

Major salivary gland cancer

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Salivary gland tumors represent 3% of head and neck tumors and 0.6% of all tumors in the body. Parotid gland tumors constitute 70% to 80% of tumors of the salivary gland, and 20% of parotid gland tumors are malignant. Four fifths of the parenchyma of the gland lies lateral to the facial nerve, in the superficial lobe, and 90% of parotid neoplasms present in the superficial lobe. Approximately 80% of parotid tumors occur in the lower part of the gland. Parotid pleomorphic adenoma is the most common parotid neoplasm, accounting for 60% to 70% of parotid tumors.

Malignant salivary gland tumors have an incidence of less than 1 per 100,000 individuals. Most malignant salivary gland tumors arise from the excretory or intercalated duct reserve cells [1]. Their origin is largely unknown. Genetic alterations, including allelic loss, chromosomal translocations, and absence or addition of a chromosome, may be factors in some cases. A heightened risk after radiation exposure [2] is not uniformly reported [3]. Malignant parotid tumors are slightly more common in women, with a peak incidence in the fifth through seventh decades of life.

Malignant salivary gland tumors generally present as painless, slow-growing tumors that are indistinguishable from benign tumors. The overall detection rate for salivary gland malignancy based on clinical features is approximately 30%; palpable cervical lymph nodes, facial nerve palsy, and deep fixation and rapid enlargement of the tumor are significant parameters for parotid gland tumors [4]. Both benign and malignant tumors can present with pain in a small percentage of patients. Approximately 10% of patients who have parotid gland malignancies present with facial paralysis, which is associated with a poor prognosis. Patients who have deep-lobe parotid tumors may present with distortion of the lateral pharyngeal wall on intraoral examination. Trismus may represent infratemporal fossa involvement.

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Cervical lymph node metastasis is observed in 10% to 20% of malignant cases. Most parotid cancers are high-grade tumors, with a global 5-year survival rate of 45% to 50%.

Submandibular gland tumors are malignant in 50% of cases, constituting 10% of all salivary gland malignancies. Fixation to the mandible or skin infiltration suggest extraparenchymal extension. Weakness or numbness of the tongue indicates perineural involvement of the hypoglossal or lingual nerve. The 5-year survival rate has recently been reported to be as high as 50% [5], but generally, submandibular gland cancers are regarded as more aggressive and are associated with a lower survival rate compared with parotid gland tumors of the same histologic type. Sublingual gland tumors are very rare; approximately 80% are malignant. They present as a submucosal mass on the anterior floor of the mouth, and survival rates are similar to those in patients who have submandibular gland tumors of the same histologic type.

The American Joint Commission on Cancer 2002 classification of major malignant salivary gland tumors follows the tumor-node-metastasis (TNM) system of staging (AJCC Cancer Staging Manual, American Joint Committee on Cancer, 6th edition. Springer-Verlag: New York; 2002.) (Box 1).

Imaging and fine-needle aspiration

Preoperative CT, MRI, or ultrasonography rarely alters the clinical course for small tumors of the superficial parotid lobe. Management of parotid tumors with fixation, facial nerve dysfunction and cervical lymph node metastasis, and deep-lobe tumors with parapharyngeal extension is enhanced with imaging. Imaging is helpful for submandibular and sublingual gland tumors. MRI provides superior resolution of soft tissue structures and is the preferred modality for evaluating a parotid tumor and neck metastasis. MRI may indicate an inferior tail of parotid mass, when clinical presentation would suggest an upper cervical nonparotid neck mass. Infiltration of the tumor into muscle or bone on MRI is predictive of malignant disease. High-resolution MRI may detect perineural involvement. Positron emission tomography categorizes only 69% of parotid tumors correctly when attempting to distinguish benign from malignant parotid masses [6].

