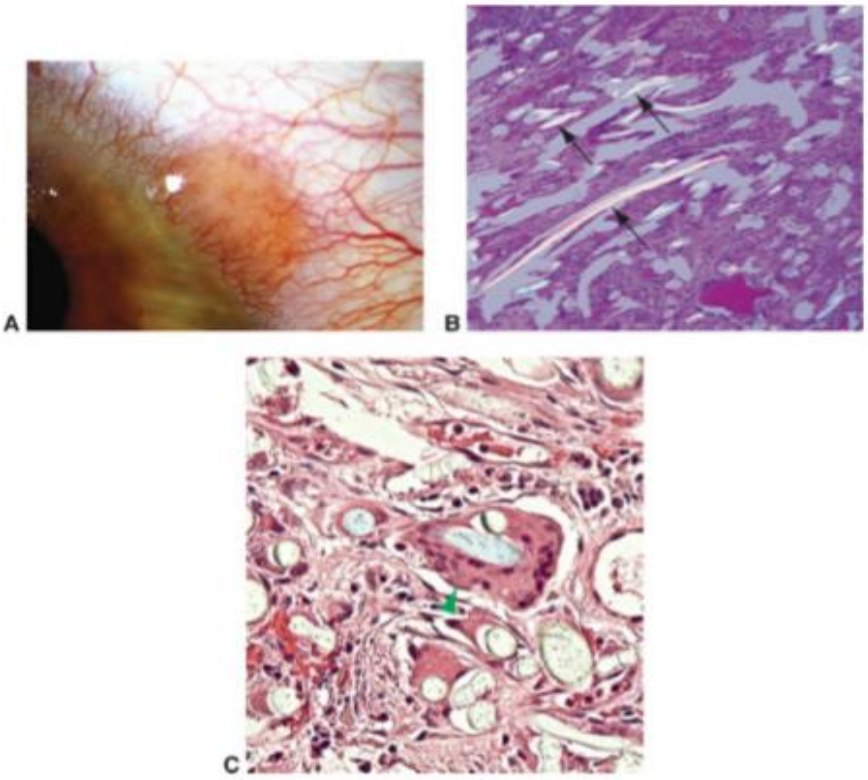
XVIII. GRANULOMATOUS CONJUNCTIVITIS

It is less common than papillary conjunctivitis and follicular conjunctivitis and has infectious and non-infectious causes. Clinically, the nodular elevations of granulomatous conjunctivitis is tough to distinguish from follicles, but the history and systemic symptoms may help in the diagnosis. Granulomatous conjunctivitis with preauricular lymphadenopathy is known as "Parinaud oculoglandular syndrome". Bacteria like Bartonella henselae (causing cat-scratch disease) & Francisella tularensis (causing tularemia), mycobacteria (Mycobacterium tuberculosis), treponemes (syphilis), and fungi (sporotrichosis) may cause. Microorganisms may be seen with Gram, acidfast / silver stains. The diagnosis is based on the culture results, serology, PCR, or combination of all. If biopsy is done, the granulomas in granulomatous conjunctivitis will show central necrosis. In non-infectious cause of granulomatous conjunctivitis like sarcoidosis, involve all ocular tissues, also the conjunctiva. It occurs as small tan nodules with no inflammatory signs, within the fornix. Conjunctival biopsy is a simple way of giving diagnostic confirmation of systemic disease. Histologically, noncaseating granulomatous "tubercles" are seen within the conjunctival stroma, with a minimal cuff of lymphocytes & plasma cells. The diagnosis of sarcoidosis is made if supported by clinical features and infectious causes of granulomatous inflammation have been ruled out by histochemical and by culture results.

FOREIGN BODY GRANULOMA

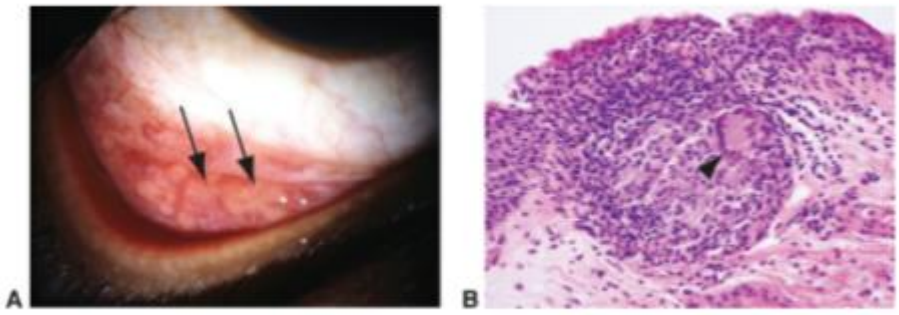
Since it is exposed surface, the conjunctiva is open to contact with foreign bodies. Some are transient & inert, others may become embedded and cause a foreign-body reaction, seen histologically as granuloma around the foreign object. Multinucleated giant cells are seen. Viewing the tissue section under polarized light may be useful in identifying the offending foreign object.

FIGURE 20: FOREIGN BODY GRANULOMA – GROSS AND HISTOPATHOLOGICAL APPEARANCE



SARCOID GRANULOMA

FIGURE 21: SARCOID GRANULOMA – GROSS AND HISTOPATHOLOGICAL APPEARANCE

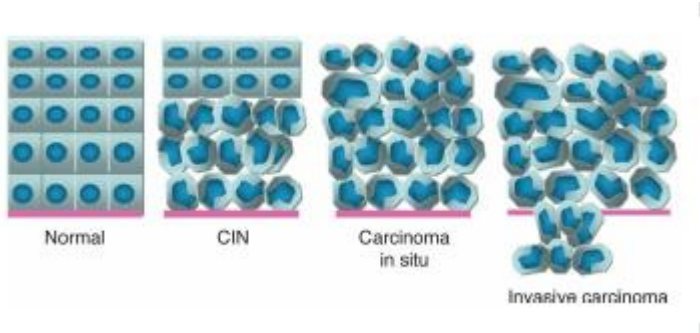


XIX**. MALIGNANT LESIONS**:

CONJUNCTIVAL- INTRAEPITHELIAL NEOPLASIA (CIN) AND SQUAMOUS CELL CARCINOMA (NON PIGMRNTED)

Epithelial neoplasia of the ocular surface is a disease complex, having a spectrum of changes within the epithelial layers. Previously known as Bowen's disease and ocular surface squamous neoplasia. Conjunctival- corneal intraepithelial dysplasia (CCIN) is used if the cornea is also involved. The earliest change is dysplasia, limited by the underlying epithelial basement membrane. Increasing degrees of dysplasia occurs if process is not stopped resulting in transgression of the basement membrane and invasion of underlying space & structures. This invasion of subjacent tissue is hallmark of squamous cell carcinoma. Histologic examination is needed for definitive diagnosis.

FIGURE 22: DIAGRAMMATIC REPRESENTATION OF HISTOPATHOLOGY OF VARIOUS CONJUNCTIVAL NEOPLASIA



Incidence and Etiology

CIN occurs in elderly, with light- complexioned men having extensive actinic exposure... The incidence of SCC of the eye has been calculated to increase 49% for every 10-degree decrease in latitude. Previous H/O skin cancer is positive prognostic indicator for CIN. Apart

from ultraviolet light, other reported risk factors are previous H/O skin cancer, smoking, ocular trauma, petroleum derivative exposure. Human papilloma virus (HPV), types 16 and 18, has been found in conjunctival epithelial neoplasia by immunohistochemical and other molecular analysis. The role of HPV in the etiology of CIN is unclear. Atypical, rapidly progressive CIN in younger patients is associated with HIV. CIN has been found in younger organ transplant patients using long- term cyclosporine. Xeroderma pigmentosum is an AR disorder characterized by inadequate repair of DNA damage due to ultraviolet radiation. Affected patients are prone to epithelial cancers, those of the conjunctiva & cornea. The limbus is the transitional zone, from columnar conjunctival to stratified squamous corneal epithelium. Within crypts of Vogt are the limbal stem cells. This area is similar to the uterine cervix. Similar to cervical tissue, the corneal limbus is the site of origin for the majority of dysplastic & neoplastic changes of the ocular surface.

Clinical Presentation

The patient with CIN presents with ocular irritation /complaints of redness /“growth on the eye.” Vision is not affected. Differentiation of benign from malignant surface tumors is difficult in slit lamp examination even for the experienced. Examination reveals a vascular limbal mass, within interpalpebral area. The affected area is thick, and may appear gelatinous /velvety. Gelatinous thickening, with superficial blood vessels, is common. CIN may mimic diffuse chronic conjunctivitis with mild thickening. Other less common presentations are sclerokeratitis, which is a focal corneal or scleral thinning with inflammation without any tumor mass. Sclerokeratitis is similar to interstitial keratitis or Mooren’s ulcer. Biopsy is needed in atypical /chronic scleritis / conjunctivitis unresponsive to standard treatment. Hyperkeratosis is a characteristic feature of CIN and manifest as a white surface plaque, / “leukoplakia”, which has no diagnostic significance. Neoplastic cells invades corneal epithelium, as a continuation of limbal CIN. Neoplastic cells may originate at the limbus and

migrate centrally. Affected epithelium looks translucently gray, with sharply demarcated border. Finger- like protrusions, and isolated islands are found on the leading edge. The epithelium inside the lesion is thickened, and blood vessels are present, especially close to limbus. Spontaneous regression may occur.

Marked thickening of a limbal lesion and fixation of the mass to underlying tissue, suggests squamous cell carcinoma. Biopsy may yield helpful diagnostic information. In exfoliative cytology and impression cytology, superficial cells are removed, fixed and stained with a Papanicolaou technique, and studied by a cytopathologist. In exfoliative cytology cells are taken away with a sterile platinum spatula, but in impression cytology cells are retained in cellulose acetate paper strips, that are pressed against the area in doubt. Cells are graded on degree of atypia, (including size, shape, nuclear and nucleolar characteristics, and mitotic figures). Cytology is positive in 77% of biopsy- proven cases.

Differential Diagnosis

i) Benign epithelial lesion– associated thickening and surface keratin.

ii) Irritation caused by stromal inflammation or by pinguecula or pterygia may cause pseudoepitheliomatous hyperplasia, and thickening of the epithelium and leukoplakia. Biopsy reveals the benign acanthosis and hyper keratosis without dysplasia. Simple excision is done.

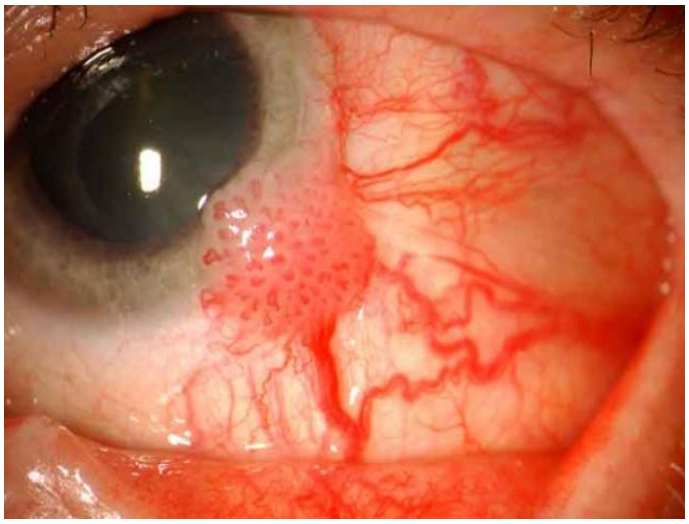
iii) Actinic keratosis of the ocular surface is due to UV radiation. These lesions occur in older, light complexioned people with previous exposure to sunlight, the same population at higher risk for CIN. Thickening with hyperkeratosis is present. Histopathologic examination may show, mild acanthosis with hyperkeratosis &inflammation, to marked acanthosis with cellular pleomorphism.

iv) Benign conjunctival papillomas,

v) Chronic conjunctivitis

vi) Inflammation of a pinguecula or pterygium

FIGURE 23: OSSN – GROSS IMAGE



Pathology

Histologic examination is needed for definitive diagnosis.In small lesion, excisional biopsy and removal of the entire mass is done. Incisional biopsy of the atypical area is performed for larger lesions. Staining with hematoxylin- eosin and PAS is sufficient for the diagnosis of CIN lesions. Biopsy helps to determine the depth of the lesion, & whether the margins are free of tumor. The transition from normal to abnormal epithelium is sudden.

Specimens are graded based on location and degree of atypia.

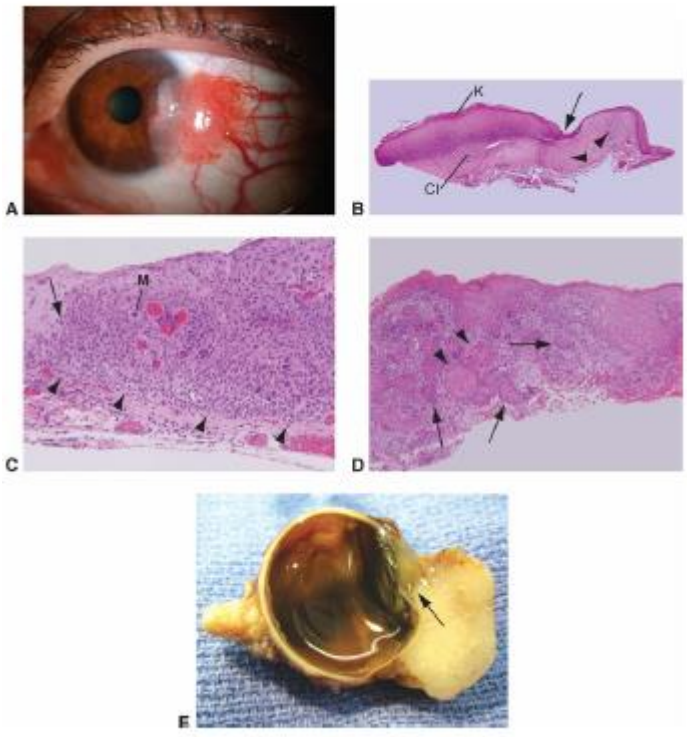
Full- thickness dysplasia indicates carcinoma- in- situ.

Extension of tumour to sub epithelial space (substantia propria, sclera, or cornea) indicates squamous cell carcinoma. Advanced tumors may enter into ciliary body, iris, and trabecular meshwork.

Mucoepidermoid carcinoma is uncommon in the conjunctiva. Clinically it is difficult to differentiate from CIN. Histopathology shows epidermoid and mucus- secreting cells. Special stains for mucin, like Alcian blue / mucicarmine are used in diagnosis.As mucoepidermoid carcinoma of the conjunctiva is locally aggressive than CIN, this diagnosis needs proper follow up for invasion and recurrence.

Spindle cell carcinoma is aggressive variant of conjunctival squamous cell carcinoma arising on the ocular surface. Clinical differentiation of this tumor is difficult. Pathologically, pleomorphic spindle cells are seen, arranged in fascicles. Immuno histochemical analysis using cytokeratin stains demonstrates the epithelial origin of spindle cell carcinoma. Transmission electron microscopy may be used in difficult cases.

FIGURE 24: OSSN – GROSS AND HISTOPATHOLOGICAL IMAGE



Treatment

Surgical excision of suspicious area is the approach to therapy, if the entire lesion can be removed in toto. Staining with rose Bengal will highlight abnormal epithelium. A wide margin of 2 to 3 mm around the visible tumor is seen.

Frozen section control can shoe lateral surgical margins, not helpful with the deep margins. Cryotherapy with a nitrous oxide probe done after surgical excision decreases the recurrence rate of CIN. After removal of the lesion with 2- to 3-mm free margins, freezing the remaining conjunctival margins and the sublesional base is done with formation of ice ball for 6 seconds, followed by slow thaw. A double freeze- thaw technique is usually done; but three cycles are better if inadequate removal of tumor is suspected. Cryotherapy destroys tumor cells by 'thermal disruption' & resultant local ischemia. Side effects of cryotherapy are elevation or decrease in IOP, corneal scarring, iris atrophy, and destruction of retina. Local application of beta- irradiation is used as primary treatment of squamous epithelial tumors, & treatment of incompletely excised squamous tumors. Other side effects of irradiation are dose related and include cataract, secondary glaucoma, local scarring, dry eye, & loss of cilia. The threshold dose to prevent cataract of surface strontium 90 is estimated to be 5,000 rads. Therapy with antimetabolite agents is beneficial in the adjunctive treatment of partially excised corneal epithelial neoplasia & initial therapy in recurrent disease, extensive disease having ill- defined borders/ situations in which excessive conjunctiva may be taken off, leading to severe dry eye /limbal stem cell deficiency. "The rationale is use the highest possible dose against the smallest amount of tumor". Both MM-C and 5-FU have a selective effect on rapid growing tumor cells. Due to dose- related local toxicity, intervening rest periods between topical chemotherapy are employed. Rest intervals spares the limbal stem cells. Punctal plugs needed to protect the NL system during therapy to reduce systemic absorption, or manual punctal occlusion may be done after each dose of drug. The ability of

topical treatment to eradicate tumor cells located in the subepithelial space is an area of concern in possible squamous cell carcinoma with scleral invasion. Long- term observation is needed, as squamous cell carcinoma may recur. Mitomycin C (MMC) is a chemotherapeutic antibiotic from Streptomyces caespitosus, which is used as an alkylating agent and inhibits DNA synthesis. MMC also has an effect on fibroblasts and stem cells. Therapeutic applications include 0.02% or 0.04% MMC QID for 14-day courses; 0.02% MMC TDS for 14 days; and 0.04% MMC QID for 1 week cycles. A combination of excision, cryotherapy, and topical MMC is effective in recurrent CIN. Adverse reactions to topical drug mild hyperemia and tearing, photophobia, hyperemia, PEK, and blepharospasm. Pain occurs if used more than 14 days; stoppage of therapy leads to decrease of pain. More severe side effects, including scleral ulceration and perforation. 5--FU drug has antimetabolite properties, rapidly growing cells accumulate lethal amounts of 5-FU. 5-FU is useful as an adjunct in recurrent or incompletely excised squamous cell carcinoma. 1% 5-FU in artificial tear base TDS- QID daily for 2- to 3-week cycles, until epithelium sloughs off. Clinical improvement or resolution of intraepithelial neoplasia seen in all cases.

