Occult Temporal Bone Facial Nerve Involvement by Parotid Malignancies with Perineural Spread

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Abstract

Objective. To characterize disease presentation and outcomes following surgical treatment of parotid malignancies with occult temporal bone facial nerve (FN) involvement.

Study Design. Case series with chart review.

Setting. Tertiary academic referral center.

Subjects and Methods. Thirty consecutive patients (mean age 58 years; 77% men) who underwent surgery for parotid malignancies with occult perineural involvement of the intratemporal FN were included. Primary outcome measures included margin status and recurrence.

Results. The mean duration of clinical follow-up was 49 months, and the most common presenting symptom was FN paresis (n = 23; 77%) followed by pain (n = 15; 50%). To obtain a proximal FN margin, 27 patients (90%) underwent mastoidectomy, and 3 patients (10%) had lateral temporal bone resection. The intratemporal FN margin was cleared in 26 patients (87%), most commonly in the mastoid segment (60%). Adjuvant therapy was given in 25 patients (83%). Ten patients (33%) experienced locoregional (4; 13%) and/or distant (8; 27%) recurrence at a median of 19 months (mean 26, 2–54 months) following surgery. Locoregional failure was significantly more common in cases with a positive intratemporal FN margin (66% vs 8%; P = .045). Overall 1-, 3-, and 5-year disease-specific survival rates were 83%, 79%, and 72%, respectively.

Conclusions. Perineural invasion of the intratemporal FN by parotid malignancy is uncommon. Normal preoperative FN function does not preclude histopathologic involvement. Temporal bone FN exploration should be considered when a positive margin is encountered at the stylomastoid foramen, as failure to do so is associated with an increased rate of locoregional recurrence.

Keywords
facial nerve, parotid, paralysis, perineural invasion, mastoid, temporal bone

Introduction

Salivary gland tumors represent less than 5% of all head and neck neoplasms, with an incidence rate of 1 per 100,000 persons.1-5 Approximately 70% to 80% of salivary gland tumors occur in the parotid gland, and, of these, less than a fifth are malignant. Primary parotid gland carcinoma may develop de novo or from preexisting pleomorphic adenoma, while metastatic disease most commonly involves lymphatic spread from cutaneous squamous cell carcinoma of the scalp or face. Prognostic factors for parotid gland malignancies include histologic type, tumor grade, clinical stage, lymph node status, extraparotid extension, facial nerve involvement, and margin status.2-6

Previous studies have found that preoperative facial nerve dysfunction occurs in less than a fourth of all parotid gland malignancies and portends a poor prognosis.2,3 With such rarity, management of the facial nerve in the setting of parotid carcinoma remains controversial. The long-standing dogma of parotid surgery has been to maintain facial nerve continuity when normal preoperative function exists. However, it has been shown that perineural invasion and facial nerve encasement may occur even without facial nerve paresis and that nerve sacrifice to achieve negative margins may augment local disease control.1,2,5,7,8

To date a limited number of studies have specifically examined management of the facial nerve with parotid gland malignancies. Even more rare are publications focusing on the unique and challenging situation of occult perineural invasion of the intratemporal facial nerve. In this setting, many important questions remain unanswered: How
often can a negative margin be achieved? Does the duration or severity of preoperative function predict proximal extent of involvement? Does achieving a negative margin improve locoregional control or survival? Herein, the authors review a 20-year experience at a high-volume tertiary referral center managing 30 consecutive parotid malignancies with occult invasion of the temporal bone from perineural facial nerve spread.

Subjects and Methods
Following Mayo Clinic Institutional Review Board approval, a retrospective case series with chart review was performed (1994-2014) including all patients who underwent surgery for primary or metastatic parotid gland malignancies with histologically confirmed perineural invasion of the intratemporal facial nerve. Malignancies of external auditory canal or periauricular cutaneous origin and those with contiguous temporal bone invasion from osseous erosion of the temporal bone were excluded. Clinical details, management strategy, operative findings, and outcome data were collected from the medical records of the 30 subjects who met inclusion criteria. Tumor staging was reported using the 7th Edition American Joint Committee on Cancer (AJCC) TNM classification for salivary gland cancer, and facial nerve function was described using the House-Brackmann (HB) scale.