Fine-needle aspiration (FNA) for a small, mobile mass of the tail of the parotid gland is not mandatory. The breadth of histologic subtypes in parotid tumors makes cytologic diagnosis a formidable goal. Furthermore, histologic patterns of pleomorphic adenoma are variable, and they can be mistaken for mucoepidermoid carcinoma or adenoid cystic carcinoma [7,8]. There is difficulty in distinguishing a benign oncocytic tumor from an acinic cell carcinoma, and a Warthin's tumor (adenolymphoma) from a low-grade mucoepidermoid carcinoma [8]. The accuracy of FNA in broadly distinguishing benign and malignant tumors, however, is more than 90% in most series [7]. In elderly, debilitated patients with a parotid neoplasm, such as

Box 1. TNM staging system for salivary gland tumors*T: tumor*

- T1 tumor smaller than 2 cm
 T2 tumor 2 to 4 cm
 T3 tumor 4 to 6 cm or tumor with extraparenchymal extension
 T4a tumor invading skin, mandible, ear canal, or facial nerve
 T4b tumor invading skull base or pterygoid plates or encasing carotid artery

N: regional lymph nodes

- N1 single ipsilateral node smaller than 3 cm
 N2a single ipsilateral node 3 to 6 cm
 N2b multiple ipsilateral nodes smaller than 6 cm
 N2c bilateral or contralateral node smaller than 6 cm
 N3 node larger than 6 cm

M: distant metastases

- M0 no distant metastases
 M1 distant metastases present

Staging

Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3, T1/T2/T3	N0, N1	M0, M0
Stage IVa	T4a, T1/T2/T3	N0/N1/N2 N2	M0, M0
Stage IVb	T4b, any T	N3, any N	M0, M0
Stage IVc	any T	any N	M1

Data from the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original and primary source for this information is the AJCC Cancer Staging Manual, 6th edition (2002) published by Springer-Verlag New York (For more information, visit www.cancerstaging.net). Any citation or quotation of this material must be credited to the AJCC as its primary source. The inclusion of this information herein does not authorize any reuse or further distribution without the expressed written permission of Springer Verlag New York, Inc., on behalf of the AJCC.

a Warthin's tumor, FNA may obviate the need for surgery. In addition, the use of FNA may avoid parotid gland surgery in sarcoidosis, tuberculosis, histoplasmosis, lymphoma, and benign cervical adenopathy in patients with HIV and in children. FNA can distinguish an upper cervical neck mass from a low tail of parotid tumor. It also is helpful in patients who have

submandibular neoplasms, and can distinguish a salivary gland neoplasm from a metastatic occult upper respiratory tract primary tumor in a patient who has a painless mass that does not enlarge with oral intake. Preoperative diagnosis is helpful to advise patients about the extent of surgery that may be required or that operative findings may dictate sacrifice of the facial nerve. More rigorous attention to the operative margin may be required when results of preoperative cytologic tests reveal malignancy. The type of malignant tumor is much more difficult to classify correctly by FNA. Finally, there have been no reports of seeding of tumor along the needle tract.

Histology, immunohistochemistry, and molecular biology

In 2002, the World Health Organization suggested the histologic typing of malignant salivary gland tumors listed in [Box 2](#).

Mucoepidermoid carcinoma

Mucoepidermoid carcinoma is the most common malignant tumor of the parotid gland and the second most common malignant tumor of the

Box 2. Histologic typing of malignant salivary gland tumors^a

Acinic cell carcinoma
Mucoepidermoid carcinoma
Adenoid cystic carcinoma
Polymorphous low-grade adenocarcinoma
Epithelial-myoepithelial carcinoma
Basal cell adenocarcinoma
Sebaceous carcinoma
Papillary cystadenocarcinoma
Mucinous adenocarcinoma
Oncocytic carcinoma
Salivary duct carcinoma
Adenocarcinoma
Myoepithelial carcinoma
Carcinoma ex pleomorphic adenoma
Squamous cell carcinoma
Small cell carcinoma
Other carcinomas

Data from: Seifert G in collaboration with Sobin LH, and pathologists in 6 countries. World Health Organization international histological classification of tumors. Histological typing of salivary gland tumors, 2nd edition. Springer-Verlag: Berlin, 1991.