Recombinant interferon- alfa-2b

It has been used successfully in the treatment of CCIN, with an initial injection of 3 million international units (IU), followed by “topical” interferon- alfa-2b drops (1 million IU/mL) QID daily. If clinical response was noted by 1 week, topical therapy was continued until resolution of the CIN. If response seen at 1week, subconjunctival and perilesional injections are given three times weekly until clinical resolution. No complications seen with topical therapy, though fever and myalgia may occur with subconjunctival dose.

Intralesional interferon alfa-2b is also successful in the treatment of squamous cell and basal cell carcinoma of the skin. The mechanism is unknown. Regression occurred after 6 weeks of

topical therapy with cidofovir (2.5 mg/mL), one drop 2 hourly initially, with a weekly taper in frequency over the next 6 weeks. A residual focus needed excision, followed by cryotherapy. If spread to the regional lymph node occurs, radical neck dissection may be done

Prognosis

Conjunctival CIN, including squamous cell carcinoma, is a low- grade malignancy. Recurrence is by the integrity of surgical margins, so need for wide margins and histopathologic examination is stressed. The degree of histologic atypia and presence of subepithelial neoplastic cells (squamous cell carcinoma) corresponds to recurrence rate. The majority of neoplasia recur before 2 years, though recurrences have occurred as late of 5 years after excision. Intraocular invasion in 3% to 11% of patients with conjunctival SCC. The mucoepidermoid variant is aggressive and invades adjacent tissues. Extension of squamous cell carcinoma commonly affects the sclera, anterior chamber, trabecular meshwork, ciliary body, and choroid. If globe is invaded iridocyclitis, ciliary body elevation, and secondary glaucoma occurs. Orbital invasion seen in 11% to 15% of invasive SCC of the conjunctiva. Exenteration is needed in cases involving the orbit. Conjunctival squamous cell carcinoma may metastasize to the preauricular and cervical LN, with an incidence of 0 to 4%. Metastases to the parotid gland, lungs and bone occur rarely.

SEBACEOUS CARCINOMA

Etiology and Incidence

Sebaceous carcinomas occur from adnexal epithelium of sebaceous glands throughout the body. The ocular adnexa contributes for 25% of sebaceous carcinoma and is the common locale for these tumors. Sebaceous carcinomas may occur in the meibomian glands of the tarsus, the glands of Zeiss at the lid margin, & sebaceous glands of the caruncle or

surrounding skin / eyebrow. The most common adnexal site is the meibomian glands of the upper and lower lids. Meibomian glands are larger compared to the sebaceous glands elsewhere & not associated with hair follicles. Sites of sebaceous carcinoma- meibomian glands, glands of Zeiss, & caruncle, eyebrows, eyelids. Other sites include -external genitalia, parotid and submandibular glands, external auditory canal, and the trunk and upper extremity. Older patients are more commonly affected, with diagnosis usually between the 5 th and 9 th decade of life, though cases in children have been reported .Sebaceous carcinoma in younger patients with HIV virus have been noted.

Sebaceous carcinoma may occur postradiation treatment for other tumors

Clinical Presentation

Sebaceous carcinoma may occur in a variety of ways, mimicking common conditions and delaying diagnosis. The usual presentation is that of a painless, slowly progressive mass arising within the eyelid. The upper lid is most commonly involved. Ulceration of the eyelid skin typically occurs late, unlike basal cell or squamous cell carcinomas, although ulceration may occur earlier in cases originating near the lid margin. Sebaceous carcinoma may cause atrophy and loss of lashes. A yellow tint is found in some cases. The eyelid tumor may remain relatively small, whereas intraepithelial spread of tumor cells leads to inflammation of the ocular surface. Thus, sebaceous carcinoma may resemble benign conditions such as conjunctivitis, blepharoconjunctivitis, blepharitis, superior limbic keratoconjunctivitis, and keratitis .Symblepharon formation and corneal neovascularization may occur. Sebaceous carcinoma presenting as a papillary growth of the palpebral conjunctiva has been described. Sebaceous carcinoma of the eyelid may be thought as a chalazion. Chalaza tend to occur rapidly, whereas sebaceous carcinoma is slowly progressive. Helpful differentiating signs in carcinoma include adhesion of the skin to a firm underlying mass, erythema, trichiasis,

destruction of the cilia, and conjunctival cicatrization. Growth or spread of a localized carcinoma may conceivably be facilitated by inappropriate incision and curettage. A longstanding recommendation has been to perform a full- thickness eyelid biopsy for all recurrent eyelid masses originally felt to be a chalazion. Clear communication by the surgeon of any suspicion or concern for sebaceous carcinoma to the ophthalmic pathologist is important...

Pathology

Sebaceous carcinoma requires biopsy for definitive diagnosis. Any suspicion of sebaceous carcinoma by the surgeon should be communicated to the ophthalmic pathologist, as special preparation of the specimen is required. Routine processing of formalin- fixed tissue will remove intracellular lipid; fresh frozen sections, however, will preserve this lipid, which can then be stained with oil red- O or other fat stains to facilitate diagnosis. Difficulties may arise in pathologic diagnosis of sebaceous carcinoma, as well as in clinical diagnosis. It is most frequently misdiagnosed as basal cell carcinoma or squamous cell carcinoma. Unlike these epithelial tumors, sebaceous carcinoma will often have an identifiable site of origin deeper within the eyelid. Well- differentiated tumors are composed of pleomorphic cells with foamy or vacuolated cytoplasm. Fresh frozen sections stained with oil red- O or other fat stains will demonstrate lipid within the cytoplasm. Less differentiated neoplasms contain less lipid and a more basophilic cytoplasm, as well as mitotic figures. These cells may be mistaken for basal cell carcinoma.Such tumors may simulate squamous cell carcinoma. Intraepithelial carcinomatous change may occur in either eyelid skin or conjunctiva, or in both. Individual cells or small clusters may be found within epithelium. This pattern is called “pagetoid” spread, as it resembles intraepithelial spread in Paget disease of the breast. Intraepithelial involvement may also resemble severe dysplasia or squamous carcinoma- in- situ, replacing the entire epithelium with malignant sebaceous cells. Intraepithelial involvement was noted in

44% of 104 specimens and in 50% of 40 specimens. Severe chronic inflammation is usually present, correlating with the clinical inflammation seen in cases mimicking chronic blepharitis, conjunctivitis, or keratitis. The various clinical and pathologic presentations of intraepithelial sebaceous carcinoma illustrate the necessity of full- thickness eyelid biopsy to find the underlying tumor. Excision of skin or conjunctiva only may lead to erroneous diagnosis. Cases of sebaceous pagetoid spread without underlying eyelid tumor have been reported. One possible reason for this phenomenon is regression of the original tarsal tumor. Residual nests of sebaceous carcinoma in areas of tarsus with fibrosis and inflammation seen in some cases lend support to this explanation.

EVALUATION OF A PATIENT WITH SEBACEOUS CARCINOMA

If sebaceous carcinoma is confirmed by biopsy, a complete history, family history, physical examination, and complete eye examination is indicated. The family history should be inquired about benign or malignant skin lesions, as well as internal malignancies that characterize Muir- Torre syndrome. Complete evaluation of the skin for other cutaneous tumors as well as palpation of the lymph nodes should be performed. Baseline studies include chest x- ray, liver function tests, and complete blood count. If the clinician suspects the possibility of Muir- Torre syndrome, further testing includes rectal examination, colonoscopy, and barium enema. Mammography may be needed.

Treatment

Wide surgical excision with eyelid reconstruction is the primary treatment for sebaceous carcinoma of the eyelid. The goal is to obtain 5- to 6-mm surgical margins clear of tumor by fresh frozen tissue control. If the conjunctiva is involved, map biopsies to determine the presence and extent of pagetoid spread is useful. As originally described by Putterman, local anesthesia of the eyelids as well as palpebral and bulbar conjunctiva is achieved with 2%

lidocaine with epinephrine. Biopsies of conjunctiva and underlying tarsus are obtained from the temporal, central, and nasal areas of the upper and lower eyelids, as well as temporal, central, and nasal bulbar conjunctiva. Full- thickness excision of the eyelid in any involved area is then performed under frozen section control, with 5-mm normal margins. Adjunctive cryotherapy to areas of affected conjunctiva has been described in six patients. In each case wide resection of the eyelid was followed by cryotherapy to affected conjunctiva as determined by mapping. A concern of any technique using representative biopsies is failure to diagnose clinically inapparent areas of involvement. Mohs micrographic surgery (MMS) of eyelid sebaceous carcinoma has been described, with primary repair of the ensuing eyelid defect by an oculoplastic surgeon. Spencer and colleagues reported a recurrence rate of 11% in 18 patients with an average follow- up of 37 months. Radiation therapy is considered palliative and not curative in sebaceous carcinoma... If diffuse spread into both eyelids is found, and extension into the orbit, orbital exenteration is recommended. A limited orbital exenteration with removal of eyelid, conjunctival sac, globe, and tenonectomy has been described for sebaceous carcinoma with pagetoid spread to conjunctiva and cornea. Biopsy should be performed if the ipsilateral parotid or cervical lymph nodes are enlarged, because inflammation alone may cause this change. If the lymph nodes contain tumor cells, radical neck dissection, superficial parotidectomy, and postoperative radiation have been recommended. Chemotherapy has also been used for recurrent sebaceous carcinoma.

Prognosis

5-year mortality rate of 30%. A number of factors, including delay in diagnosis, tumor location and size, and pathologic features, have been associated with a poorer prognosis. Pathologic features associated with a poor prognosis included multicentric origin, poor degree of differentiation, highly infiltrative pattern, intraepithelial carcinoma, invasion of

vascular or lymphatic channels, and extension into the orbit. Metastases may occur in the ipsilateral parotid and cervical lymph nodes, as well as in lungs, liver, brain, bone.

CONJUNCTIVAL MELANOMA

Clinical Presentation

The term melanoma was first introduced by Carswell in 1838. These uncommon lesions make up less than 1% of all ocular malignancies and only 2% to 5% of all ocular melanomas. Conjunctival melanomas are less common than uveal and skin melanomas.The increased incidence of conjunctival melanomas may be due to increased sun exposure. Malignant melanomas of the uvea and conjunctiva are histopathologically and clinically different and therefore should be considered separate entities. In fact, melanomas of the conjunctiva have more in common with melanomas of the skin than with melanomas of the uveal tract. Conjunctival melanomas are extremely rare in blacks and Asians. They usually develop after the third decade of life. The mean age at diagnosis is 52 to 60 years. In most series, males and females are equally affected. Conjunctival melanomas in children are also very rare. Approximately 75% of conjunctival melanomas arise from pre-existing PAM. The rest occur de novo, from a nevus or a blue nevus, or secondary to metastasis from a melanoma elsewhere. A rare aggressive form of amelanotic melanoma arises from PAM without pigmentation (“sine pigmento”). Chronic exposure to ultraviolet radiation has been implicated in the etiology of conjunctival melanomas. Several case reports have described conjunctival and uveal melanomas in patients with the dysplastic nevus syndrome of the skin, suggesting an association between these malignancies. The “dysplastic nevus syndrome “consists of atypical cutaneous nevi, which may be sporadic or familial. This skin nevus has a typical clinical appearance, but nuclear atypia is found on histologic exam. Conjunctival malignant melanoma lesions are nodular. They may invade the globe or extend posteriorly

into the orbit. Some lesions are pedunculated. Multicentric cases have been reported. Pigmentation is variable and are heavily vascularized. The bulbar conjunctiva and limbus are the most commonly involved sites. Primary malignant melanoma of the cornea is extremely rare. Most melanomas of the cornea, however, are secondary to extension from the neighbouring conjunctiva and usually involve the superficial layers of the cornea anterior to the basement membrane.

Histopathology

Histopathology of malignant melanomas of the conjunctiva reveals four different cell types:

-small polyhedral cells

-spindle cells

- Balloon cells and

-round epithelioid cells.

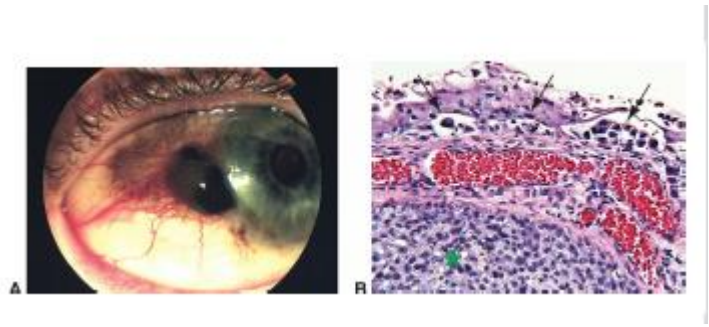
Lesions composed mostly of spindle cells have the lowest potential for metastasis.

Prognosis and Metastatic Potential

The overall 10 year survival rate following conjunctival melanoma varies from 70% to 87%. Risk factors for death from tumor metastasis include a lump as the presenting symptom, a melanoma arising de novo, and the technique of initial surgery. Prognosis also depends in part on the location of the lesion and its cytologic characteristics. Bulbar conjunctival melanomas -favourable prognosis than palpebral conjunctival tumors or tumors involving the fornix or caruncle. Large, multicentric, thick, or recurrent tumors, pagetoid growth, and lymphatic invasion increased risk for metastasis. Tumors composed mostly of spindle cells have a better prognosis than those composed of mixed cell types. Up to 30% to 40% of tumors metastasize at an average of 3.2 years after initial diagnosis. Risk factors for

metastasis include tumor location away from the limbus and lateral tumor margin involvement on pathologic examination .Metastasis is related to the presence of PAM sine pigmento, forniceal, palpebral, or caruncular location, lesion thickness of more than 2 mm, and histologic evidence of intralymphatic spread. Metastasis of conjunctival melanomas occurs through the lymphatics to regional lymph nodes especially the parotid (preauricular) and submandibular nodes. Palpation of these areas is an important part of the follow up of patients with conjunctival melanoma. Once metastasis has occurred, the survival rate declines markedly. Sentinel lymph node mapping and selective lymphadenectomy may help detect early metastasis. Local intraocular extension of tumor may occur, although this is infrequent

FIGURE 25: CONJUNCTIVAL MELANOMA – GROSS AND HISTOPATHOLOGICAL APPEARANCE



Treatment

In the past, melanomas of the conjunctiva were considered so malignant, and their behaviour so unpredictable, that orbital exenteration was commonly performed even for small lesions. Currently, therapy involves less drastic approaches. If a melanoma is confirmed on histopathologic analysis, complete excision with cryotherapy of the conjunctival margins and scleral base should be performed.

The surgical technique used to manage conjunctival melanomas is important, as incomplete tumor removal increases the risk of recurrence. In general, one should avoid incisional

biopsies when a lesion is suspicious for malignant melanoma as this can lead to “seeding” of tumor cells onto the conjunctival surface. Complete surgical excision of nodular or vascularized conjunctiva with superficial lamellar dissection of underlying sclera for adherent tumors, using the “no-touch” technique decreases recurrences, tumor cell seeding, and metastasis. A 3- to 5-mm tumor-free margin is ideal. Cryotherapy, using a double freeze-thaw approach, can be applied to the cut edges of conjunctiva and to the scleral base at the time of excision. Extension of tumor cells onto the cornea, which is usually superficial and does not penetrate Bowman’s membrane, can be managed using alcohol-assisted epithelial removal. One should avoid penetrating Bowman’s layer during surgery, as this layer serves as a natural barrier against tumor extension into the corneal stroma. Map biopsies of surrounding PAM and even of uninvolved conjunctiva should be done at the time of tumor excision to determine the extent of the disease and the degree of histologic atypia. Amniotic membrane transplantation may be used to restore the conjunctival surface following tumor excision, especially for large tumors in which the conjunctival defect is too large to close primarily. Amniotic membrane grafting reduces scarring and symblepharon formation, thereby improving postoperative cosmesis and ocular motility. Adjunct treatments are very useful postoperatively, especially for conjunctival melanoma in the setting of diffuse PAM with atypia. Cryotherapy, the historical standard of care for extensive PAM that cannot be completely removed surgically, can cause significant ocular surface morbidity when applied over a large area. Topical chemotherapy using mitomycin C has been shown to be effective, and in general, is well tolerated. It has the added advantage of treating the entire ocular surface, as opposed to cryotherapy, which treats only the areas to which it is applied. The optimal strength and duration of mitomycin C treatment has not been established in clinical trials. However, 0.02% to 0.04% eyedrops applied four times daily for 1- to 2-week cycles have been used with good success and minimal side effects. Serious complications from

mitomycin C use have occurred in other settings and one should approach this medication with caution. We wait until the ocular surface is completely healed following surgical manipulations before starting mitomycin C drops. Patients are cautioned to avoid contact of the medication with their skin, as it can cause contact dermatitis. Punctal plugs are placed in both the upper and lower punctum before beginning a course of mitomycin C and are replaced as needed during treatment to reduce systemic absorption. Manual punctal occlusion following each application of medication is an alternative to punctal plugs. We typically give 0.04% mitomycin C drops for times daily for 1 week, followed by a 3-week holiday. Patients are examined prior to beginning the next course of mitomycin C. Usually two to three cycles are needed to see a reduction in conjunctival pigment. Conjunctival injection occurs almost universally, especially during later treatment courses. An ointment such as erythromycin or a steroid-antibiotic ointment combination can be given to soothe the eye. Refrigerated artificial tears and cold compresses may also be suggested. Map biopsies are repeated several months after the last course of mitomycin C to assess for residual disease. Orbital exenteration may be considered in aggressive, advanced, or bulky tumors especially if the eyelids and/or orbit are involved. This procedure, however, does not improve survival. Exenteration should not be performed in the elderly because of the associated morbidity in this population, or in cases in which distant metastasis have already occurred. Risk factors for exenteration included poor vision, amelanotic or red coloured tumor, and extralimbal tumor location. Conjunctival melanomas are not very radiosensitive. Iodine-125 brachytherapy, however, may be a useful alternative in patients who might otherwise require exenteration, or as an adjunct to surgical excision. Good local control was achieved with an average dose of 37 Gy. Proton beam therapy and beta irradiation are also other alternatives.

