Lacrimal gland tumors represent 5% to 25% of orbital tumors. It has been described that about 50% of lacrimal masses are epithelial and 50% are nonepithelial (Table 1). But the recent literature shows that the inflammatory lesions and lymphoid tumors of the lacrimal gland are two to three times more common than epithelial tumors.

Nonepithelial Lacrimal Gland Lesions
Most of the nonepithelial lesions of the lacrimal gland represent lymphoid proliferations or inflammations. Preoperative characterization of the particular lesion is key in the management, which is based on the duration of symptoms, the presence of pain, and radiologic findings.

Inflammatory
Acute onset of swelling associated with periorbital pain, chemosis and indurated lid indicate an inflammatory process of either idiopathic (pseudotumor) or of infective etiology (dacryoadenitis). A computed tomography scan usually reveals a diffuse lacrimal enlargement with irregular margins, frequently demonstrating contrast enhancement and no bony change. Idiopathic orbital inflammatory disease (pseudotumor) is treated with a short course of corticosteroids. In case of failure to resolve over a few weeks, an incisional biopsy should be taken should, since acute inflammatory episodes may be related to an underlying carcinoma (Figure 1).

Lymphoproliferative lesions
These are characterized by insidious onset, painless proptosis in a slightly older population and is often bilateral. CT scans show that all lymphoid tumors mold themselves around the existing orbital structures, such as the globe and the bony orbit, without eroding bone or enlarging the orbit (Figure 2).

Table 1: Classification of Lacrimal Gland Tumors

*50% of the Orbital Lymphoproliferative lesions occur in the Lacrimal Gland.
Epithelial tumors of the lacrimal gland

A pathologic classification of the epithelial tumors of the lacrimal gland (Table 2) is recently proposed, based on the current WHO classification of salivary gland tumors.

Pleomorphic Adenoma

It is the most common benign neoplasm of the lacrimal gland. The term “benign mixed tumor” denotes that these tumors are derived from a mixture of epithelial and mesodermal elements.

Clinical Features

Pleomorphic adenoma usually occurs in the fourth and fifth decade of life, and incidence is equal for both genders. It presents with symptoms of painless, progressive proptosis and downward and inward displacement of the globe. A non tender palpable mass in the superotemporal orbital quadrant is present in most patients (Figure 3a). Although pleomorphic adenoma usually involves the orbital lobe of the lacrimal gland, palpebral lobe involvement is seen in 10% of cases. These palpebral lobe tumors are freely movable and do not produce proptosis or bony changes.

Radiologic Features

CT images (Figure 3b) show well-defined, round to oval lesions that are smooth in outline and are associated with prominent lacrimal fossa formation due to pressure erosion. Long-standing large tumors may show lobulations and radiolucent areas of cystic degeneration. On MRI, the tumor is hypointense on the T1-weighted image and hyperintense on the T2-weighted image.

Pathology

Grossly (Figure 4), the tumor is greyish white, solitary, bosselated and well circumscribed by a thin pseudocapsule formed by compressed adjacent tissue.

Histopathologic examination (Figure 3c) shows the mixture of epithelial and mesenchymal elements. Focal squamous metaplasia may also be present.

Management and Prognosis

The management is complete excision of the tumor. Lateral orbitotomy is described for the complete surgical removal.