^a World Health Organization, 2002.

submandibular and sublingual glands. There is a slight female predilection. Mucoepidermoid carcinoma is located in the parotid gland in 80% to 90% of patients, comprising approximately one third of parotid malignancies. Mucoepidermoid carcinomas contain mucin-producing cells and epithelial cells. Differentiation between high-grade mucoepidermoid carcinoma and poorly differentiated squamous cell carcinoma (SCC) may require special staining with periodic acid–Schiff stain for the presence of glycogen in the mucin or positive staining for mucicarmine in the mucous cells. Subclassification includes low-grade, intermediate-grade, and high-grade tumors. Low-grade tumors are circumscribed but not encapsulated and have a predominance of mucin cells (Fig. 1), whereas high-grade tumors are dominated by poorly differentiated squamous cells with poorly defined margins, high mitotic activity, neural invasion, and tumor necrosis. Most mucoepidermoid carcinomas are low grade, with less than 10% of patients presenting with facial nerve dysfunction. Wide excision without radiation therapy results in 5-year survival rates for low-grade tumors that approach 75%. High-grade mucoepidermoid carcinoma presents with facial nerve

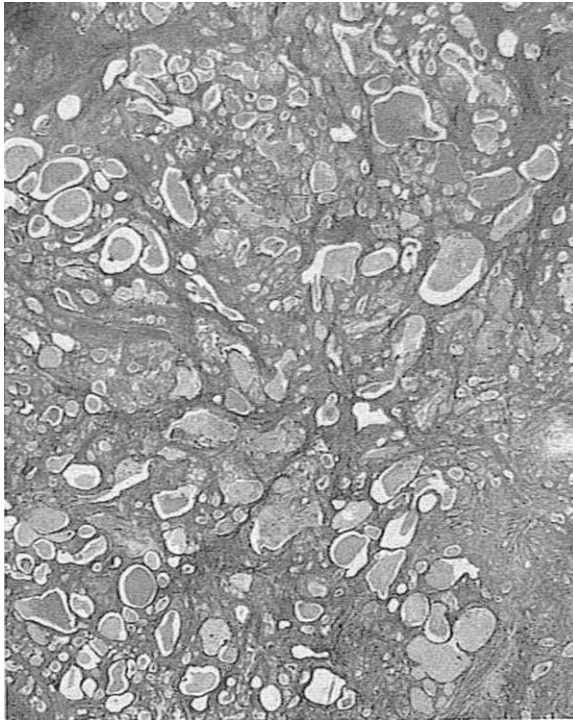


Fig. 1. Photomicrograph of low-grade mucoepidermoid carcinoma (magnification 40 $\times$ with H&E stain). (From Ellis GL, Auclair PL. Tumors of the salivary gland. In: Rosai J, editor. Atlas of tumor pathology. Washington, DC: Armed Forces Institute of Pathology; 1996. p. 164; with permission.)

dysfunction in 25% of patients and has a propensity for locoregional and distant recurrence. Recommended treatment is surgery and radiation therapy, which yields a 5-year survival rate of 50%. Grading is not as successful in predicting clinical outcome in submandibular mucoepidermoid carcinoma.

Adenoid cystic carcinoma

Adenoid cystic carcinoma is the second most common salivary gland malignancy, representing 10% to 20% of major salivary gland cancers. Women are more commonly affected. It is the most common malignancy of the submandibular gland and sublingual glands; half of all sublingual tumors are adenoid cystic carcinomas. Perineural involvement by direct invasion is the hallmark of adenoid cystic carcinoma, allowing distant spread, including the skull base in 42% of patients [8]. Invasion into salivary gland parenchyma and soft tissues is common. The incidence of facial nerve dysfunction in adenoid cystic carcinoma is 20%, although most of these tumors present as an asymptomatic mass. Lymphatic spread is less common than distant metastasis to bone and lung. Histologic subtypes include the most common “Swiss cheese–appearing” cribriform pattern (Fig. 2). The tubular subtype, with a more glandular histology, has the best prognosis. The solid subtype has sheets of cells and is associated with a grim prognosis. Most tumors display more than one histologic subtype, with the classification depending on the predominant subtype. Recurrences generally develop within 5 years, but late recurrences develop 10 to 20 years later. The factors with the greatest impact on survival are the stage of the disease and histologic grade; other significant factors include the site of origin, surgical