Recurrences after treatment have been estimated to occur in 35% of patients, at an average of 3.5 to 4.5 years after primary treatment. Patients with a history of conjunctival melanoma,

therefore, should be examined several times each year. Tumor recurrence is more common in melanomas arising from pre-existing PAM, in extralimbal lesions, and in multifocal tumors. Major risk factors for recurrence included nonlimbal location of the tumor and tumor cells at the margin after excision. Adjunctive cryotherapy decreases the chance of recurrences after surgical excision. Treatment of recurrent conjunctival melanoma is similar to the treatment of the primary tumor. Recurrent tumors may occasionally be nonpigmented, even if the original tumor was pigmented. Metastatic spread occurs in 16% of patients at 5 years, 26% at 10 years, and 32% at 15 years. Metastasis occurs more commonly following recurrent melanoma. The prognosis is extremely poor after metastasis. These sobering statistics underscore the importance of accurate diagnosis and meticulous surgical and medical management of patients with conjunctival melanoma and primary acquired melanosis.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of primary melanocytic lesions of the conjunctiva includes secondary melanocytic lesions and nonmelanocytic pigmentary lesions.

Addison’s disease and pregnancy may lead to conjunctival melanosis due to hormonal changes.

Topical medications containing epinephrine products or silver and systemic medications such as the phenothiazines may lead to pigmentary deposits in the conjunctiva.

After ocular surgical procedures.

Congenital blue sclera and areas of scleral thinning from any cause may mimic primary pigmentary conjunctival lesions.

Intraocular melanomas may extend to the conjunctiva or cornea, or conjunctival metastasis from the skin or other melanomas may occur.

REVIEW OF LITERATURE

1.CONJUNCTIVAL BIOPSIES AND OPHTHALMIC LESIONS : A HISTOPATHOLOGIC STUDY IN EASTERN INDIA

Conjunctiva is a thin and flexible mucus membrane that provides a protective barrier to the eye. Very few histopathological studies have been conducted on conjunctival biopsies in eastern India 120 cojunctival biopsies from 117 patients received during 8 years were included in the study.

RESULTS : Histologic diagnosis were degenerative lesions in 38 cases, benign epithelial lesions in 23 cases ,premalignant and malignant epithelial lesions in 27 cases , melanocytic lesions in 10 cases , lymphoid in 7 cases and miscellaneous in 15 cases.

CONCLUSION:

Squamous papilloma was the commonest benign tumour whereas commonest malignant tumour was squamous cell carcinoma .melanocytic lesions were less prevalent compared to western studies.

2.LYMPHOID LESIONS OF THE CONJUNCTIVA: RELATION OF HISTOPATHOLOGY TO CLINICAL OUTCOME

JESSE SIGELMAN, MD FREDERICK A. JAKOBIEC, MD

A retrospective clinicopathologic study of 40 patients with lymphoid lesions of the conjunctiva demonstrated the validity of current histologic criteria in predicting clinical outcome. Overall histologic architecture as well as cytologic detail must be used to differentiate benign reactive lymphoid hyperplasia from lymphoma. Lesions verified clinically as being malignant had obvious malignant cytologic features. Clinical signs of surface follicularity, multifocality, and minimal elevation suggest benignancy. All the benign lesions, on histopathologic examination, were either follicular in architecture or composed of

mature lymphocytes, and were generally restricted to the substantia propria. Bilaterality and clinical recurrence do not necessarily imply a malignant disease

3. .**MELANOCYTIC LESIONS OF CONJUNCTIVA**

Hardeep S Mudhar

This article reviews the clinic pathological details of common benign and malignant melanocytic lesions of the conjunctiva .Melanocytic lesions clinically present as flat or nodular and it is in this way this review covers the commonest benign and malignant entities. Several types of naevi can be identified in the conjunctiva with some site specific peculiarities,familiarisation with which will allow a correct interpretation.Benign and atypical 'flat intraepithelial melanocytic lesions are covered in detail as they constitute many cases of referred material to specialist ophthalmic pathologists .The various classification schemes for atypical intraepithelial melanocytes are covered.Common histological and prognostic details for melanoma are mentioned.Ambuguous lesions are alluded to and how ancillary molecular investigations help in this regard along with a brief summary of the recent advancements in the molecular biology for conjunctival melanomas.

4. **CLINICAL AND HISTOPATHOLOGICAL ANALYSIS OF CONJUNCTIVAL TUMOURS AT A TERTIARY CARE CENTRE IN INDIAN POPULATION**

Hemalatha Krishnamurthy, Manjuladevi N, Tanushree V, Venkategowda H.T4, Bharathi M, Archana S, Shivani Nayak, Valijwala Ehatesham Ul Hak

The broad spectrum of conjunctival tumors ranges from non-neoplastic benign tumors to very aggressive malignancies, such as melanoma or Kaposi's sarcoma which threat visual function and life of the patient. There is a relative paucity of large published studies documenting conjunctival lesions. In the Indian population, reported 46% of epithelial origin (benign, premalignant, and malignant neoplasm), degenerative lesions (14%), chronic non-specific inflammation (12%), melanocytic tumors (12%), and lymphoid tumors (6%). Squamous cell

carcinoma (20%), miscellaneous (22%), pterygium (10%), squamous papilloma (8%), and OSSN (8%). A review of a large series of conjunctival biopsy specimens from an adult US population documented the following distribution: inflammatory/degenerative lesions (12%), benign epithelial (2%), pigmented (53%), premalignant and malignant epithelial (11%), lymphoid (8%), miscellaneous (12%) and congenital lesions (2%).

AIM: To study the clinical and histopathological features of conjunctival tumors at a tertiary care hospital in south Indian population.

In this study, 134 patients with conjunctival tumors followed between January 2009 and September 2010 were retrospectively reviewed. Clinical data were collected from medical records and analyzed. Of the 134 patients with conjunctival tumor, 80 were male (59.70%) and 54 were female (40.29%). The mean age of the134 patients was 35 years (range1to 95 years). In our series, the most common diagnosis of 134 lesions were, nevus 18.66% (n=25), carcinoma in situ 10.44% (n=14), dysplasia 5.97%(n=8), squamous cell carcinoma(SCC) 5.22% (n=7), haemangioma 3.73% (n=5), squamous papilloma 3.73%(n=5), limbal dermoid 2.98%(n=4), malignant melanoma 1.49% (n=2) and lymphoma 0.74 %(n=1).

CONCLUSION: Nevus was found to be the most common conjunctival benign tumor. Even though squamous cell carcinoma is a rare conjunctival malignant tumor, it may be encountered in younger male population.

DETAILED STUDY PROPOSAL

AIMS AND OBJECTIVES:

1. To analyse the importance of histopathological examination in confirming the diagnosis of various conjunctival lesions like ocular surface squamous neoplasia, malignant melanoma, granulomas.

2. To analyse the clinical presentation of various conjunctival lesions

3. To differentiate between benign and malignant lesions histopathologically (for early diagnosis of malignancy)

MATERIALS AND METHODS:

1 All patients with conjunctival lesions should undergo a detailed slit lamp examination and photograph the lesion preoperatively

2. In case of malignant lesions clinical staging of the lesion is done

3. Basic blood investigations like – random blood sugar , bleeding time and clotting time should be done before procedure

4. Informed written consent to be obtained from the patient

5. Patient is admitted as inpatient in ophthalmology ward

6. The procedure is done in Eye OT under strict aseptic precautions under suitable anasthesia

7. The eye is draped and speculum is applied and specimen is obtained with 11 blade and forceps and scissors from the base and edge of the lesion

8. In case of doubtful malignant lesion cryotherapy has to be applied

9. In cases with large conjunctival lesions after excision leaving a large conjunctival defect – amniotic membrane graft should be done

10. The specimen collected has to be sent in a sterile container with formalin and sent immediately to the pathology laboratory for the histopathological examination of the same.

STUDY CONUCTED AT:

Department of Ophthalmology, GRH, Madurai medical college

STUDY DESIGN

Cross Sectional study

STUDY POPULATION:

Patients attending Eye OPD, GRH with bulbar conjunctival lesions indicating excision to restore smooth ocular surface and HPE to determine the etiology

INCLUSION CRITERIA:

1. Consenting patients

2. Age more than 12 years, of either sex

3. Presenting with conjunctival lesions of bulbar conjunctive requiring excision and HPE.

EXCLUSION CRITERIA:

1. Patients with infective conjunctival lesions like bacterial, chlamydial, viral, fungal, rickettsial, protozoal, parasitic, spirocheal conjunctivitis.
2. Patients with bleeding diathesis
3. Patients on anticoagulants
4. Patients not consenting to participate in the study
5. Patients less than 12 years of age.

SAMPLE SIZE:

A total number of 40 patients attending to the Eye OPD, GRH Madurai with bulbar conjunctival lesions requiring biopsy and HPE and satisfying the above inclusion and exclusion criteria were taken for the study.

STUDY DURATION:

Study is conducted for a period of 5 months.

FINANCIAL SUPPORT:

Nil

ETHICAL CLEARANCE:

Ethical committee approval letter obtained

INFORMED CONSENT:

Consent was obtained for all patients/ guardians involved in the study. Visual acuity and a detailed anterior and posterior segment examination was done

RESULTS AND INTERPRETATION

STATISTICAL ANALYSIS:

The data was analaysed with SPSS statistical software package (version 16.0 SPSS Inc. Chicago ,USA).The distribution of the conjunctival lesions were analysed using chi square test and p value < 0.05 will be considered as statistically significant.

OBSERVATIONAL ANALYSIS

TABLE 1: AGE DISTRIBUTION OF CONJUNCTIVAL LESIONS

Among the 40 patients of the study group 12 were less than 20 years, 4 were between 21-40 years, 13 were between 41 – 60 years and 11 were more than 60 years.

Age in years	No.of cases	Percentage
< 20	12	30%
21 - 40	4	10%
41 - 60	13	32.5%
> 60	11	27.5%
Total	40	

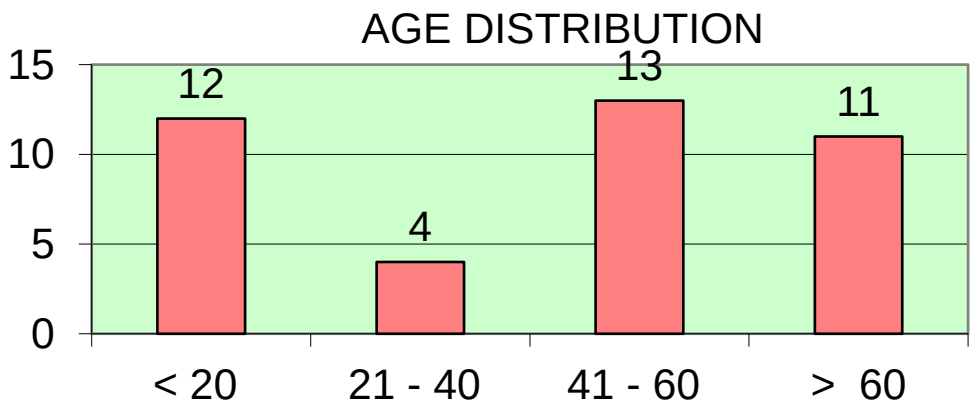


TABLE 2: AGE DISTRIBUTION OF CONJUNCTIVAL LESIONS BASED ON HISTOPATHOLOGICAL DIAGNOSIS

Age in years	Benign Non pigmented	Pre malignant-non pigmented	Malignant-nonpigmented	Benign pigmented	Malignant pigmented	premalignant Pigmented	Cyst	Degeneration
< 20	4	0	1	4	1	0	2	0
21 - 40	3	0	0	0	0	0	1	0
41 - 60	2	3	2	0	1	0	1	4
> 60	1	0	3	0	1	1	0	5
Total	10	3	6	4	3	1	4	9

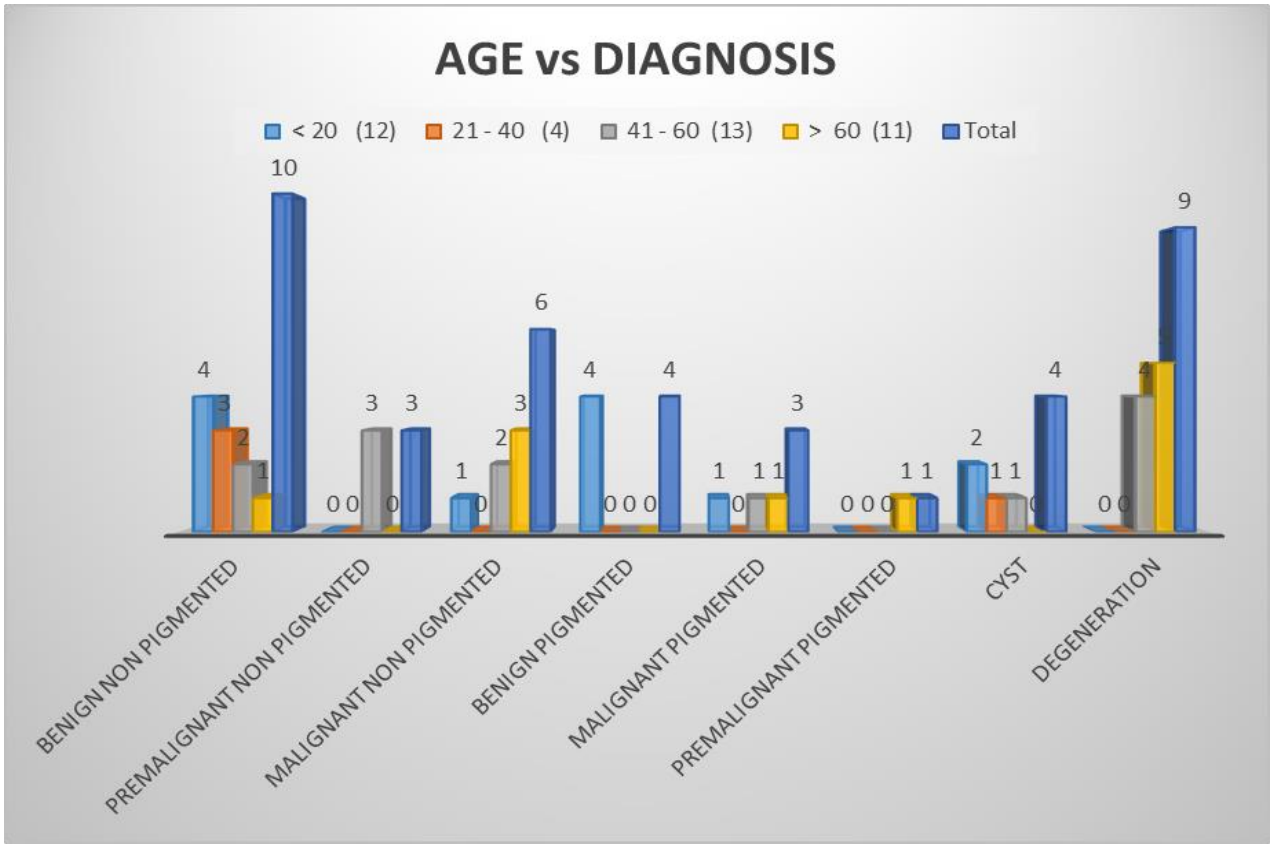


TABLE 3: PERCENTAGE DISTRIBUTION OF VARIOUS CONJUNCTIVAL LESIONS

Among 40 patients, 25% cases were non pigmented benign lesions, 22.5% were degeneration ,15 % were nonpigmented malignant lesions, 10 % were benign pigmented lesions, 10% were cysts , 7.5% were nonpigmented premalignant lesions, 5% were premalignant pigmented lesions and 5% were malignant pigmented lesions.