Results
We identified 47 patients with parotid malignancies involving the temporal bone who had been treated between 1994 and 2014. Of these, 17 had evidence of direct extension through bone erosion and were excluded. Thus, 30 patients met inclusion criteria and were analyzed, representing 1.1% of all parotid surgeries performed during this time period. Twenty-three patients (77%) were men and the median age at diagnosis was 58 years (mean 58.4 years; range, 34-80 years). Twenty-five patients (83%) presented with primary disease, while 5 patients (17%) were evaluated for recurrent parotid malignancy. The most common presenting symptom was facial paresis (n = 23; 77%) followed by pain (n = 15; 50%); only 5 patients (17%) presented with a painless mass. Of the 23 patients presenting with facial nerve paresis, the median duration of preoperative facial nerve paresis was 6 months (mean 7.6 months; range, 0.25-24 months), and the median HB facial nerve score immediately prior to surgery was 6 (mean 5; range, 3-6). Notably, 7 patients (23%) did not have a preceding history of facial nerve symptoms. All patients had a normal-appearing external auditory canal and middle ear on otoscopy.

Primary radiologic workup included computed tomography (CT) in 23 patients (77%), positron emission tomography (PET)-CT in 18 (60%), and contrast-enhanced magnetic resonance imaging (MRI) in 25 (83%). Imaging confirmed abnormal, albeit often subtle, asymmetrical enhancement of the facial nerve with or without enlargement in 71% of cases (Figure 1). Per study inclusion criteria, none of the cases demonstrated radiologic evidence of temporal bone cortex invasion or gross mastoid or middle ear disease. A total of 20 patients (67%) underwent fine-needle aspiration (FNA); 12 of these procedures (60%) confirmed malignancy, while 8 (40%) were either nondiagnostic or interpreted as benign. Preoperative acoustic reflex threshold data were available in 9 cases. Of these, 3 ipsilateral ears had elevated or absent stapedial reflexes, while 6 cases demonstrated normal responses. Both the level of facial nerve involvement based on pathologically confirmed margins and the severity of preoperative paralysis did not reliably correlate with acoustic reflex test results. All patients underwent total parotidectomy, 27 (90%) received selective cervical lymphadenectomy, and 6 (20%) additional infratemporal fossa dissection.
proximal facial nerve margin, 27 (90%) underwent cortical mastoidectomy with facial nerve decompression, and 3 (10%) received lateral temporal bone resection when disease abutted the ear canal (Figure 2). The intratemporal facial nerve margin was cleared within the stylomastoid foramen in 5 ears (17%), the mastoid segment in 18 (60%), and the horizontal tympanic segment in 3 (10%); in 4 ears (13%), a negative margin was not achieved. The intratemporal facial nerve was cleared on the first margin in only 7 cases (23%), while the remaining required more than one margin secondary to perineural invasion beyond grossly normal appearing nerve. A negative overall tumor margin was achieved in 20 cases (67%). The median duration of preoperative paralysis was 5 months (mean 3.75 months; range, 0.25-6 months) for disease extending to involve the stylomastoid foramen, 5 months (mean 7.8 months; range, 0.5-24 months) for extension to the mastoid segment, and 10 months (mean 9.2 months; range, 3-12 months) for extension proximal to the second genu (P > .05). The median preoperative HB score was 2 (mean 2.5; range, 0-6) for disease extending to involve the stylomastoid foramen, 5.5 (mean 4.4, range, 1-6) for extension to the mastoid segment, and 3 (3.4 mean, range, 1-6) for extension proximal to the second genu (P > .05). Notably, perineural spread was present in the mastoid segment or proximal in 4 patients without clinical preoperative facial palsy. Thus, duration and severity of preoperative paresis did not reliably predict extent of proximal facial nerve involvement.