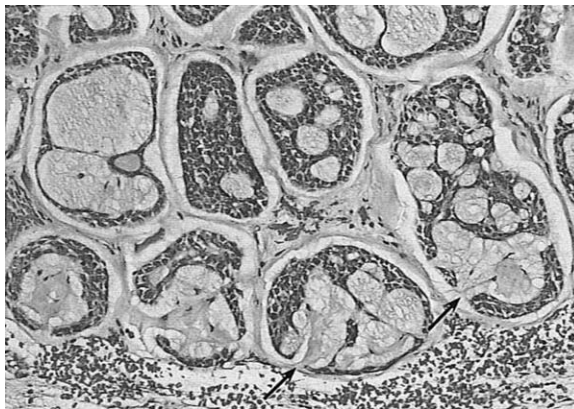


Fig. 2. Photomicrograph of the cribriform type of adenoid cystic carcinoma demonstrating the “Swiss cheese” appearance (magnification 100 $\times$ with H&E stain). Arrows show pseudolumens that are in continuity with the stroma of the tumor. (From Ellis GL, Auclair PL. Tumors of the salivary gland. In: Rosai J, editor. Atlas of tumor pathology. Washington, DC: Armed Forces Institute of Pathology; 1996. p. 206; with permission.)

margin, and previous radiation therapy. The 10-year survival rates for the solid and cribriform subtypes have been reported as 0% and 62%, respectively [9]. Many patients survive for several years after recurrence, but up to 80% ultimately succumb to this malignancy.

Acinic cell carcinoma

Acinic cell carcinoma constitutes 10% to 15% of malignant salivary gland tumors. Two thirds of the patients are female. Approximately 3% of acinic cell carcinomas occur bilaterally, making this tumor second only to Warthin's tumor for bilateral presentation [10]. This low-grade tumor occurs primarily in the parotid gland and rarely presents with facial nerve dysfunction (Fig. 3). Regional lymph nodes are the most likely site of metastasis. There are numerous subtypes, including solid, papillary cystic, follicular, medullary, and microcystic, which do not correlate with

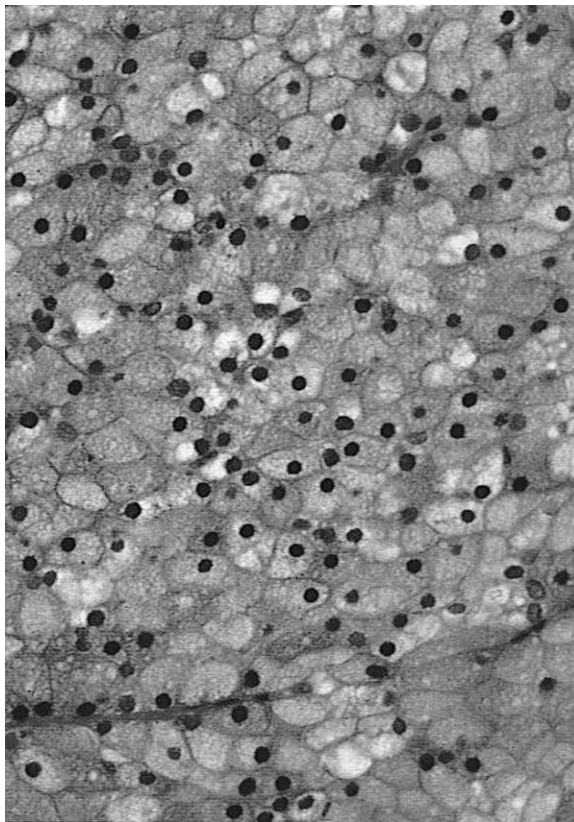


Fig. 3. Photomicrograph of acinic cell carcinoma (magnification 200 $\times$ with H&E stain). (From Ellis GL, Auclair PL. Tumors of the salivary gland. In: Rosai J, editor. Atlas of tumor pathology. Washington, DC: Armed Forces Institute of Pathology; 1996. p. 186; with permission.)

prognosis. Surgery without radiation is recommended for this well-circumscribed tumor. Five-year survival rates of 75% are achieved but these rates decrease with longer follow-up periods. Local recurrences are treated with further surgery. Acinic cell carcinoma is the second most common pediatric salivary gland malignancy after mucoepidermoid carcinoma.

