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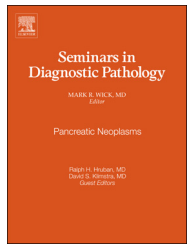

Tumors of the lacrimal gland

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ABSTRACT

Tumors of the lacrimal gland comprise a wide spectrum, of which the most common demonstrate epithelial and lymphoid differentiation. The diagnosis of lacrimal gland tumors depends primarily on histological evaluation, as do the choice of treatment and prognosis. For some lacrimal gland neoplasms, such as adenoid cystic carcinoma, the outlook is grave. Optimal treatment for several lacrimal gland tumors is also a matter of controversy. However, recent progress has been made in the molecular and genetic understanding of tumorigenesis for such lesions. This article presents an overview of the histopathology of lacrimal gland tumors, together with their epidemiological features, clinical characteristics, and treatment strategies.

Tumors of the lacrimal gland have an estimated incidence of 1 per 1 million people per year.[1] They represent 22–28% of all orbital space-occupying lesions and approximately 50% are benign.[2–4] Epithelial tumors are the most common lesions of the lacrimal gland, constituting 50–60%. Lymphoid tumors comprise 20–35% and secondary tumors approximately 10%, with the remaining 10% being mesenchymal, neuroepithelial, and vascular tumors.[1,5] The most common epithelial, lymphoid, and mesenchymal tumors of the lacrimal gland (Table) will be described in this review.

Epithelial tumors of the lacrimal gland

Distribution

The most common neoplasm of the lacrimal gland is the pleomorphic adenoma (Fig. 1A, B, and D), which accounts for up to 90% of benign tumors and 50% of primary epithelial tumors. The most common form of carcinoma is the adenoid cystic type (Fig. 1E–H), comprising 20–30% of cases. Carcinoma ex pleomorphic adenoma (Fig. 1C) accounts for approximately 10%, adenocarcinoma not otherwise specified (NOS) comprises another 5–10%, and mucoepidermoid carcinoma (Fig. 1I–L) constitutes 1–2%.[1,5–7] Other epithelial tumors are rare, including oncocytoma, myoepithelioma, Warthin's tumor, ductal carcinoma, sebaceous carcinoma, and squamous cell carcinoma.[8]

Clinical characteristics

Epithelial tumors of the lacrimal gland are generally seen in middle-aged adults. Patients with pleomorphic adenoma and adenoid cystic carcinoma have a mean age at diagnosis of 40 years, whereas individuals with other forms of carcinoma

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Table – Tumors of the lacrimal gland.

Epithelial tumors	
Benign tumors	Pleomorphic adenoma
	Oncocytoma
	Epithelioma
	Warthin's tumour
Malignant tumors	Adenoid cystic carcinoma
	Mucoepidermoid carcinoma
	Carcinoma expleomorphic adenoma
	Squamous cell carcinoma
	Sebaceaus carcinoma
	Ductal carcinoma
	Acinic cell carcinoma
	Myoepithelial carcinoma
	Epithelial–myoepithelial carcinoma
	Carcinosarcoma
	Polymorphous low-grade adenocarcinoma
	Basal cell carcinoma
	Cystadenocarcinoma
Lymphoid tumors	
Benign tumors	Reactive lymphocytic hyperplasia
Malignant tumors	Extranodal marginal zone lymphoma
	Follicular lymphoma
	Diffuse large B-cell lymphoma
	Mantle cell lymphoma
	Chronic lymphocytic leukemia/small lymphocytic lymphoma
Mesenchymal tumors	
Benign tumors	Capillary and cavernous hemangioma
	Epitheloid hemangioendothelioma
	Angiolymphoid hyperplasia with eosinophilia
	Granular cell tumour
	Fibrous histocytoma
	Solitary Fibrous tumour
	Neurofibroma
Malignant tumors	Extremely rare

have a mean age of 50 years.[6,7,9,10] However, these tumors may occur in patients of all ages, including teenagers and children.[10,11] Mucoepidermoid carcinoma is slightly more common in females (3:2), and adenocarcinoma NOS is more common in males.[12,13]