Diagnosis	No.of cases	Percentage
Benign non pigmented	10	25
Premalignant non pigmented	3	7.5
Malignant non pigmented	6	15
Benign pigmented	4	10
Malignant pigmented	2	5
Premalignant pigmented	2	5
Cyst	4	10
Degeneration	9	22.5
Total	40	100

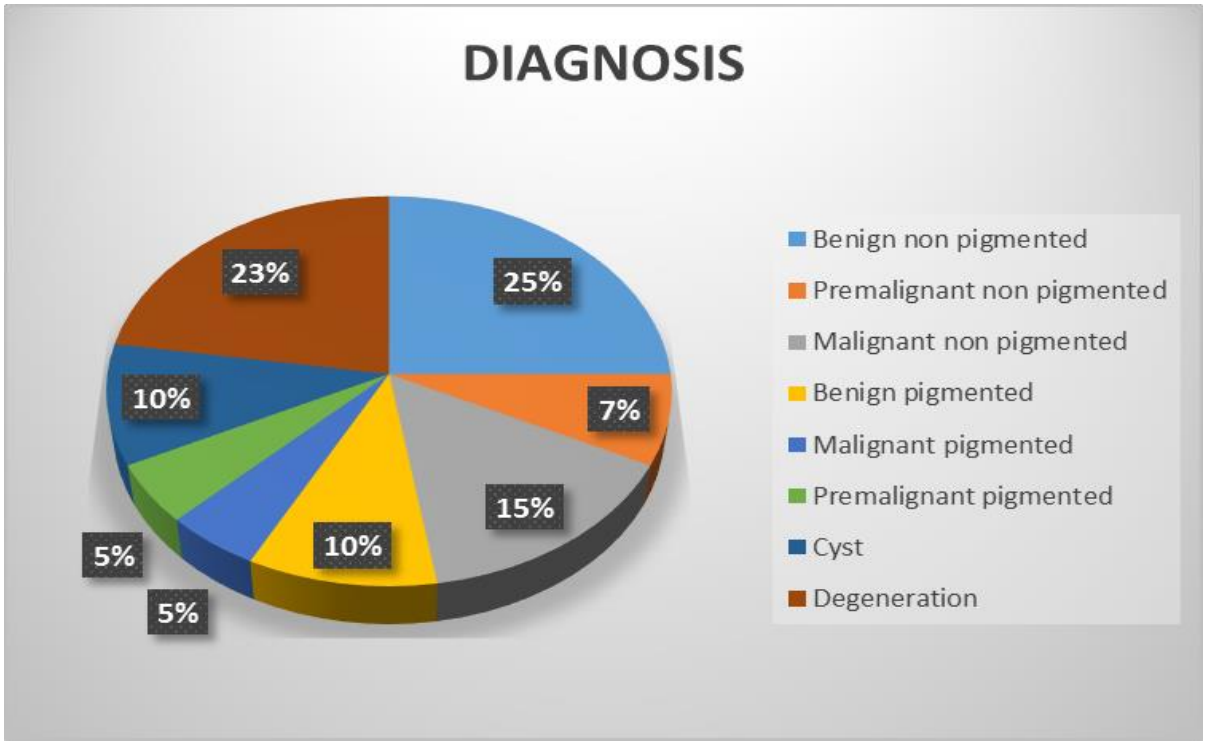


TABLE 4: SEX DISTRIBUTION OF CONJUNCTIVAL LESIONS

Among the study group of 40 patients, 23 were males and 17 were females.

Sex	No.of cases	Percentage
Male	23	57.5%
Female	17	42.5%
Total	40	

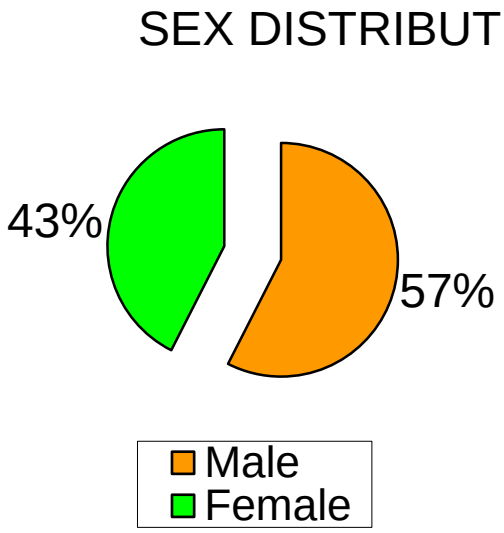


TABLE 5: SEX DISTIBUTION BASED ON THE HISTOPATHOLOGICAL DIAGNOSIS:

Among the 40 cases the following sex distribution was noted

Sex	Benign nonpigmented	Pre malignant non pigmented	Malignant non pigmented	Benign pigmented	Malignant pigmented	premalignant Pigmented	Cyst	Degeneration
Male (23)	3	3	4	2	2	2	2	5
Female (17)	7	0	2	2	0	0	2	4
Total	10	3	6	4	2	2	4	9

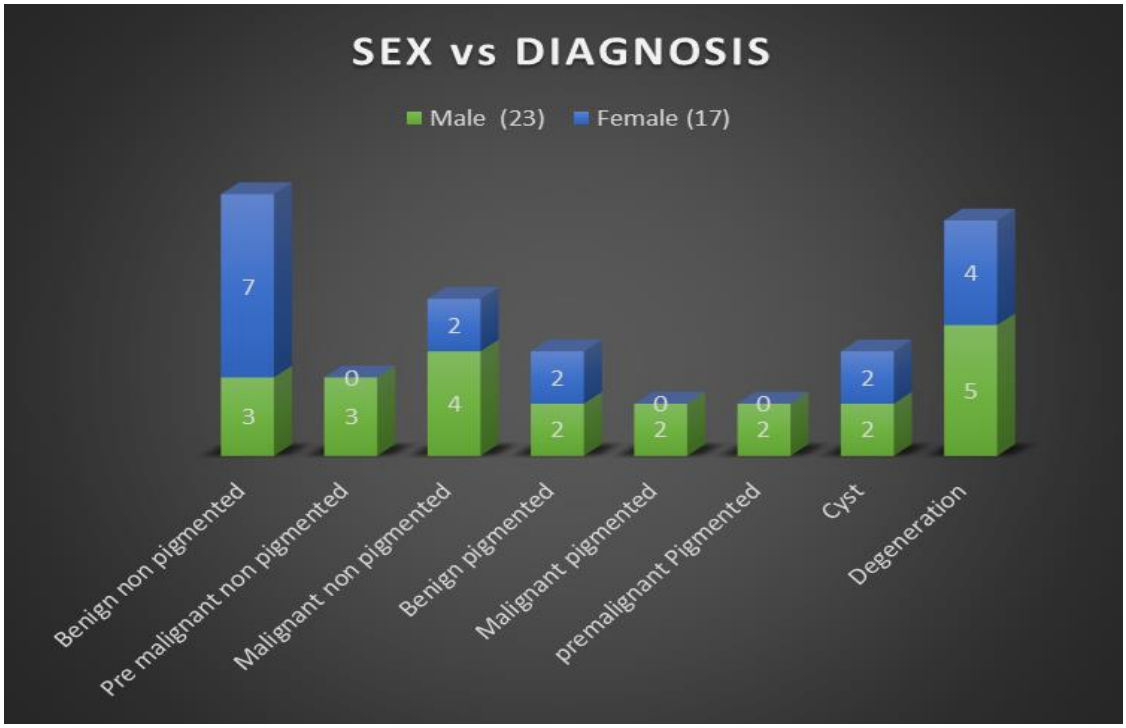


TABLE 6: DISTRIBUTION OF CONJNCTIVAL LESION BASED ON LATERALITY

Among the study group of 40 cases , in 13 cases right eye was involved and in 1 cases left eye was involved and in 11 cases both eyes were involved.

Laterality	No.of cases	Percentage
Right eye	13	32.5%
Left eye	16	40%
Both eye	11	27.5%
Total	40	

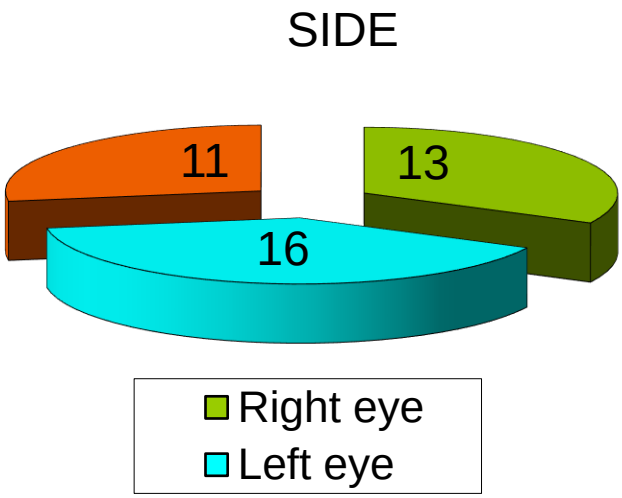


TABLE 7: DISTRIBUTION OF CONJUNCTIVAL LESIONS BASED ON THEIR GROSS FEATURES:

Among the study group of 40 cases the following range of gross features were noted the most common being pinkish lesion.

Gross features	No.of cases
Pinkish	13
Yellowish	8
Brownish	5
Whitish	4
Flat pigmented	3
Leucoplaciform	2
Reddish	1
Salmon	2
Soft	1
Transparent	1
Total	40

Consistency/ colour	Benign non pigmented	Pre malignant non pigmented	Malignant Non pigmented	Benign pigmented	Malignant pigmented	premalignant Pigmented	Cyst	Degeneration
Pinkish	4	0	1	0	0	0	2	6
Yellowish	3	0	0	0	0	0	0	3
Brownish	0	0	0	3	1	1	0	0
Whitish	0	3	1	0	0	0	0	0
Flat pigmented	0	0	0	1	1	1	0	0
Leucoplaciform	0	0	2	0	0	0	0	0
Reddish	1	0	0	0	0	0	0	0
Salmon	0	0	2	0	0	0	0	0
Soft	0	0	0	0	0	0	1	0
Transparent	0	0	0	0	0	0	1	0
Total	8	3	6	4	2	2	4	9

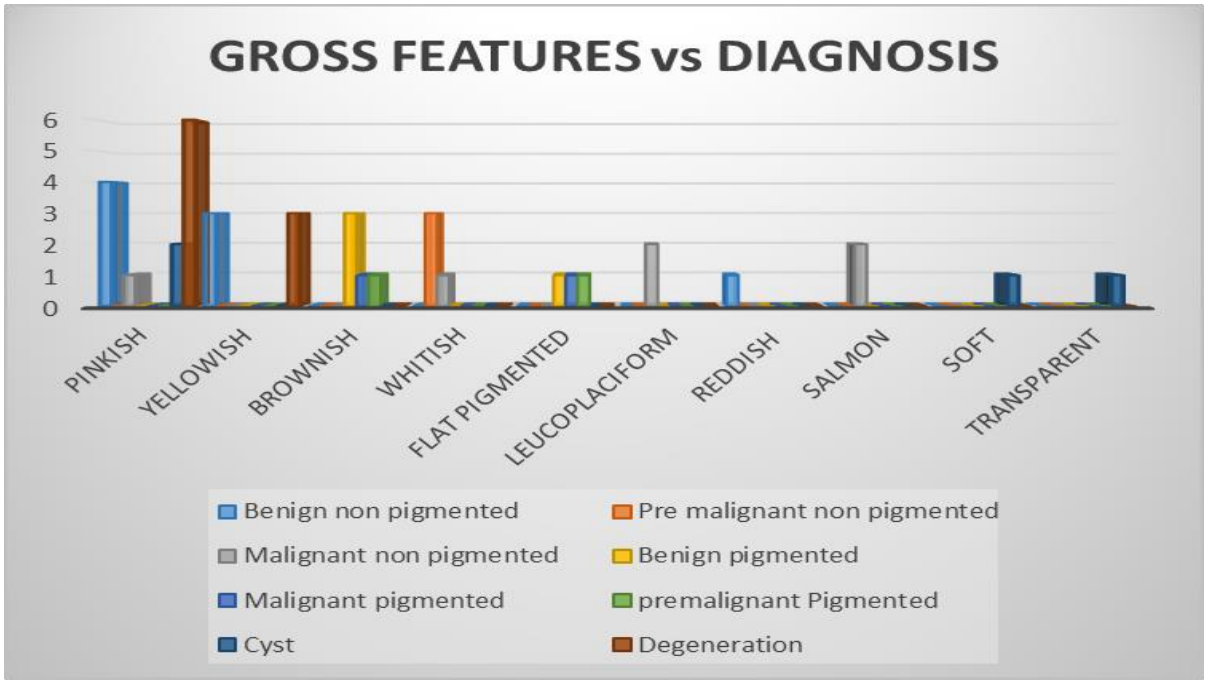


TABLE 8: SMOKING VS CONJUNCTIVAL LESIONS:

Among the study group 27.5% cases are smokers, among which all were males.Among the males 47.8% were smokers. And it is found that there is a high preponderance of malignant and premalignant (both pigmented and non-pigmented) among the smokers.

Smoking	Benign non pigmented	Pre malignant non pigmented	Malignant non pigmented	Benign pigmented	Malignant pigmented	premalignant Pigmented	Cyst	Degeneration
Present	1	2	4	0	1	1	0	2
Absent	9	1	2	4	1	1	4	7

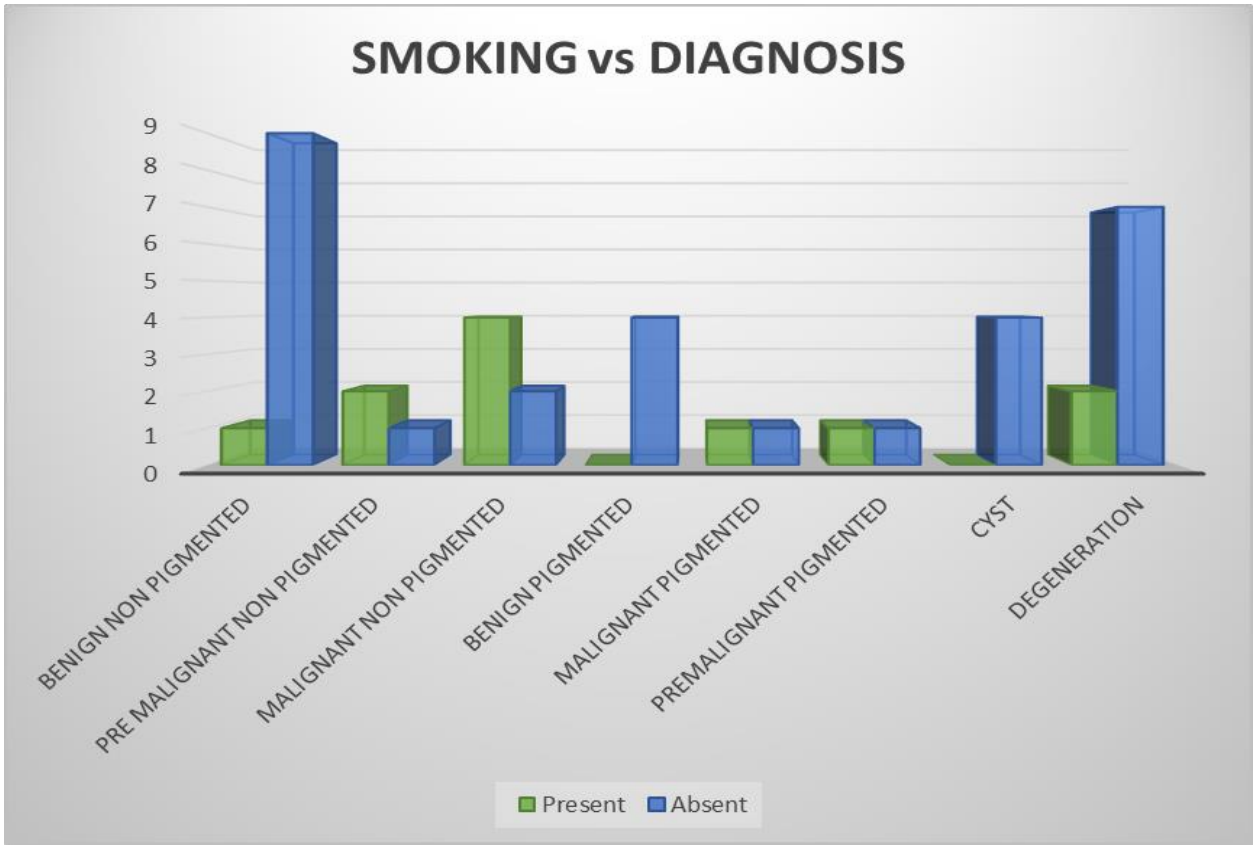


TABLE 9: PRESENCE OF SCLERAL FIXITY IN THE CONJUNCTIVAL LESIONS

Among the study group of 40 cases, scleral fixity was absent in 31 cases, present in 7 cases and minimal in 2 cases.

SCLERAL FIXITY	No.of cases
Present	7
Absent	31
Minimal	2
Total	40

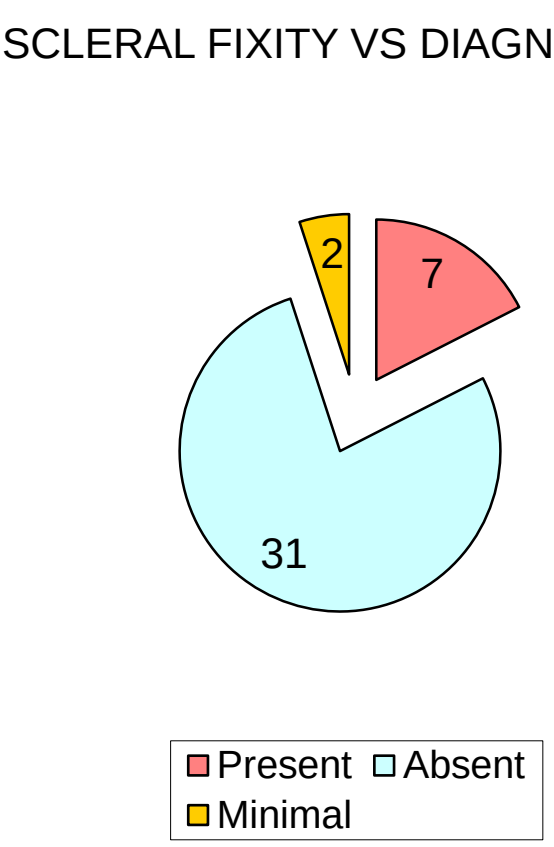


TABLE 10 : DISTRIBUTION OF SCLERAL FIXITY AMONG VARIOUS CONJUNCTIVAL LESIONS BASED ON HISTOPATHOLOGICAL DIAGNOSIS

Among the 40 cases in study group, it was noted that scleral fixity was associated with malignant lesions (pigmented / non pigmented) and chi square test was used and the p value was found to be 0.029 which was significant.