Malignant mixed tumors

Malignant mixed tumors comprise 5% to 10% of salivary gland malignancies, with most occurring in the parotid gland. Gender is not a factor in presentation. The most common of the three types of malignant mixed tumors, carcinoma ex pleomorphic adenoma (CEPA), arises from a pleomorphic adenoma that has been untreated for many years or from a previously treated pleomorphic adenoma that has recurred. Sudden enlargement may represent malignant transformation. Clinical findings and histologic features at the initial diagnosis that indicate a greater likelihood of malignant transformation are as follows: older patient age, large tumor size, submandibular gland location, and prominent zones of hyalinization or at least moderate mitotic activity [11]. The rate of malignant transformation approaches 10% in tumors that have been present for 15 years [12]. Only the epithelial component metastasizes, typically presenting as an adenocarcinoma. A noninvasive subtype with either complete encapsulation or only limited microscopic invasion has an excellent prognosis, but the invasive subtype is associated with regional and distant metastasis [13]. Immunohistochemistry has demonstrated that activation of *c-myc* and *ras p21* proto-oncogenes and the involvement of the *p53* mutation may play an important role in the malignant transformation of pleomorphic adenoma [14]. Ploidy results do not predict tumor behavior in CEPA. Cervical neck node metastasis occurs in 25% of patients. Surgery and postoperative radiation therapy are recommended and lead to an overall 5-year survival rate of 40%. In addition, the degree of invasion and histologic grade have an impact on survival.

The malignant mixed tumor also can present as a true carcinosarcoma from the beginning, with both epithelial and mesenchymal metastasizing components. The most common epithelial types are SCC and adenocarcinoma, and the most common mesenchymal tumor is chondrosarcoma, a lethal tumor with few survivors. Finally under this category is the rare histologic curiosity known as benign metastasizing pleomorphic adenoma. These tumors have an absence of cytologic atypia, and they are histologically indistinguishable from pleomorphic adenoma; however, these tumors are associated with a mortality rate of 22% [15].

Adenocarcinoma and related classifications

Adenocarcinoma is a shrinking category (as is undifferentiated carcinoma). These tumors have been reclassified into subtypes with similar histopathology

and biologic behavior based on electron microscopy and immunohistochemistry. Carcinomas with ductal features without other distinguishing characteristics are termed “adenocarcinoma, not otherwise specified.” Adenocarcinoma is generally an aggressive tumor. Approximately 20% of patients present with facial nerve dysfunction, with frequent regional and distant metastasis. Treatment consists of wide excision and postoperative radiation therapy. A 5-year survival rate of less than 50% is generally predicted.

Immunoreactivity of smooth muscle-specific proteins helps differentiate adenocarcinoma from the high-grade salivary duct carcinoma. Salivary duct carcinoma, which originates from the excretory duct reserve cell and resembles intraductal carcinoma of the breast, is an extremely aggressive tumor with low survival rates [16].

Differentiating salivary duct carcinoma from the more indolent polymorphous low-grade adenocarcinoma (PLGA) is important. PLGA has a female predominance (2:1) and arises primarily from intraoral minor salivary glands. PLGA has a varied histologic (polymorphic) appearance of papillae, glandular structures, and solid aggregates. Local and regional spread is limited, and this tumor is associated with low recurrence rates and a high rate of expected survival. Perineural involvement can make distinction from the more aggressive adenoid cystic carcinoma difficult. The immunoreactivity of smooth muscle-specific proteins also helps differentiate adenoid cystic carcinoma from PLGA [16]. Invasion helps distinguish PLGA from the benign pleomorphic adenoma, for which it can also be mistaken. Before histologic refinements, salivary duct carcinoma and PLGA were classified as adenocarcinoma.