Table 2: Classification of Epithelial Lacrimal Gland Tumors

<table>
<thead>
<tr>
<th>Classification</th>
<th>Epithelial Lacrimal Gland Tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>Pleomorphic adenoma, Pleomorphic adenoma with atypia Myoepithelioma, Oncocytoma, Cystadenoma</td>
</tr>
<tr>
<td>Malignant</td>
<td>Carcinoma ex pleomorphic adenoma/ malignant mixed tumor (where the carcinoma is noninvasive or minimally invasive [≤ 1.5mm] as defined by the WHO classification) Polymorphous low-grade carcinoma Mucoepidermoid, grades 1 and 2 Epithelial-myoepithelial carcinoma, Acinic cell carcinoma, Basal cell carcinoma Mucinous adenocarcinoma</td>
</tr>
<tr>
<td>Low grade</td>
<td>Carcinoma ex plomorphic adenoma/ malignant mixed tumor, which includes adenocarcinoma and adenoid cystic carcinoma arising in a pleomorphic adenoma (where the carcinoma is invasive (&gt;1.5 mm) as defined by the WHO classification) Adenoid cystic carcinoma not otherwise specified Adenocarcinoma not otherwise specified Mucoepidermoid, grade 3 Ductal acenocarcinoma Squamous cell carcinoma Sebaceous adenocarcinoma Myoepithelial carcinoma Lymphoepithelial carcinoma Other rare and unclassifiable carcinomas Dedifferentiation in any of the above carcinomas</td>
</tr>
<tr>
<td>High grade</td>
<td>Carcinoma ex plomorphic adenoma/ malignant mixed tumor, which includes adenocarcinoma and adenoid cystic carcinoma arising in a pleomorphic adenoma (where the carcinoma is invasive (&gt;1.5 mm) as defined by the WHO classification) Adenoid cystic carcinoma not otherwise specified Mucoepidermoid, grade 3 Ductal acenocarcinoma Squamous cell carcinoma Sebaceous adenocarcinoma Myoepithelial carcinoma Lymphoepithelial carcinoma Other rare and unclassifiable carcinomas Dedifferentiation in any of the above carcinomas</td>
</tr>
<tr>
<td>Histologic grade</td>
<td>Grade cannot be assessed Well differentiated Moderately differentiated, includes adenoid cystic carcinoma without basaloid (solid) pattern Poorly differentiated, includes adenoid cystic carcinoma with basaloid (solid pattern Undifferentiated.</td>
</tr>
</tbody>
</table>
of these tumors, however anterior orbitotomy can be performed especially if the mass is primarily located in the anterior orbit. Stallard-Wright incision or lid-crease incision can be used. To minimize any tumor seeding, adjacent periorbita should be removed. Removal of the palpebral lobe of the lacrimal gland is also advocated to reduce the recurrence rate. However, sacrificing the palpebral lobe may lead to postoperative dry eye and the need for topical lubricants.

These tumors have high recurrence rate following incomplete excision or incisional biopsy. The 5-year recurrence rate for completely excised lesions is 3% and for incompletely excised tumors, it is 32%. Recurrent pleomorphic adenoma can also undergo malignant change. As biopsy of pleomorphic adenomas can have disastrous consequences, these tumors should be diagnosed before surgery, so that biopsy can be avoided. In patients with pleomorphic adenoma who have undergone biopsy, the biopsy track and skin scar are excised in continuity with a total removal of lacrimal gland.

**Adenoid Cystic Carcinoma**

Adenoid cystic carcinoma is the most common malignant epithelial tumor of the lacrimal gland. A bimodal peak in the fourth and sixth decades is described. As this tumor may present at an earlier age, a high index of suspicion is required for any unilateral mass in the upper temporal quadrant, in young adults, where it might be mistaken for pseudotumor or dermoids.

**Clinical Features**

It usually presents with a shorter history of proptosis, globe displacement and pain; which may be associated with motility disturbance, diplopia, ptosis, lacrimation, numbness and decreased vision. Pain is a characteristic feature of this malignancy due to perineural invasion. The reported incidence of pain ranges from 37.5 to 79%.

**Radiologic Features**

CT shows more elongated, irregular mass extending along the lateral orbital wall, with bone invasion. In a series, CT abnormalities in adenoid cystic carcinoma consisted of bone erosion (75%), bone destruction (34%), and calcification (22%). High-resolution CT with bone windows is recommended. Contrast enhancement helps to reveal involvement of the dura and intracranial extension.

Intracranial extension of the tumor in cavernous sinus and brain can be best assessed by contrast enhanced MRI. The tumor is hypointense on the T1-weighted image and hyperintense on the T2-weighted image.

**Pathology**

Grossly, this tumor is firm, nodular, with ill-defined borders. Microscopically, five histologic patterns have been described: (i) cribriform ("Swiss cheese") (Figure 1b), (ii) solid (basaloid), (iii) sclerosing, (iv) comedocarcinomatous, and (v) tubular (ductal), in order of frequency. The "Swiss cheese" pattern is associated with longer survival and basaloid pattern has poorer prognosis. Perineural invasion is frequently observed, accounting for the symptoms of pain and numbness.