Scleral Fixity	Benign non pigmented	Pre malignant non pigmented	Malignant non pigmented	Benign pigmented	Malignant pigmented	premalignant Pigmented	Cyst	Degeneration
Present (7)	0	1	4	0	2	0	0	0
Absent (31)	10	0	2	4	0	2	4	9
Minimal (2)	0	2	0	0	0	0	0	0
Total	10	3	6	4	2	2	4	9

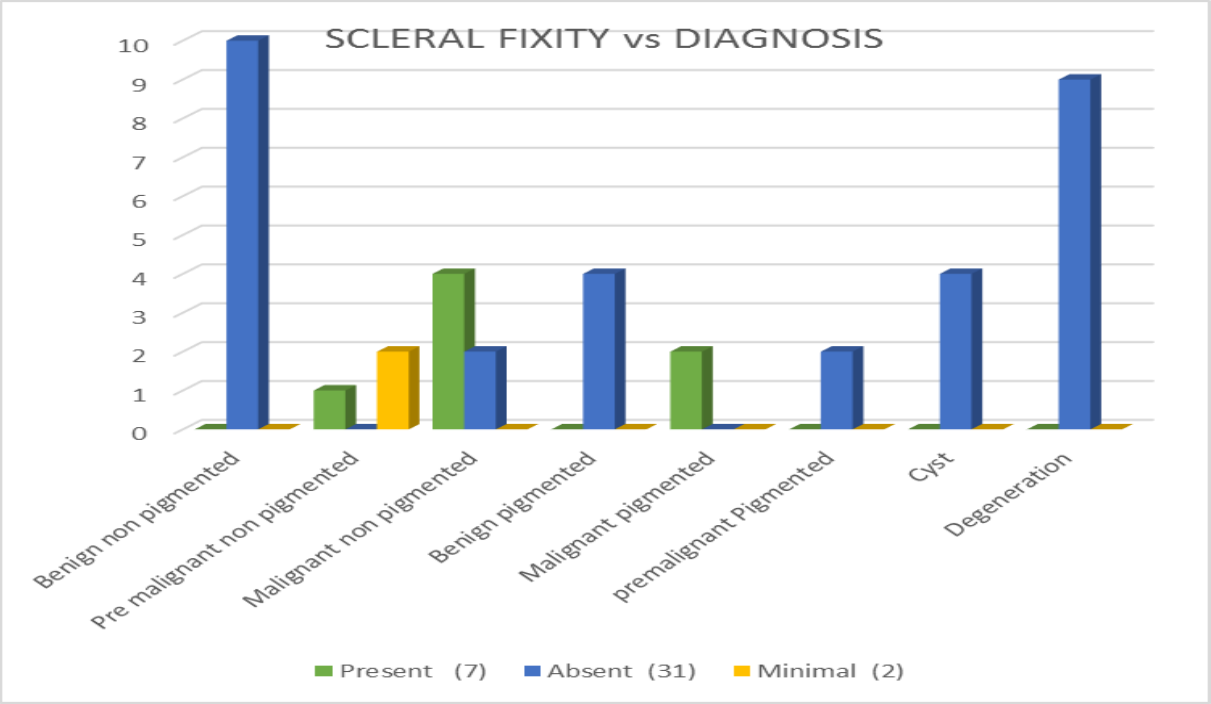


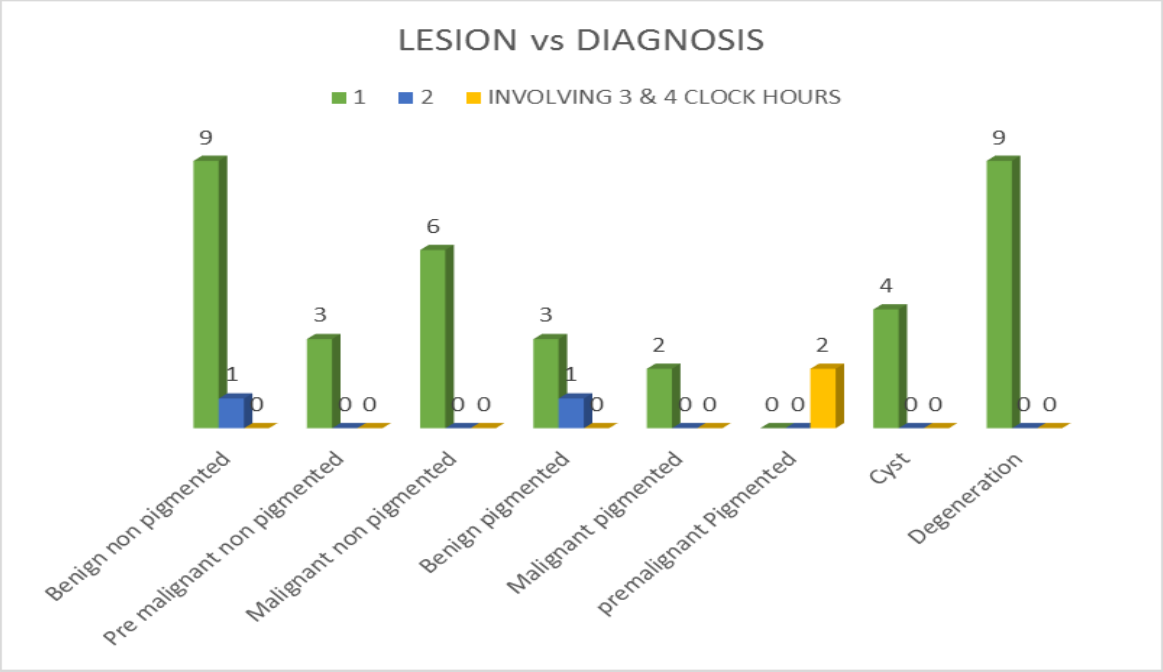
TABLE 11: DISTRIBUTION OF CONJUNCTIVAL LESIONS BASED ON THE NUMBER OF CONJUNCTIVAL LESIONS

Among the study group of 40 cases around 36 cases were having single lesion, 2 cases had 2 lesions, and 2 cases had single large lesion involving 3-4 clock hours.

Lesion	No.of cases
1	36
2	2
INVOLVING 3 & 4 CLOCK HOURS	2
Total	40

TABLE 12: NUMBER OF CONJUNCTIVAL LESIONS VS HISTOPATHOLOGICAL DIAGNOSIS OF LESION

Among the study group of 40 cases the following distribution of conjunctival lesions based on number of lesions and histopathological diagnosis was noted.



Lesion	Benign non pigmented	Pre malignant non pigmented	Malignant non pigmented	Benign pigmented	Malignant pigmented	premalignant Pigmented	Cyst	Degeneration
1	9	3	6	3	2	0	4	9
2	1	0	0	1	0	0	0	0
INVOLVING 3 & 4 CLOCK HOURS	0	0	0	0	0	2	0	0
Total	10	3	6	4	2	2	4	9

TABLE 13: DISTRIBUTION OF CONJUNCTIVAL LESIONS BASED ON SIZE:

Among the study group of 40 cases 25 cases were <3 mm and 15 cases were 4-7 mm in size.

Size of lesions	No.of cases
2- 3 mm	25
4 - 7 mm	15
Total	40

TABLE 14: DISTRIBUTION OF VARIOUS CONJUNCTIVAL LESIONS BASED ON HISTOPATHOLOGICAL DIAGNOSIS AND SIZE:

Among the study group of 40 cases following pattern of distribution was noted based on the size.

Size of lesions	Benign non pigmented	Pre malignant non pigmented	Malignant non pigmented	Benign pigmented	Malignant pigmented	premalignant Pigmented	Cyst	Degeneration
2- 3 mm (25)	9	0	2	4	0	0	4	6
4 - 7 mm (15)	1	3	4	0	2	2	0	3
Total (40)	10	3	6	4	2	2	4	9

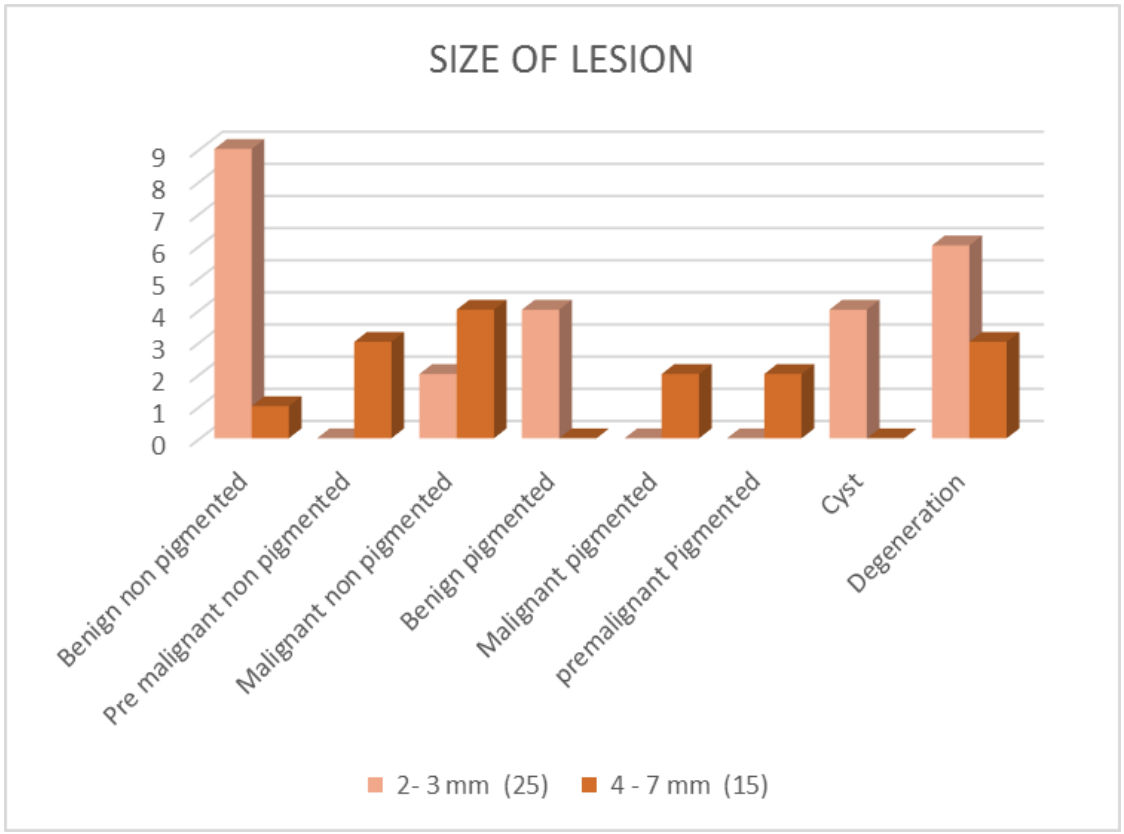


TABLE 15: DISTRIBUTION OF CONJUNCTIVAL LESIONS BASED ON THEIR MANAGEMENT:

Among the 40 cases in the study group 10 cases underwent 3 mm tumour free margin excision.

Type of Biopsy	No.of cases
Excision	30
Excision with 3mm free margin	10
Total	40

TABLE 16: DISTRIBUTION OF CONJUNCTIVAL LESIONS BASED ON THEIR HISTOPATHOLOGICAL DIAGNOSIS AND THE TYPE OF BIOPSY DONE:

Among the 40 study cases the management was done as follows for various lesions. It was noted that 3 mm tumour free margin was excised for malignant cases most commonly.

Type of Biopsy	Benign non pigmented	Pre malignant non pigmented	Malignant non pigmented	Benign pigmented	Malignant pigmented	premalignant Pigmented	Cyst	Degeneration
Excision (30)	10	0	1	4	0	2	4	9
Excision with 3mm tumour free margin (10)	0	3	5	0	2	0	0	0
Total	10	3	6	4	2	2	4	9

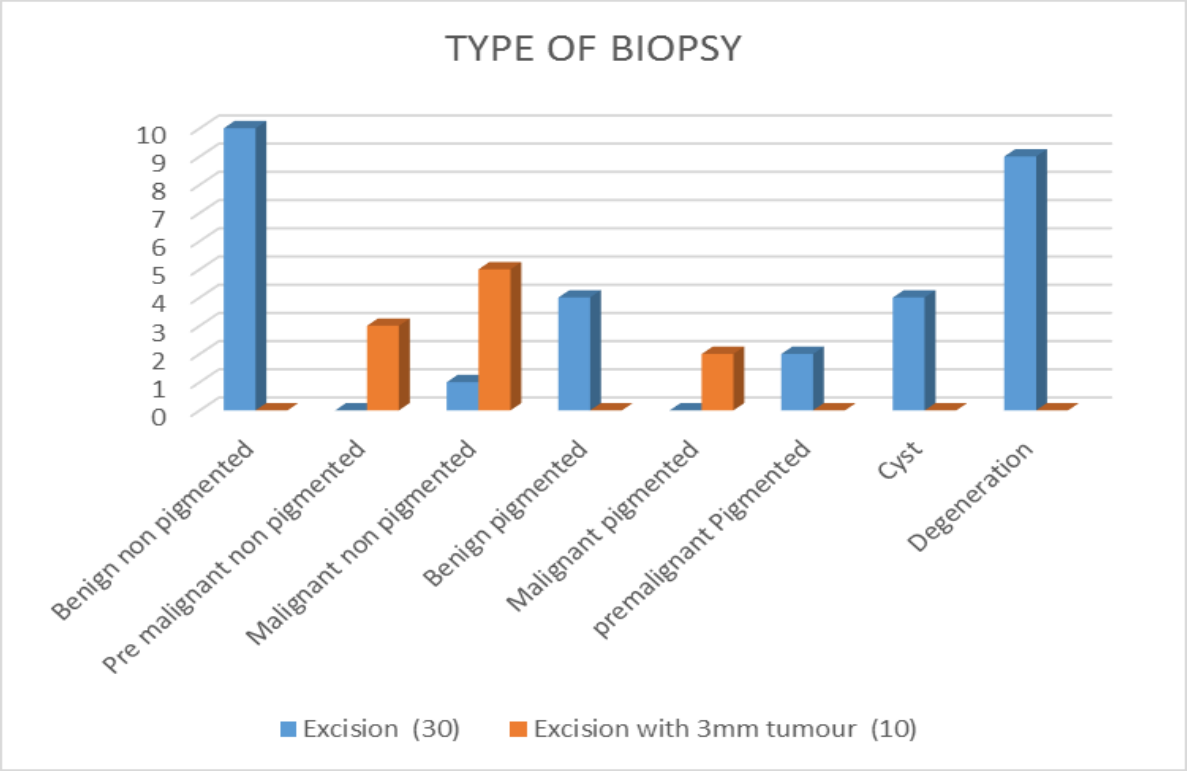


TABLE 17: DISTRIBUTION OF CONJUNCTIVAL LESIONS BASED ON THE DURATION OF THE LESION:

Among the study group of 40 cases 17 cases were present for < 1 year duration, 10 cases were present for 1-3 years duration, and 13 cases were present for a duration of > 3 years.

Duration of lesions	No.of cases
< 1 year	17
1 - 3 years	10
> 3 years	13
Total	40

TABLE 18: DISTRIBUTION OF CONJUNCTIVAL LESIONS BASED ON HISTOPATHOLOGICAL DIAGNOSIS AND DURATION OF THE LESIONS:

Among the study group of 40 cases the following pattern of distribution was noted depending on the duration of lesion.

Duration of lesions	Benign non pigmented	Pre malignant non pigmented	Malignant non pigmented	Benign pigmented	Malignant pigmented	premalignant Pigmented	Cyst	Degeneration
< 1 year (17)	5	3	4	0	2	0	3	0
1 - 3 years (10)	3	0	2	1	0	0	0	4
> 3 years (13)	2	0	0	3	0	2	1	5
Total	10	3	6	4	2	2	4	9

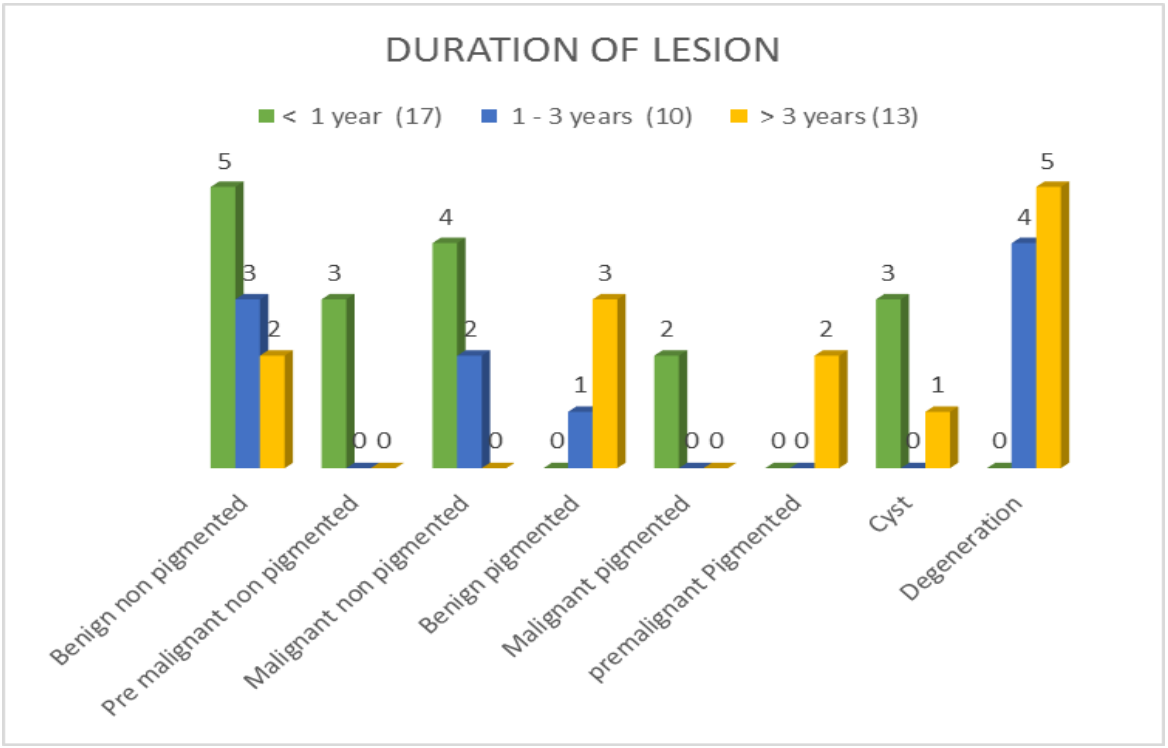


TABLE 19: DISTRIBUTION OF CONJUNCTIVAL LESIONS BASED ON THE CORNEAL INVOLVEMENT:

Among the 40 study group cases corneal involvement was present in 7 cases and absent in 33 cases.