Squamous cell carcinoma

Primary SCC of the parotid gland is rare, representing 1% of cases. There is a 2-to-1 male preponderance. Metastatic disease to an intraparotid lymph node from a skin primary tumor, contiguous spread of SCC from an adjacent skin primary tumor, poorly differentiated mucoepidermoid carcinoma (mucin stains must be negative to exclude mucoepidermoid carcinoma), and squamous metaplasia must be excluded. Primary SCC arises from metaplastic parotid duct epithelium. These tumors often act in an aggressive fashion, widely infiltrating the parotid gland. Up to 60% of patients who have this SCC present with cervical lymph node metastasis and facial nerve dysfunction. With advanced-stage disease, survival rates are less than 50%. Radical surgery and postoperative radiation therapy are required for this highly malignant tumor.

Melanoma

Most malignant melanomas arise from cutaneous primary sites, with the parotid gland being a frequent metastatic location. The prognosis is generally poor. Mucosal and ocular primary sites also must be considered.

Identifying the primary tumor of a parotid metastasis can be exceptionally difficult when the rare spontaneous regression of the primary tumor occurs. The complex lymphatic drainage of the head and neck has slowed the use of sentinel node biopsy. Many patients have multiple positive nodes, and primary melanomas may be near or overlap the nodal basin in the head and neck. Preoperative lymphoscintigraphy using intradermal injections of technetium Tc 99m antimony trisulfide colloid, followed within 4 hours by intraoperative handheld gamma-probe localization, has been used to improve sentinel node biopsy. This procedure can be coupled with intraoperative injection of 1% isosulfan blue dye. Technical success rates have risen to 95%. The routine elective use of superficial parotidectomy for patients who have primary melanoma of the scalp, auricle, and face has been questioned. Sentinel node biopsy in the parotid gland has been performed without facial nerve dissection, with a 2.6% rate of facial nerve dysfunction (and one case of temporary facial nerve paresis) [17]. Further study to define the role of sentinel neck nodes in the parotid gland and the surgical procedures to address them is required.

Lymphoma

Lymphoma of the parotid gland represents 1% to 2% of parotid malignancy presenting either primarily or as part of disseminated disease. The incidence is equal in men and women, and this tumor rarely occurs before the age of 50. Patients with Sjögren's syndrome have a 40-fold greater risk for a parotid lymphoma than the general population. Most are B-cell, non-Hodgkin's lymphomas, with 80% of patients presenting in stage I or II disease [18]. Primary lymphomas are usually low grade; however, even intermediate- and high-grade lymphomas of the parotid gland can have a satisfactory prognosis with chemotherapy and radiation therapy. Immunohistochemical analysis can help differentiate the low-grade mucosa-associated lymphoid tissue lymphoma from myoepithelial sialadenitis. In many cases, lymphoma can be diagnosed with FNA using immunohistochemistry.

Undifferentiated carcinoma

Undifferentiated carcinomas include large cell undifferentiated carcinoma, small cell undifferentiated carcinoma, and lymphoepithelial carcinoma. Primary lymphoepithelial carcinoma may arise from a benign epithelial lesion. It has been reported in Asians and Greenland Eskimos, with an associated Epstein-Barr virus infection [19].

Molecular biology

DNA flow cytometry can assist in the characterization and diagnosis of salivary gland malignancies, which can be difficult to diagnose. Bang et al [20] reported that 43% of salivary gland tumors were reclassified after DNA

flow cytometry. The development and progression of cancer are regulated by various oncogenes and tumor-suppressor genes. Genetic alterations, such as those involving *p53* and *c-erbB-2*, play an important role in the progression of malignant salivary gland tumors, specifically adenocarcinoma, CEPA, and salivary duct carcinoma [21]. The *p53* tumor-suppressor gene may be involved in salivary gland carcinogenesis, and its oncoprotein expression is an independent indicator of clinical aggressiveness in parotid cancer [22]. Collagen IV and tenascin are extracellular matrix constituents. Weak immunoreactivity for collagen and intense staining of tenascin are determinants of recurrent disease. Tenascin immunoreactivity is intimately associated with *c-erbB-2* positivity and weak staining of collagen IV [23]. DNA aneuploidy noted in undifferentiated adenocarcinoma or squamous carcinomas is associated with reduced survival times compared with those of predominantly diploid tumors, such as mucoepidermoid, acinic cell, and adenoid cystic carcinomas [20].