**Management and Prognosis**

There are no clear guidelines regarding the optimal treatment for adenoid cystic carcinoma. Tumor removal and postoperative radiotherapy comprise the most common treatment. The surgical techniques of tumor removal include local resection, en bloc removal, exenteration, and radical exenteration. Even with the radical approach, the survival rate is reported to be 20% at 10 years, with the median survival of 5 years. Mortality in this tumor is primarily due to intracranial spread as a result of perineural invasion and pulmonary metastasis.
Post operative radiotherapy in the dose of 50 to 60 Gy following local resection of the tumor significantly delays the onset of tumor recurrence and prolongs the survival. Use of neoadjuvant chemotherapy is also described for patients with inoperable tumors to shrink them to a more surgically amenable size. Intra-arterial chemotherapy with intracarotid cisplatin has recently been advocated for supplemental management. Role of adjuvant chemotherapy is not clear. We have reported survival of 6 and 4 years respectively in 2 patients of adenoid cystic carcinoma after they received adjuvant chemotherapy following local resection of tumor.

**Malignant Mixed Tumor**

A malignant mixed tumor represents malignant degeneration of pleomorphic adenoma. It accounts for 4 to 15% of lacrimal gland epithelial tumors. Font and Gamel described that adenocarcinoma arising from pleomorphic adenoma is more common in males, whereas adenoid cystic carcinoma arising from pleomorphic adenoma is more often seen in females.

**Clinical Features**

Malignant mixed tumors usually present in three clinical ways.

1. Incompletely excised benign mixed tumor may develop a sudden recurrence several years later.
2. Long-standing lacrimal tumor presents with sudden expansion of the mass, as well as pain and swelling of the upper eyelid.
3. De novo presentation, where patient has rapidly develops symptoms of pain and bone destruction.

**Radiologic Features**

On CT, lacrimal fossa mass with bone destruction suggests malignant tumors, which is best seen in bone window. It is indistinguishable from the other carcinomas of the lacrimal gland on CT.

**Pathology**

Malignant mixed tumors have the microscopic features of a benign mixed tumor with areas of malignant change. Mostly, the malignant elements are poorly differentiated adenocarcinoma. Less commonly there are adenoid cystic carcinoma, squamous cell carcinoma, and, rarely, spindle cell sarcoma.

**Management and Prognosis**

A transseptal biopsy should be taken to confirm the diagnosis if malignancy is suspected in preoperative evaluation, which should be followed by en bloc resection of the neoplasm with periorbita. Postoperative radiotherapy is also recommended. Even with extensive surgery, patient mortality remains high.

**Adenocarcinoma**

Adenocarcinoma tends to occur in an older population and is associated with a shorter patient survival time than adenoid cystic carcinoma. It often manifests as a rapidly growing mass, exceeding the limits of adequate surgical excision at the time of presentation and metastasize earlier.

---

Table 3: Clinico-radiological features, management and prognosis of lacrimal gland tumors

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Imaging features</th>
<th>Management</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic Inflammatory (Pseudotumor)</td>
<td>Acute onset swelling with periorbital pain, chemosis and lid edema</td>
<td>Diffuse mass with ill-defined margins, Moderately enhancing and No bony changes.</td>
<td>Short course of oral corticosteroids</td>
</tr>
<tr>
<td>Lymphoproliferative Mass</td>
<td>Insidious onset, painless older age often bilateral</td>
<td>Characteristic molds around the globe and the bone without eroding</td>
<td>Radiotherapy (moderate-low dose RT) ± Chemotherapy</td>
</tr>
<tr>
<td>Benign (Pleomorphic adenoma)</td>
<td>Painless, without inflammation &gt;1 year duration</td>
<td>Round to oval, well circumscribed, Enlargement of the lacrimal fossa without invasion of underlying bone</td>
<td>Complete excision with periorbita (Incisional Biopsy is Contraindicated)</td>
</tr>
<tr>
<td>Malignant (Adenoid cystic carcinoma)</td>
<td>Painful swelling Shorter duration Steroid unresponsive</td>
<td>More elongated mass extending along the lateral orbital wall with bone invasion. Calcifications are more common</td>
<td>Biopsy followed by En bloc resection/ Exenteration ± Radiotherapy</td>
</tr>
</tbody>
</table>
Histopathologically, the tumor consists of pleomorphic cells with many mitotic figures and lumen formation with mucin production, which can be demonstrated with mucicarmine and alcian blue stains.

The shorter survival of the patients with this malignancy probably is related to early lymphatic dissemination to regional lymph nodes and pulmonary metastasis. Radical management with monobloc craniofacial orbitectomy and regional lymph node dissection is recommended for longer survival.