Corneal involvement	Benign non pigmented	Pre malignant non pigmented	Malignant non pigmented	Benign pigmented	Malignant pigmented	premalignant Pigmented	Cyst	Degeneration
Present (7)	2	0	1	0	0	1	0	3
Nil (33)	8	3	5	4	2	1	4	6
Total	10	3	6	4	2	2	4	9

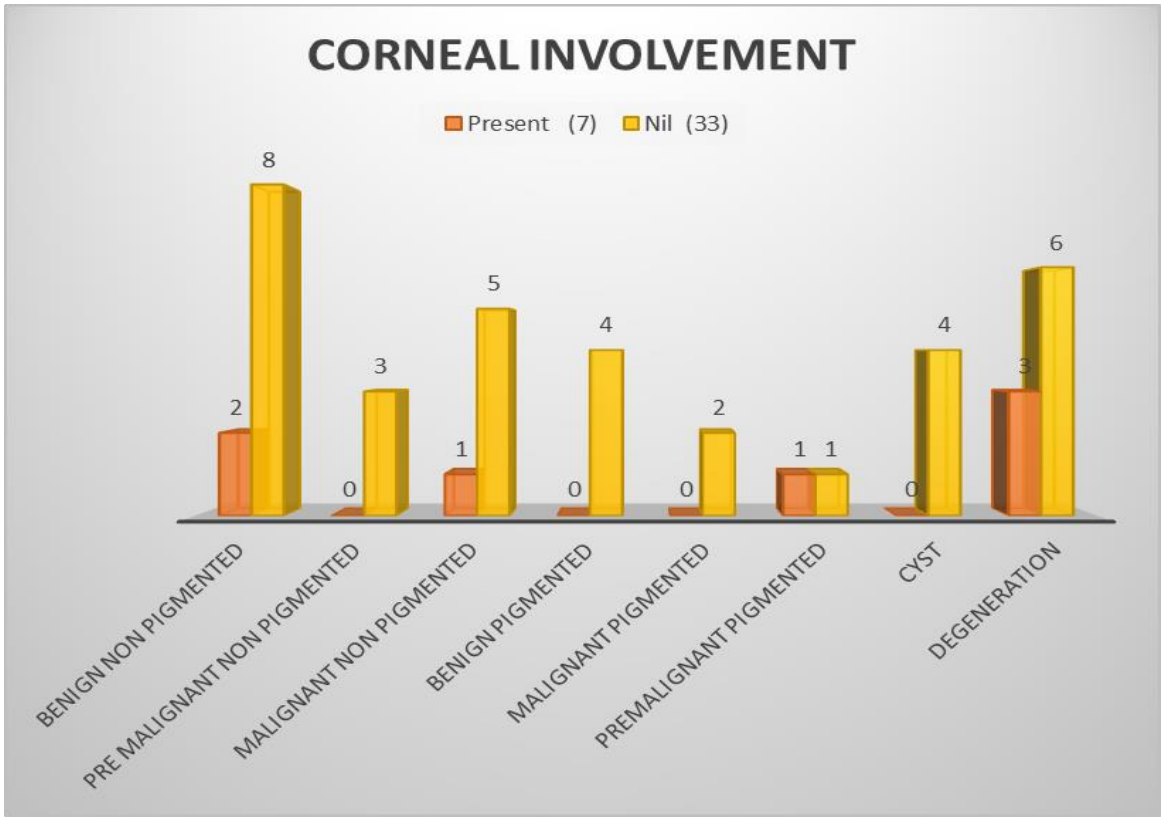


TABLE 20: DISTRIBUTION OF CONJUNCTIVAL LESIONS BASED ON PAIN:

Among the study group of 40 cases the following pattern of distribution was noted.

Pain	Benign non pigmented	Pre malignant non pigmented	Malignant non pigmented	Benign pigmented	Malignant pigmented	premalignant Pigmented	Cyst	Degeneration
Mild	2	2	1	0	1	0	2	0
Mild on and off	0	0	0	0	0	0	0	1
Moderate	1	0	2	0	1	0	0	0
Nil	7	1	3	4	0	2	2	8
Total	10	3	6	4	2	2	4	9

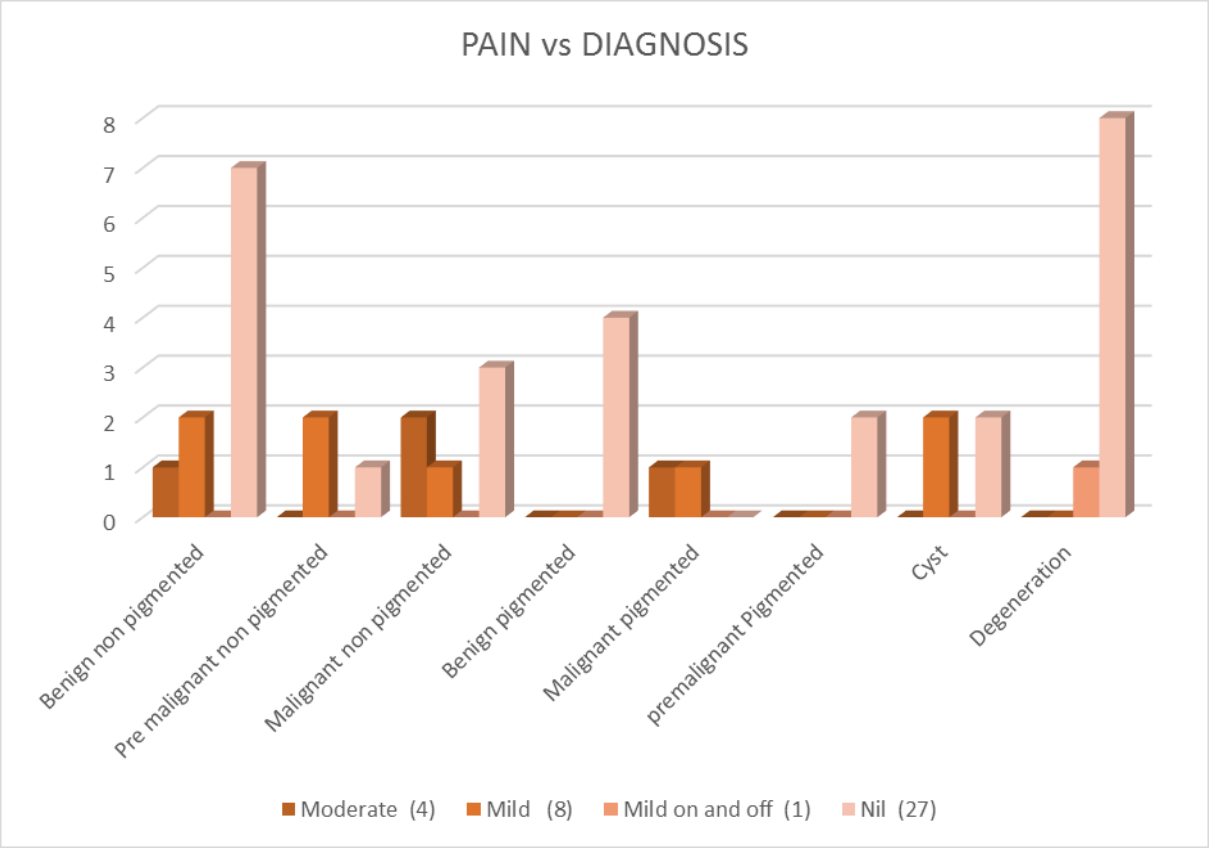


TABLE 21: DISTRIBUTION OF CONJUNCTIVAL LESIONS BASED ON PROGRESSION

Among the 40 study cases progression was noted in 28 cases and absent in 12 cases.

Progression	No.of cases
+	28
-	12
Total	40

TABLE 22: DISTRIBUTION OF CONJNCTIVAL LESIONS BASED ON HISTOPATHOLOGICAL DIAGNOSIS AND PROGRESSION:

Progression	Benign non pigmented	Pre malignant non pigmented	Malignant non pigmented	Benign pigmented	Malignant pigmented	premalignant Pigmented	Cyst	Degeneration
Present	4	3	5	3	2	2	1	8
Absent	6	0	1	1	0	0	3	1
Total	10	3	6	4	2	2	4	9

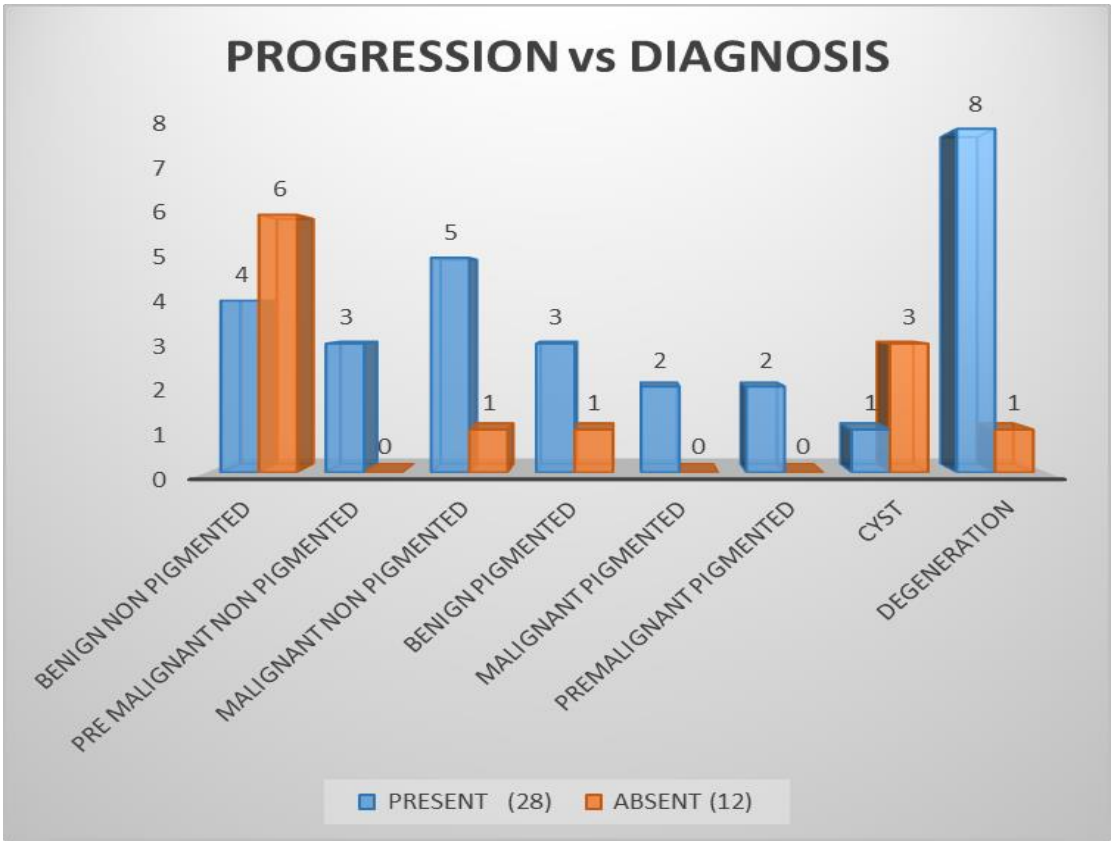


TABLE 23: DISTRIBUTION OF CONJUNCTIVAL LESION BASED ON NATURE OF DISEASE

Among the 40 cases studied only 2 were congenital others were acquired.

	Benign non pigmented	Pre malignant no n pigmented	Malignant non pigmented	Benign pigmented	Malignant pigmented	premalignant Pigmented	Cyst	Degeneration
ACQ (38)	9	3	6	4	2	2	3	9
CONG (2)	1	0	0	0	0	0	1	0
Total (40)	10	3	6	4	2	2	4	9

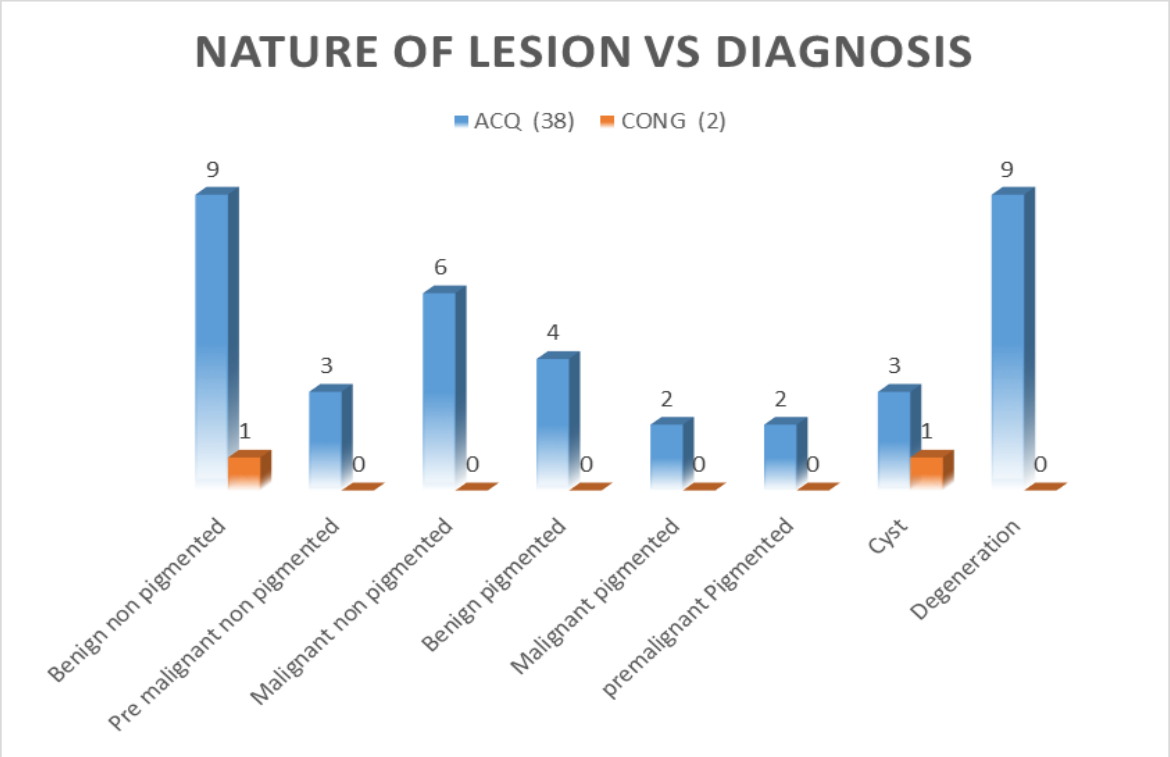


TABLE 24: DISTRIBUTION OF CONJUNCTIVAL LESIONS BASED ON ADDITIONAL MANAGEMENT DONE AFTER EXCISION BIOPSY:

Among the 40 cases studied additional intervention was done for 19 cases. Cryotherapy with amniotic membrane graft was done for 9 cases, conjunctival autograft was done for 8 cases, plain amniotic membrane graft was done for 1 case and alcohol ablation of cornea was done for 1 case.It was noted that all malignant cases underwent cryotherapy with AMG

Additional Management	No.of cases
CONJ AUTOGRAFT	8
CRYOTHERAPY WITH AMG	9
AMG	1
CRYOTHERAPY WITH AMG,CORNEA- ALCOHOL ABLATION	1
Nil	21
Total	40

	Benign non pigmented	Pre malignant non pigmented	Malignant non pigmented	Benign pigmented	Malignant pigmented	premalignant Pigmented	Cyst	Degeneration
CRYO WITH AMG =/- CORNEAL ABLATION (10)	0	3	5	0	2	0	0	0
AMG (1)	0	0	0	0	0	0	0	1
CONJ AUTOGRAFT(8)	3	0	0	0	0	2	0	3
NIL (21)	7	0	1	4	0	0	4	5
Total (40)	10	3	6	4	2	2	4	9