Treatment

Salivary gland surgery

Surgery is the primary treatment for salivary gland malignancy. The minimal operation for a parotid mass is superficial parotidectomy with facial nerve dissection. Enucleation will result in higher rates of recurrence and facial nerve dysfunction. Low-grade parotid tumors may be treated with superficial parotidectomy. Facial nerve monitoring for a mobile tumor of the superficial lobe will not decrease the rate of facial nerve dysfunction [24]. Deep-lobe tumors, facial nerve dysfunction, recurrent tumors, fixed tumors, tumors larger than 4 cm, and nodal metastasis are indications for nerve monitoring.

The incision in the preauricular skin curves gently 2 mm below the ear lobule to prevent distortion of the ear lobule, and subsequently 3 cm below the mandible so as not to traumatize the marginal mandibular branch of the facial nerve. Electrosurgical dissection is eschewed. The sternocleidomastoid muscle is separated from the parotid gland. The facial nerve trunk emanating from the stylomastoid foramen is superior to the cephalic margin of the digastric muscle. The cartilaginous tragal pointer leads to the tympanomastoid suture. The pes anserinus of the facial nerve is invariably located 2 mm to 4 mm inferior to this most important anatomic landmark. Facial nerve dissection can be performed atraumatically with a fine hemostat, bipolar coagulation, and plastic scissors. Bipolar scissors, the harmonic scalpel, and hemostat/stimulator probes with a dedicated nerve monitor have been advocated.

Deep-lobe dissection or total parotidectomy is indicated for deep-lobe tumors, superficial tumors that extend to the deep lobe, high-grade tumors, and tumors involving the parapharyngeal space. After completion of the superficial parotidectomy, the facial nerve branches are elevated from surrounding parotid tissue or tumor, and the deep lobe is separated from the

masseter and other muscles. Parapharyngeal parotid tumors can present as an oropharyngeal submucosal mass and can pass posteroinferiorly or posterosuperiorly to the stylomandibular ligament. The cervical-parotid approach is successful for most cases. Anterior or lateral mandibulotomy is required more commonly for malignant tumors approaching the skull base. Suction drainage will minimize the risk of hematoma and allow the wound to be readily observed without a dressing. Infrequently, retrograde identification of peripheral nerve branches is required for large, bulky tumors or for surgical procedures for recurrent tumors. Cortical mastoidectomy can be used to identify the intratemporal course of the facial nerve and to follow it to the stylomastoid foramen. Involvement of the middle cranial fossa and medial neurovascular structures of the jugular foramen may require subtotal petrosectomy.

A balance between eradicating the tumor and preserving the facial nerve is warranted. Facial nerve branches should be spared unless they are involved with tumor. In cases in which the tumor extends close to the nerve, the tumor potentially can be peeled off the nerve and treated with postoperative radiation therapy. Although this procedure transgresses the classic oncologic principle that malignant tumors should be resected with a wide margin, high rates of survival confirm the efficacy of postoperative radiation therapy in eradicating microscopic remnants of tumor after surgery. Preoperative facial nerve weakness suggests a very high likelihood of facial nerve sacrifice intraoperatively. A facial nerve surrounded by tumor is best treated with resection. If direct neurorrhaphy is not possible, cable nerve graft reconstruction is performed, most commonly with the greater auricular or sural nerve. Facial skin involvement requires reconstruction with local or regional flaps or free-tissue transfer. Complications include facial nerve dysfunction, Frey's syndrome, ear numbness, hematoma, and salivary fistula.