The typical symptoms of all lacrimal gland tumors are those of facial asymmetry, due to displacement of the globe; swelling of the lacrimal gland; reduced ocular motility; diplopia; and ptosis (Fig. 1A, E, and I).[12–15] Pain is uncommon in patients with benign tumors, but it is a cardinal symptom in patients with adenoid cystic carcinoma.[10,14] The mean duration of complaints before initial ophthalmic consultation averages 2 years for patients with pleomorphic adenoma and 6 months for patients with adenoid cystic carcinoma.[9,15,16]

Preoperative diagnosis is based on the clinical history and imaging analyses. In CT and MRI scans pleomorphic adenoma typically appears as a solid, well-defined, round or oval space-occupying lesion that occasionally shows calcification and remodeling of adjacent bones. This contrasts with malignant tumors that may have irregular margins and signs of bony erosion (Fig. 1F and J).[12,17] In addition, adenoid cystic carcinomas may be nodular with infiltration of adjacent tissue and bony destruction.[17]

The primary treatment of lacrimal gland tumors is operative removal. For malignancies, in most cases surgery will be followed by radiotherapy, or chemotherapy, or both.[18,19] However, the optimal treatment of lacrimal gland carcinomas, particularly of the adenoid cystic type, is somewhat controversial. The type of surgery (e.g., globe-sparring vs. exenteration) has not been demonstrated convincingly to correlate with prognosis,[14,16,20] and the use of adjuvant treatments has also been debated.[14,21–23]

The prognosis of pleomorphic adenoma is generally good, but those tumors have a tendency to recur locally. Multiple recurrences increase the risk of malignant transformation, especially in patients who are >45 years old.[10,24–26] The clinical course of lacrimal gland carcinomas is often aggressive. Most patients with CEPA die within a few years, with a mean survival of only 36 months.[7,14] Adenoid cystic carcinoma is often called the "slow killer," because recurrences and metastases may become manifest several years after initial treatment. The likelihood of surviving 10 years is only 20–30%.[10,14,27] "Solid pattern" histology and tumor size correlate with a worsened prognosis for patients with adenoid cystic carcinoma.[28,29]

Mucoepidermoid carcinoma is classified as low-, intermediate-, and high-grade according to a scoring system defined by the World Health Organization (WHO).[30] Low- and intermediate-grade mucoepidermoid lesions have a favorable prognosis, but high-grade mucoepidermoid carcinomas do not.[12]

Histopathology

Pleomorphic adenoma is usually well-defined and characterized by epithelial and modified myoepithelial elements that intermingle with mesenchymal components (Fig. 1B).[30] The epithelial elements comprise a mixture of well-formed ductal structures and non-ductal cells with fusiform, round, stellate, plasmacytoid, oncocytoid, and polygonal shapes. Occasional clear cells and squamous elements may also be present. The mesenchymal component demonstrates varying degrees of myxoid, hyaline, cartilaginous or osseous differentiation. Immunohistochemically, the epithelial and myoepithelial cells express cytokeratin, with the latter also potentially labeling for muscle specific actin and glial fibrillary acidic protein.[30,31]

Carcinoma ex pleomorphic adenoma (Fig. 1C) is defined as a malignant tumor that arises from pleomorphic adenoma. Histological analysis reveals residual elements of the "parent" tumor with zones of transition between the benign and malignant portions of the lesion. In the majority of cases, there is an obviously infiltrative growth pattern accompanied by significant cytological atypia. The carcinomatous element can be represented by any type of carcinoma—including sarcomatoid carcinoma—but adenocarcinoma NOS and mucoepidermoid carcinoma are most frequently seen.[10]

Adenoid cystic carcinoma is composed of modified myoepithelial and differentiated ductal cells (Fig. 1E and G).[10,30] It is characterized by three histologic growth patterns: cribriform ("Swiss cheese" or sieve-like), solid, and tubular, seen in varying combinations. The cribriform pattern is most common, while the solid pattern is least frequent. Within the