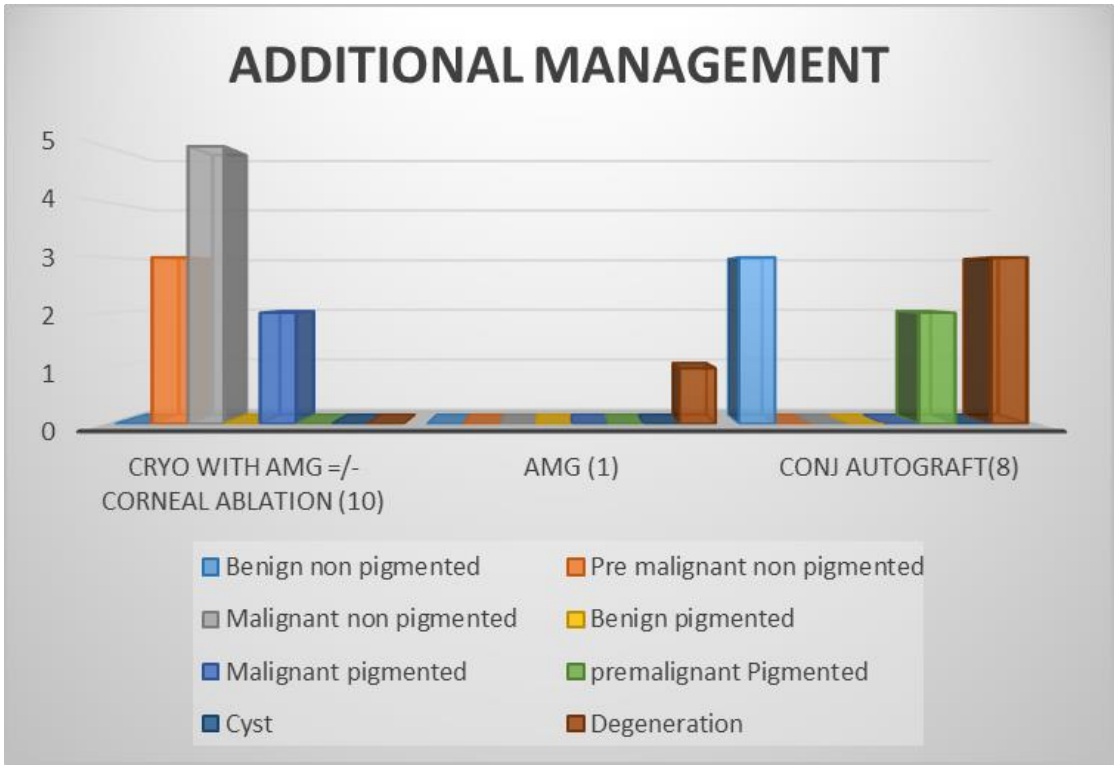


TABLE 25: DISTRIBUTION OF CONJUNCTIVAL LESIONS AND OCULAR ASSOCIATIONS

Among the 40 cases studied various ocular associations have been identified as follows

OCULAR ASSOCIATION	NO.OF CASES
Cataract	3
BE -Cataract	5
BE - PCIOL With Diabetic Retinopathy	2
BE PCIOL	3
H/O Trauma	4
H/O Cataract Surgery Re- F/B H/O Trauma	1
Corneal Pigmentation	1
RE PCIOL, LE - Cataract	1
LE- Neurofibroma Of Lid,,Mild Sphenoid Dysplasia ,BE - Lisch Nodules	1
PCIOL	1
Cataract , Lepra Nodule In Iris	1

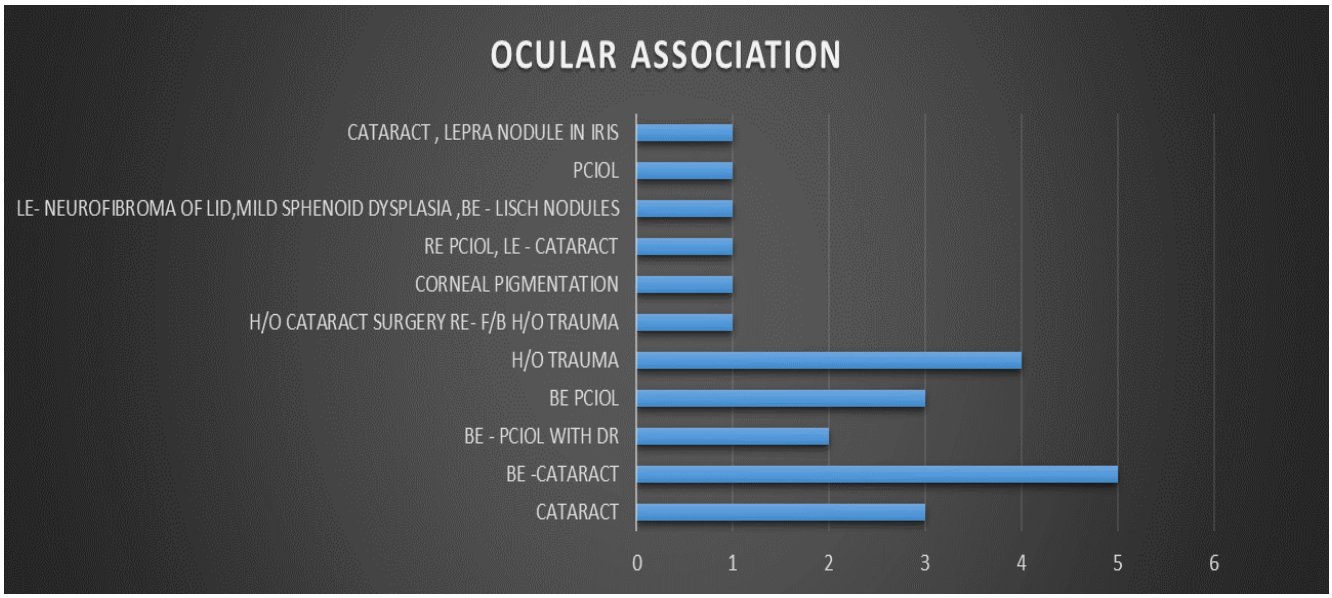
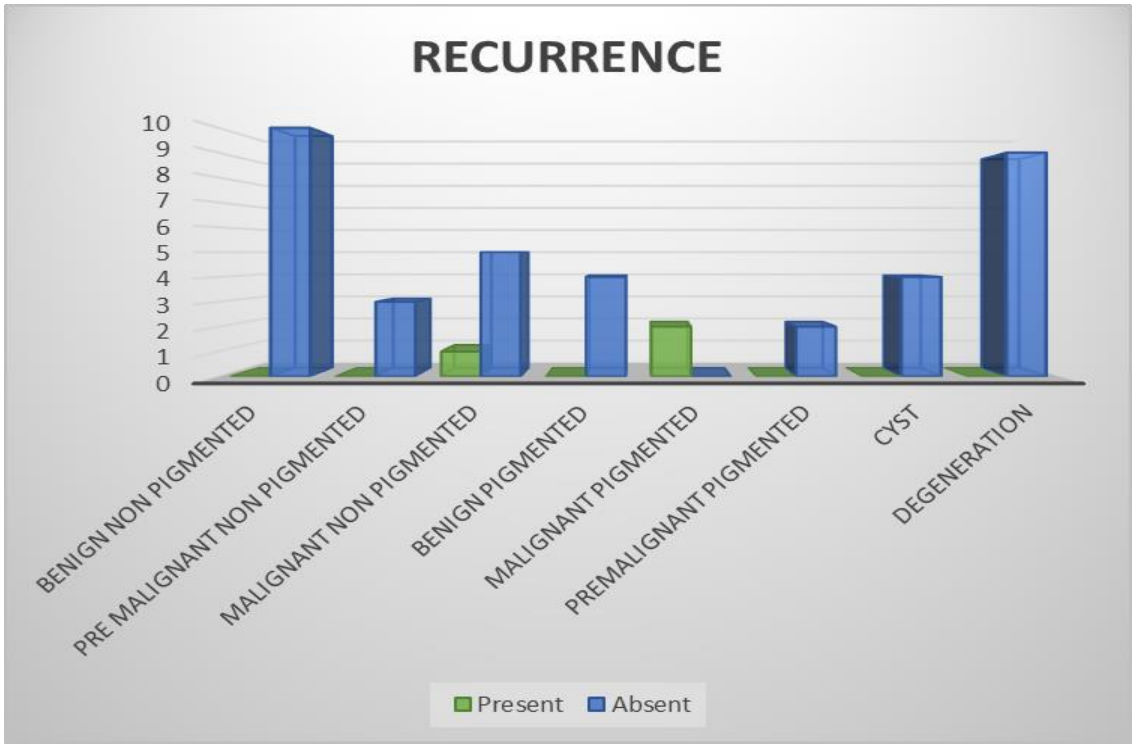


TABLE 26: DISTRIBUTION OF CONJUNCTIVAL LESION AND THEIR RECURRENCE:

Among the study group of 40 cases 3 cases were recurrent and chi square test showed the association between the malignant lesion and recurrence with p value 0.029 which is significant.

Recurrence	Benign non pigmented	Pre malignant non pigmented	Malignant non pigmented	Benign pigmented	Malignant pigmented	Premalignant Pigmented	Cyst	Degeneration
Present	0	0	1	0	2	0	0	0
Absent	10	3	5	4	0	2	4	9



SUMMARY:

- In this study, 40 patients participated and the conjunctival biopsies were sent for the histopathological analysis. The following observations were made.
- Among them, 30% were < 20 years, 10% between 21-40 years, 32.5% between 41-60 years, and 27.5% more than 60 years.
- It was noticed that benign non pigmented tumours and benign pigmented lesions are more common in less than 40 years.
- In more than 60 years, degenerations and malignancies are more common
- Among the distribution of various lesions based on their histopatholoical diagnosis – benign non pigmented tumours are most common around 25%, degenerations are second most common – 22.50%.Third most common includes non-pigmented malignant lesions 15%.
- Among the benign non pigmented tumours –squamous papilloma (33%) is most common and among degeneration- pterygium (33%) and pingecula (33%) are most common .Among malignancies – squamous cell carcinoma (37.5%) is most common.
- In this study 42.5% were females and 57.5% were males.It was noted that there is a markedly high percent of malignant (75%) and premalignant (100%) lesions in males than females.
- There is no significant predilection of laterality of eyes in conjunctival lesions
- The most common site for conjunctival lesions is the bulbar conjunctiva (87.5%)
- In this study, from the gross features of conjunctival lesions indicates that non pigmented malignancies most often (50%)are leukoplakic white growth and benign non pigmented lesions are most often (46%) pinkish in colour
- In this study it was noted that scleral fixity of the lesion is associated with malignancy most commonly (85%) and it was statistically significant with p value of 0.029

- In this study there were 27.5% smokers and all of them were males. Among males 47.8% were smokers (11 patients), Among the 11 patients 3 lesions were premalignant and 5 lesions were malignant, which constitutes about 72%. In this study 2 patients with OSSN were also PLWHA. CIN, lymphoma, metastatic lung cancer could have been because of its association with smoking.
- From the study it is noted that the number of lesions does not conclude the nature of the lesion
- In the study it is obvious that larger the lesion size >4mm it is more likely to be malignant or premalignant (73%) and most smaller lesions <3mm are benign (36%)
- It was also concluded that all malignant lesions need wide excision with tumour free margin of about 3 mm (70%) and also additional application of cryotherapy and AMG (70%)
- From the study it was noted that chronic lesions >3 years are more likely to be either degenerative (38%) or benign (38%)
- In this study it is seen that the presence of corneal involvement in conjunctival lesions does not conclude the nature of the lesion.
- In this study it is found out that pain is commonly associated with any type of malignant lesions (38.4%) and mild pain may be a feature of traumatic granuloma or inclusion cysts (30%)
- It is noted that progression is characteristically absent in benign lesions (50%)
- It is also noted that acquired lesions are more common (95%) than congenital lesions (5%)
- It is also found that most OSSN are associated with HIV (50%)

- From the study it was found that visual acuity cannot be correlated with the severity of the lesion because of lot of confounding factors like refractive error, cataract and diabetic retinopathy in these patients with conjunctival lesions
- In this study it is found that recurrence after excision is markedly associated with malignant lesions (pigmented/ non pigmented) (30%) and it was found to be statistically significant with p value of 0.029.

DISCUSSION:

Tumours of the conjunctiva have large spectrum that range from benign to aggressive life and vision threatening malignancies. The conjunctiva spawns neoplastic lesions from both its epithelial & stromal structures. Conjunctiva being visible, tumours and lesions that occur are easily recognized at a relatively early stage. Tumours having typical clinical features and small benign appearing tumours do not need a biopsy usually. If a smaller tumour does require a biopsy, it is often better to completely remove the lesion, by excisional biopsy. In cases of larger lesions, however, it is appropriate to remove a portion of the tumour (incisional biopsy) to obtain a histopathologic diagnosis before embarking on more extensive therapeutic approach.

In a study by Hemalatha Krishnamurthy, Manjuladevi N on the clinical and histopathological analysis of conjunctival tumours in tertiary care centre in Indian population showed that (59.70%) patients were male and (40.29%) patients were female. The mean age of the134 patients was 35 years. (76.12%) were benign, (5.97%) were premalignant and (17.91%) were malignant cases.

The most common diagnosis of 134 conjunctival lesions were, nevus 18.66%, chronic inflammation 15%, followed by foreign body granuloma 13.4% , carcinoma in situ 10.44% ,

Squamous cell dysplasia 5.97%, tendons cyst 5.97% , squamous cell carcinoma (SCC) 5.22% , epithelial cysts 5.22%, dermolipoma in 4.48, haemangioma 3.73% , squamous papilloma 3.73%, dermoid 2.98, pyogenic granuloma 2.98%,malignant melanoma 1.49% and lymphoma 0.74 %

The most common indication for resection of tumour was suspected growth of the tumour. In all cases of suspected growth, the tumour was excised surgically, (1.49%) SCC was treated with topical mitomycin C after tumour resection. Malignant lesions had no systemic metastasis and local recurrence.

Amoli and Heidari reported that the most common benign primary conjunctival tumour was nevus 38.7% (mean age of the patients 22.27) and the most common malignant tumour (25.1%) was SCC (mean age of the patients 58.63) in their series

Shield et al reported a change in tumour colour detected in 13% and a change in tumour size detected in 8% from his study. Regarding the symptoms and clinical appearance of the conjunctival nevus, most patients reported noticing a spot on the eye (65%), 5% noted inflammation, and 30% of patients were unaware of the lesion. The symptoms were present for a mean of 12 years. Enlargement or colour change in the lesion over the years prior to our examination was reported by 54% of patients, but support for such enlargement was rarely photographed.

The tumour was most commonly found in the bulbar conjunctiva (79%), caruncle (18%), or plica semilunaris (3%).

Shield et al reports conjunctival nevus found most commonly in the bulbar conjunctiva (72%), caruncle (15%), or plica semilunaris (11%). Rarely was the tumour found in the fornix (1%), tarsal conjunctiva (1%), or within the cornea (1%). It has been suggested that the

presence of a nevus in the palpebral and forniceal region should raise the suspicion of malignancy and early biopsy.

In a Danish study by Gerner et al provided a clinicopathologic study on 343 conjunctival nevi. They described the following tumour locations: the bulbar conjunctiva in 33% caruncle in 29%, limbal conjunctiva in 27%, and at the eyelid margin in 1%

In our study group the most common lesion isolated was benign pigmented and nonpigmented lesions were common in < 40 years and in >60 years degenerative and malignancies are common.

Overall the most common lesion was squamous papilloma followed by degenerative lesions like pterygium and pingecula and thirdly squamous cell carcinoma. This difference is due to the geographic variation in the study group.

In this study also the most common location of the conjunctival lesions was bulbar conjunctiva. The indication for conjunctival biopsy is ambiguity of clinical diagnosis and cosmetic blemish. Also in our study OSSN was markedly associated with HIV.Also OSSN, CIN, lymphoma, conjunctival metastasis of lung cancer has been found to be associated with smoking.

Most patients included in the study group experienced no symptom other than cosmetic blemish due to visible conjunctival mass but few malignant and traumatic granuloma and inclusion cyst patients had mild – moderate pain. Also it was concluded that scleral fixity and recurrence are most common in malignancies.

CONCLUSION

It is observed that in subjects below 50 years benign non pigmented lesions like squamous papilloma are common and they are asymptomatic, mostly <3mm size , freely mobile , have a chronic course and do not recur after simple excision.

It is also observed that in subjects > 50 years in our study the malignant lesion like squamous cell carcinoma are more common and have predilection towards males.They have pain, grossly appear leucoplakic (in malignant non pigmented lesions),> 4mm size mostly and scleral fixity is present. They require cryo therapy and AMG after excision and they recur often after excision. It was also observed that the smokers had more incidence of premalignant- malignant lesions and OSSN was seen more in HIV positive patients.