Submandibular gland tumor resection calls attention to the following anatomic sites: the marginal mandibular branch of the facial nerve deep to the platysma (ligation of the facial vein and upward traction protects this branch); the lingual nerve, identified by its looping course along the hyoglossus muscle; and the hypoglossal nerve deep to the posterior belly of the digastric muscle. En bloc excision may require resection of the floor of the mouth or marginal or segmental mandibulectomy. Sublingual gland resection should proceed with cannulation of Wharton's duct using a lacrimal probe and identification of the lingual nerve. These structures, the mucosa of the floor of the mouth, and the associated alveolar mandible may require resection if sublingual gland cancer is present. Complications of submandibular and sublingual gland surgery revolve around the cranial nerves dissected.

Neck dissection

Neck metastases are present in 10% to 20% of parotid gland malignancies. These generally occur in levels II and III. The survival rate

for parotid gland malignancies without metastasis is 75%. Nodal metastasis reduces the survival rate by 50%. Clinically positive neck metastases are treated with neck dissection. In N0 neck disease, the odds of neck micro-metastasis being present are increased in adenocarcinoma, SCC, high-grade mucoepidermoid carcinoma, CEPA, high-grade tumors (excluding adenoid cystic carcinoma, in which lymph node metastasis is rare), facial nerve involvement, and extraglandular tumor extension. T1 and T2 tumors have a reported 12% risk of metastasis, and T3 and T4 tumors have a 27% risk of nodal metastasis [25]. Selective neck dissection at levels IB, II, III, and the upper part of level V should be considered in patients who have high-risk N0 disease. Selective neck dissection may assist in determining the need for postoperative radiation therapy. The risk of neck recurrence is higher in patients with node-positive disease [25].

Immunohistochemistry, molecular analysis, cell culture techniques, and serial sectioning of lymph nodes have increased the rate of reported micrometastasis. Neck dissection for N0 neck disease remains a debated topic. In a reported series of N0 parotid gland malignancies treated with parotidectomy and radiation therapy without neck dissection, the risk of subsequent nodal metastasis was only 4% (7 of 164 cases) [26].

Radiation therapy

Patients who have advanced-stage disease, positive margins, nodal metastasis, preoperative facial nerve dysfunction, and high-grade tumors are candidates for postoperative radiation therapy. Combined therapy with surgery followed by radiation therapy has resulted in improved 5-year disease-free survival rates as high as 77%, with few sequelae from radiation [27]. Retrospective reviews have not defined a radiation dose–response relationship, and treatment has ranged from 50 to 70 Gy. Radiation therapy as the primary treatment may be appropriate for patients with unresectable tumors or those with overwhelming comorbidities. Postoperative radiation therapy for patients with positive surgical margins was reported to be effective for T1 and T2 disease but not for advanced-stage disease [28]. Chemotherapy or combined radiation therapy and chemotherapy have not improved survival (excluding lymphoma), although chemotherapy has been used in palliative settings.

Recurrence

The pattern of recurrence for most parotid gland malignancies, in order of frequency, is local recurrence, cervical neck metastasis, and distant metastasis [26]. Significant factors for survival are as follows: advanced age, tumor stage, positive nodal disease, facial nerve involvement, high-grade tumors, extraparenchymal spread, and positive margins.

Recurrence in submandibular gland cancer is most significantly related to the initial stage at presentation, with most deaths caused by metastatic disease. Other factors include clinical skin or soft tissue invasion, lymph node metastasis, and perineural growth. Lower recurrence rates with positive margins can be achieved with postoperative radiation therapy. Survival rates for sublingual gland cancer are similar to those for submandibular gland malignancy. All salivary gland malignancies require follow-up periods of 20 years for true measures of clinical outcomes.

Summary

Major salivary gland cancers are rare, with many histologic types and subtypes. The tumor stage at presentation will dictate the need for imaging, FNA, and facial nerve monitoring. Immunohistochemistry has enhanced diagnosis. In addition, precise attention to surgical landmarks and technique will reduce complications. Tumor stage, histologic type, tumor grade, surgical margin, facial nerve dysfunction, perineural involvement, extra-parenchymal spread, and nodal metastasis are factors influencing the indication for neck dissection, postoperative radiation therapy, and survival rate.

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