**Mucoepidermoid carcinoma**

It is the most common primary carcinoma of the salivary glands, however rare to involve the lacrimal gland. It usually presents as a painless, slowly growing mass of the lacrimal gland that is sometimes mistaken preoperatively for benign mixed tumor.

Histologically, these tumors comprise a mixture of mucus-secreting cells (signet ring cells) interspersed with epidermoid and basal cells. It is classified as either low or high grade depending on the number of mucin-producing cells and degree of differentiation.

Low grade tumors (grade 1) have large, well-differentiated cells with abundant cytoplasm, a relative paucity of the epidermoid cells, and no mitotic figures.

High grade tumors (grade 3) have smaller cells with hyperchromatism and frequent mitotic figures predominated by epidermoid elements.

The clinical behavior and prognosis parallel the histologic grading.

**Other tumors**

The following are the few rare lacrimal gland tumors, which are infrequently encountered even in busy ocular oncology practices.

**Acinic Cell Carcinoma**

Acinic cell carcinoma is a rare tumor of salivary gland origin and even fewer cases are reported in the lacrimal gland. The peak incidence is in the sixth decade with female preponderance. It usually presents as a painless, slow-growing mass but can invade intracranially in a more aggressive manner.

Microscopically, there are four growth patterns described: solid, microcystic, papillary cystic, and follicular. The solid and microcystic patterns are considered to be the most common.

**Spindle Cell Myoepithelioma**

Myoepithelioma is a monomorphic adenoma with proliferation of only myoepithelial cells, in contrast to the pleomorphic adenoma which has proliferation of both epithelial and myoepithelial elements in various combinations. It is defined as a tumor composed of myoepithelial cells with ≤ 10% ductal elements. These are benign tumors and biologically behaves like pleomorphic adenoma.

**Oncocytoma (Oxyphil Cell Adenoma)**

Oncocytes are also called oxyphil cells because of their eosinophilic cytoplasm. These cells are found in mucous membranes such as the caruncle, conjunctiva, lacrimal sac, and lacrimal glands and increases in number with age. So the tumor tends to occur in older patients. Benign and malignant oncocytes have been reported in the lacrimal gland. Malignant oncocyto can be associated with intracranial extension.

**Solitary Fibrous Tumor**

Solitary fibrous tumor is a rare spindle cell neoplasm that has a clinical presentation is similar to that of pleomorphic adenoma. Careful follow-up is required for this tumor because there may be recurrence after several years.

**References**


Forthcoming Academic Events

6th DOS Teaching Programme**
14th & 15th June, 2014 (Saturday & Sunday)

Safdarjung Hospital*
(DOS Monthly Clinical Meeting)*
27th July, 2014 (Sunday)

Dr. R.P. Centre for Ophthalmic Sciences
(DOS Monthly Clinical Meeting)*
24th August, 2014 (Sunday)

Army Hospital (R&R)
(DOS Monthly Clinical Meeting)*
21st September, 2014 (Sunday)

Dr. Shroff’s Charity Eye Hospital
(DOS Monthly Clinical Meeting)*
26th October, 2014 (Sunday)

DOS Winter Conference
1st & 2nd November, 2014 (Saturday & Sunday)

Guru Nanak Eye Centre
(DOS Monthly Clinical Meeting)*
30th November, 2014 (Sunday)

Dr. Ram Manohar Lohia Hospital
(DOS Monthly Clinical Meeting)*
28th December, 2014 (Sunday)

Sir Ganga Ram Hospital
(DOS Monthly Clinical Meeting)*
25th January, 2015 (Sunday)

Bharti Eye Hospital
(DOS Monthly Clinical Meeting)*
22nd February, 2015 (Sunday)

Centre For Sight
(DOS Monthly Clinical Meeting)*
29th March, 2015 (Sunday)

DOS Winter Conference
1st & 2nd November, 2014
(Saturday & Sunday)

DOS Teaching Programme**
10th & 11th January, 2015
(Saturday & Sunday)

AIOS 2015
5th to 8th February, 2015
(Thursday, Friday, Saturday & Sunday)

DOS Annual Conference 2015
10th to 12th April, 2015
(Friday, Saturday & Sunday)

*Monthly Academic & Teaching Programme
**Teaching Programme for postgraduate students in Ophthalmology