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PROFORMA

NAME

AGE / SEX

PRESENT HISTORY

PAST HISTORY

VISIT NUMBER

DATE

HPE SAMPLE REFERENCE NUMBER:

OBLIQUE EXAMINATION

RIGHT EYE		LEFT EYE
	UCVA	
	LIDS	
	CONJ	
	CORNEA	
	ANTERIOR CHAMBER	
	IRIS	
	PUPIL	
	LENS	

SLIT LAMP EXAMINATION

RIGHT EYE		LEFT EYE
	UCVA	
	LIDS/LASHES /MEIBOMIAN GLANDS	
	CONJ	
	SIZE , LOCATION OF THE LESION	
	CORNEA	
STAINING		
	ANTERIOR CHAMBER	
	IRIS	
	PUPIL	
	LENS	

Corneal sensitivity:

Schirmer‘s test:

FUNDUS:

RIGHT EYE		LEFT EYE
	MEDIA	
	DISC S/S/C/M	
	C: D	
	VESSELS	
	A:V	
	MACULA	
	FR	

HISTOPATHOLOGY REPORT:

S.NO	NAME	AGE	SEX	EYE	HPE DIAGNOSIS	DIAGNOSIS	NATURE	SMOKING	GROSS	SF	NUMBER	SIZE	BX TYPE	DURN	LOCN	VISION	CORNEAL INV	PAIN	PROGRESN	OCULARASSOCN	RECURRENCE	SYSTEMIC	ADDITIONAL MANAGEMENT
1	LAKSHMI	16	F	RE	DERMOID	CYSTS	CONG	A	PINK,SOFT	A	1	S	E	3	BC	BE 6/6	A	A	+	A	A	A	NIL
2	MUNIANDI	13	M	LE	BENIGN MELANOSIS	BENIGN PIGMENTED	ACQ	A	FLAT PIGMENTED	A	1	S	E	3	BC	BE 6/6	A	A	+	A	A	A	NIL
3	SOUNDARAPANDI	45	M	RE	OSSN	MALIGNANT NON PIGMENTED	ACQ	P	LEUCOPLAKIC,FIRM	P	1	L	E+TFM	1	BC	BE 6/9	A	A	+	A	A	HIV -ON ART	CRYO+AMG
4	PARTHIBAN	50	M	RE	DEGENERATION	DEGENERATION	ACQ	A	YELLOW	A	1	S	E	1	BC	BE 6/60	A	A	+	C,LEP	A	LEPROSY ON MDT	AUTO
5	RAJARAM	60	M	BE	PINGECULA	DEGENERATION	ACQ	A	YELLOW	A	1	S	E	2	BC	BE 6/36	A	A	+	C	A	A	NIL
6	PONNI	65	F	BE	PTERYGIUM	DEGENERATION	ACQ	A	PINK	A	1	L	E	2	BC	BE 6/60	P	A	+	C	A	A	AUTO
7	KARUPPU	70	M	LE	LYMPHOMA	MALIGNANT NON PIGMENTED	ACQ	P	SALMON	P	1	S	E+TFM	1	FC	BE 6/18	A	M	+	PCIOL	A	HT	CRYO+AMG
8	SEETHAMAL	65	F	BE	PINGECULA	DEGENERATION	ACQ	A	YELLOW	A	1	S	E	3	BC	BE 6/24	A	A	+	PCIOL	A	A	NIL
9	SANKARAN	40	M	LE	FOREIGN BODY GRANULOMA	BENIGN NON PIGMENTED	ACQ	P	YELLOW	A	1	S	E	1	BC	BE 6/9	A	M	-	A,T	A	A	NIL
10	PECHIAMMAL	60	F	BE	PTERYGIUM	DEGENERATION	ACQ	A	PINK	A	1	L	E	3	BC	RE 6/18,LE 6/36	P	A	+	C	A	DM	AMG
11	MUTHUKUMAR	45	M	RE	CARCINOMA IN SITU	PRE MALIG NON PIGMENTED	ACQ	P	WHITE	P	1	L	E+TFM	1	BC	BE 6/12	A	M	+	A	A	A	CRYO ,AMG
12	AZHAGAR	67	M	BE	DEGENERATION	DEGENERATION	ACQ	P	YELLOW	A	1	S	E	3	BC	RE6/60,LE-6/36	A	A	-	C	A	DM	NIL
13	AMMASI	30	M	RE	INCLUSION CYST	CYSTS	ACQ	A	TRANSPARENT	A	1	S	E	1	BC	BE 6/6	A	M	-	T	A	A	NIL
14	VIJAYALAKSHMI	65	F	RE	FOREIGN BODY GRANULOMA	BENIGN NON PIGMENTED	ACQ	A	REDDISH	A	1	L	E	1	BC	RE-1/60,LE-6/12	A	P	-	T	A	A	AUTO
15	RAJAMMAL	45	F	LE	SQUAMOUS PAPILLOMA	BENIGN NON PIGMENTED	ACQ	A	PINK	A	1	S	E	1	FC	BE 6/12	P	A	+	A	A	A	AUTO
16	SARANYA	16	F	RE	BENIGN LYMPHOID HYPERPLASIA	BENIGN NON PIGMENTED	ACQ	A	PINK	A	1	S	E	1	BC	BE 6/6	A	A	-	A	A	LN	NIL
17	RAKESH	17	M	BE	JUNCTIONAL NEVUS	BENIGN PIGMENTED	ACQ	A	BROWN	A	2	S	E	3	BC	BE 6/9	A	A	-	A	A	A	NIL
18	MAHARAJAN	16	M	BE	PAM	PIGMENTED PRE MALIG	ACQ	A	BROWN	A	4' HRS	L	E	3	BC	BE 6/12	P	A	+	COR PIGMN	A	?LEOPARD SYNDROME	AUTO
19	PADMA	14	F	LE	SQUAMOUS PAPILLOMA	BENIGN NON PIGMENTED	ACQ	A	PINK	A	2	S	E	2	BC	BE 6/6	A	A	+	A	A	A	AUTO
20	RANI	28	F	RE	LIPOMA	BENIGN NON PIGMENTED	ACQ	A	YELLOW	A	1	S	E	3	FC	BE 6/9	A	A	+	A	A	A	NIL
21	RAJALAKSHMI	68	F	BE	DEGENERATION	DEGENERATION	ACQ	A	YELLOW	A	1	S	E	3	BC	RE 6/60 LE 5/60	A	A	+	C	A	CAD	NIL
22	BASKARAN	55	M	LE	MALIGNANT MELANOMA	PIGMENTED MALIGNANT	ACQ	P	PIGMENTED	P	1	L	E+TFM	1	MC	RE 6/18,LE 6/24	A	P	+	PCIOL,C	P	A	CRYO+AMG
23	ESAKIPANDI	61	M	LE	PAM	PIGMENTED PRE MALIG	ACQ	P	PIGMENTED FLAT	A	3'HRS	L	E	3	BC	RE 5/60, LE 6/60	A	A	+	C	A	DM, HT	AUTO
24	RAMESH	29	M	RE	DERMOLIPOMA	BENIGN NON PIGMENTED	CONG	A	PINK	A	1	S	E	3	FC	BE 6/6	A	A	-	A	A	A	NIL
25	MARIAMMAL	68	F	LE	SQUAMOUS CELL CARCINOMA	MALIGNANT NON PIGMENTED	ACQ	A	WHITE,FIRM	P	1	L	E+TFM	1	BC	RE - 6/36,LE -4/60	P	P	+	PCIOL	P	DM	CRYO+AMG,CORNEAL ALC ABLATION
26	GANESHAN	66	M	RE	METASTATIC LESION	MALIGNANT NON PIGMENTED	ACQ	P	PINK	A	1	L	E+TFM	2	BC	RE-1/60,LE-6/12	A	P	+	PCIOL	A	K/C/O CA	CRYO+AMG
27	KESAVAN	68	M	BE	PINGECULA	DEGENERATION	ACQ	A	PINK	A	1	S	E	3	BC	BE 6/18	A	A	+	PCIOL	A	DM,CAD	NIL
28	ANNAKODI	20	F	LE	NEUROFIBROMA	BENIGN NON PIGMENTED	ACQ	A	YELLOW	A	1	S	E	3	BC	BE- 6/12	P	M	-	NF	A	NF	NIL
29	SANTHANAMARY	13	F	RE	LEUKEMIC INFILTRATES	MALIGNANT NON PIGMENTED	ACQ	A	SALMON	A	1	S	E	1	BC	BE 6/12	A	A	-	A	A	K/C/O LEUKEMIA	NIL
30	ANTHONY	55	M	LE	DYSPLASTIC PAPILLOMA	PRE MALIG NON PIGMENTED	ACQ	P	WHITE	M	1	L	E+TFM	1	BC	BE 6/24	A	A	+	C	A	A	CRYO+AMG
31	DHARMARAJ	48	M	RE	SQUAMOUS PAPILLOMA	BENIGN NON PIGMENTED	ACQ	A	PINK	A	1	S	E	2	BC	BE 6/12	A	A	+	A	A	HT	NIL
32	ELAKIYA	13	F	LE	COMPOUND NEVUS	BENIGN PIGMENTED	ACQ	A	BROWN	A	1	S	E	3	BC	BE 6/6	A	A	+	A	A	A	NIL
33	DHIVAKAR	19	M	RE	EPIDERMOID CYST	CYSTS	ACQ	A	PINK	A	1	S	E	1	BC	BE 6/6	A	A	-	T	A	A	NIL
34	MUNIASAMY	58	M	BE	PTERYGIUM	DEGENERATION	ACQ	P	PINK	A	1	L	E	3	BC	RE 6/18, LE 6/24	P	O	+	C , DR	A	DM	AUTO
35	AKSHAYA	18	F	LE	BENIGN LYMPHOID HYPERPLASIA	BENIGN NON PIGMENTED	ACQ	A	PINK	A	1	S	E	1	BC	BE 6/6	A	A	-	A	A	LN	NIL
36	DIVYA	16	F	BE	BENIGN MELANOSIS	BENIGN PIGMENTED	ACQ	A	BROWN	A	1	S	E	3	BC	BE 6/9	A	A	+	A	A	A	NIL
37	MOHAMMAD	72	M	LE	MALIGNANT MELANOMA	PIGMENTED MALIGNANT	ACQ	A	BROWN	P	1	L	E+TFM	1	BC	BE 6/60	A	M	+	PCIOL, DR	P	DM	CRYO+AMG
38	GUNASEELAN	55	M	RE	SQUAMOUS PAPILLOMA WITH DYSPLASIA	PRE MALIG NON PIGMENTED	ACQ	A	WHITE	M	1	L	E+TFM	1	BC	BE 6/24	A	M	+	C	A	HT	CRYO+AMG
39	PITCHAI	48	M	RE	OSSN	MALIGNANT NON PIGMENTED	ACQ	P	LEUCOPLAKIC,FIRM	P	1	L	E+TFM	1	BC	BE 6/9	A	A	+	A	A	HIV -ON ART	CRYO+AMG
40	JAKAMAL	44	F	RE	INCLUSION CYST	CYSTS	ACQ	A	PINK	A	1	S	E	1	MC	BE 6/12	A	M	-	T	A	A	NIL

LIST OF ABBREVATIONS

OSSN – Ocular Surface Squamous Neoplasia

PAM – Primary Acquired Melanosis

RT – Radiotherapy

AD – autosomal dominant , AR – autosomal recessive

CGy – Centi Gray

5-FU- 5 Fluoro uracil

MM C – Mitomycin C

PLWHA – People living with HIV AIDS

LIST OF ABBREVATIONS FOR MASTER CHART

ART – Anti retroviral treatment (for HIV)

ACQ – acquired

CONG – congenital

CIN – Carcinoma in situ

HPE – Histopathological examination

HIV – Human immunodeficiency virus

AMG – Amniotic membrane graft

RE –Right eye LE – Left eye BE – Both eye

PCIOL- Posterior chamber intraocular lens

DR – Diabetic retinopathy

CONJ – Conjunctiva

LN – lymph node enlarged

CA- carcinoma

C - Cataract

K/C/O – Known case of

SIZE <3 mm –S

>4 mm –L

A- Absent

P- Present

M-Minimal

Group 1 - <1 year duration

Group 2 – 1-3 years duration

Group 3 - >3 years duration

BC – Bulbar conjunctival location

FC – Forniceal conjunctival location

MC – Medial canthal location

SF – Scleral fixity

O – Occasional

T- Trauma

NF – Neurofibroma lid, Lisch nodule, sphenoid dysplasia

LEP – Lepra nodule in iris

E – Excision

E+TFM –Excision with 3 mm tumour free margin

BX – Biopsy

CRYO +AMG- Cryotherapy with Amniotic membrane graft

AUTO – Conjunctival autograft

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ETHICS COMMITTEE CERTIFICATE

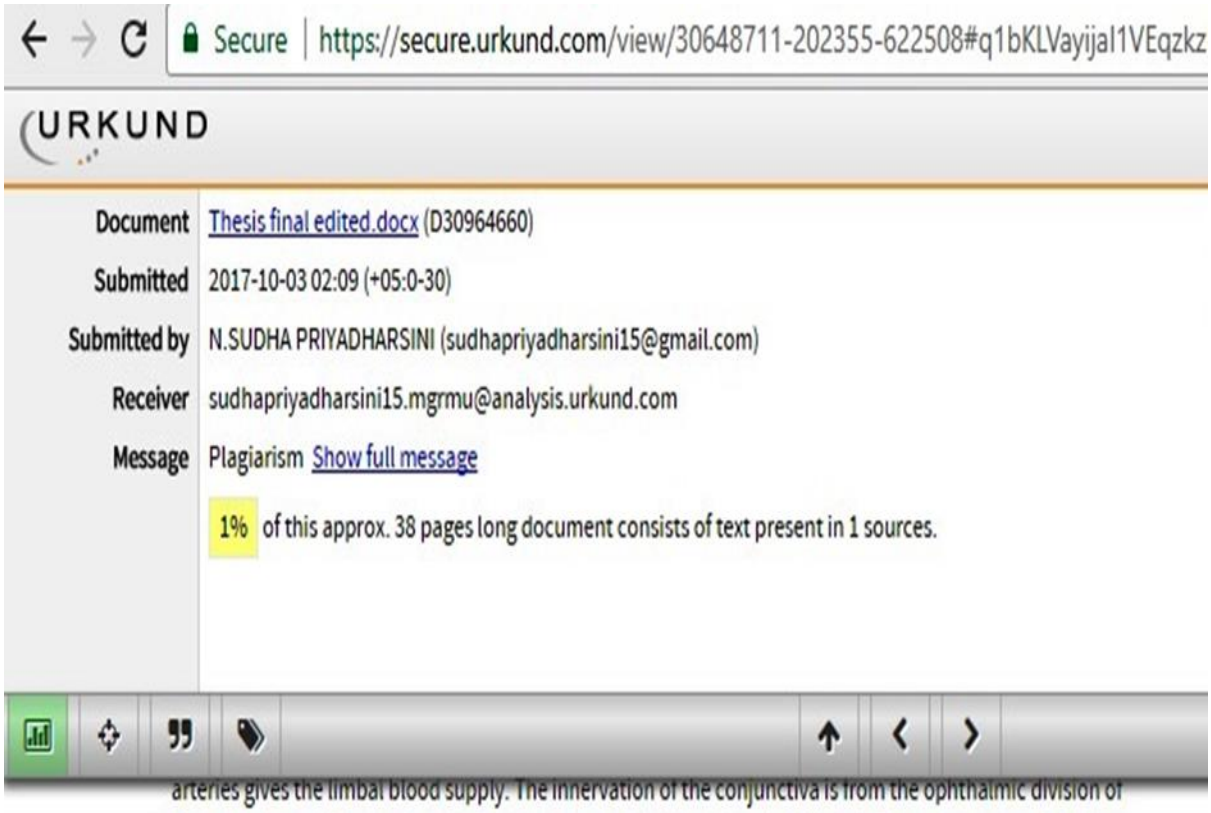
Name of the Candidate	:	Dr.Sudha priyadharsini .N
Course	:	PG in MS., Ophthalmology
Period of Study	:	**2015-2018**
College	:	**MADURAI MEDICAL COLLEGE**
Research Topic	:	A clinicopathological study to analyse the importance of histopathological examination in diagnosis of excised conjunctival lesions of the bulbar conjunctiva
Ethical Committee as on	:	21.04.2017

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

Member Secretary Chairman Dean / Convenor

Prof Dr V Nagaraajan
M.D., MNAMS, D.M., Dsc.,(Neuro), Dsc (Hon)
CHAIRMAN
IEC - Madurai Medical College
Madurai

DEAN
Madurai Medical Colleg
Madurai-20



arteries gives the limbal blood supply. The innervation of the conjunctiva is from the ophthalmic division of trigerminal nerve. The conjunctiva is a mucous membrane made of non keratinizing squamous epithelium with lot of goblet cells and richly vascularized substantia propria having lymphatic vessels, plasma cells, macrophages,mast cells. A lymphoid layer is presents from the bulbar conjunctiva to sub tarsal folds.Specialized aggregations of conjunctiva-associated lymphoid tissue (CALT) correspond to mucosa associated lymphoid tissue (MALT) and have collections of T and B lymphocytes under the epithelium. They help in antigen processing. The conjunctival epithelium is 2 to 5 cells thick. The basal cells are cuboidal in shape and become flattened polyhedral cells at the surface. The goblet cells (mucous glands) are found in the inferior and medial part of the conjunctiva more in the region of the caruncle and plica semilunaris. They are sparsely found in the remainder of the conjunctiva and absent in the limba1 area.

The conjunctiva is readily visible and so the tumors and other lesions in the conjunctiva are generally recognized at a early stage. Clinical diagnosis can often be made by ocular examination and slit- lamp biomicroscopy, if features are characteristics. A biopsy is not necessary in cases of smaller tumors that appear benign. Small tumours can be better removed completely in one setting(excisional biopsy). Larger lesions, remove a portion of the tumor (incisional biopsy) to get a histopathologic diagnosis prior to more extensive therapy.It is rarely needed to do exfoliative cytology or fine- needle aspiration biopsy, as incisional biopsy is readily available. Slit- lamp examination of the cornea is needed in patients with suspected conjunctival

CERTIFICATE - II

This is certify that this dissertation work title **"A CLINICOPATHOLOGICAL STUDY TO ANALYSE THE IMPORTANCE OF HISTOPATHOLOGICAL EXAMINATION IN DIAGNOSIS OF EXCISED CONJUNCTIVAL LESIONS OF BULBAR CONJUNCTIVA"** of the candidate **Dr. N.SUDHA PRIYADHARSINI** with registration Number 221513105 for the award of M.S. Degree in the branch of Opthalmology (III). I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion page and result shows 1 percentage of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.