An interposition nerve graft was performed in 17 cases (57%), using either a sural or greater auricular nerve donor graft. Interposition grafting was not pursued in patients with a prolonged duration of facial palsy or when suitable proximal or distal nerve stumps were not available.

Final pathological analysis confirmed primary salivary gland origin in 22 cases (73%) and metastatic disease in 8 (27%); all but 3 cases demonstrated high-grade histology (Table 1). In all cases, there was concordance between intraoperative frozen and permanent section facial nerve margins. Twenty patients (67%) had T4a disease, 10 (33%)...
had T4b disease, 12 (40%) had regional cervical nodal involvement, and none had evidence of distant metastasis at time of treatment. Tumor involved both lobes of the parotid gland in the majority of cases; isolated superficial lobe involvement occurred in only 6 cases (20%) and isolated deep lobe in 2 (7%); 9 patients (30%) had 1 or more intraparotid lymph nodes involved by carcinoma.

Adjuvant radiation (n = 18; 60%) or adjuvant radiation with chemotherapy (n = 7; 23%) was pursued in most cases. Indications for radiotherapy included advanced disease, high-grade histology, or positive margin status. The median duration of clinical follow-up was 30.9 months (mean 49.2 months; range, 0-208 months). Overall, 10 patients (33%) experienced locoregional (n = 4; 13%) and/or distant (n = 8; 27%) recurrence at a median of 19 months (mean 26 months; 2-54 months) following surgery. Four of 9 patients (44%) with a positive margin status experienced disease recurrence, compared with 6 of 19 (32%) with a negative surgical margin (P = .68). When we specifically analyzed facial nerve margin status, 2 of 3 patients (67%) with a positive facial nerve margin experienced disease recurrence, compared with 8 of 25 patients (32%) with a negative margin (P = .28). Locoregional failure was significantly more common in patients with a positive intratemporal facial nerve margin (n = 2/3; 66%) compared with those in whom a negative margin was achieved (n = 2/25; 8%) (P = .045) (Figure 3). Only 3 of the 4 cases with a positive facial nerve margin were analyzed, since 1 patient did not have follow-up at the authors’ institution.

A total of 7 patients (23%) died as a result of progressive disease at a median of 47 months (mean 45 months; range, 3-78 months) following surgery. Analysis of facial nerve margin status showed that 2 of 3 patients (66%) with a positive proximal facial nerve margin died from disease, compared with 5 of 20 patients (25%) with a negative margin (P = .15). Overall, the 1-, 3-, 5-year disease-specific survival rates were 83%, 79%, and 72%, respectively.

When we analyzed the unique subgroup of 5 patients (17%) who did not receive adjuvant therapy, 2 were alive at the time of data collection whereas 3 had died from progressive disease. The reasons for not receiving adjuvant therapy in these cases included limited, intermediate grade carcinoma without lymph node involvement and negative margins, cases of salvage surgery where radiation had been previously used, very advanced disease in an elderly patient with limited chance of cure, or patient refusal. The patient with an intermediate grade mucoepidermoid carcinoma and negative margin status has been followed for a total of 208 months without clinical or radiologic evidence of recurrence. One patient with high-grade mucoepidermoid carcinoma treated with salvage surgery for recurrent disease developed subsequent cervical nodal recurrence 21 months after revision parotidectomy and facial nerve sacrifice with negative margins; this patient is still alive following further salvage treatment some 10 years later. The remaining 3 patients succumbed to progressive disease between 3 months and 4 years following surgery.

Discussion

There is a paucity of literature addressing occult intratemporal perineural spread of parotid malignancies. The majority of the large published clinical series on salivary gland or temporal bone malignancies do not include specific details pertaining to this unique and challenging subset of patients.2,4-8,11-14 The estimated frequency of perineural invasion of the facial nerve with parotid malignancy is between 10% and 30%.6 Regarding the incidence of occult temporal bone facial nerve perineural spread, we identified only 30 cases (1.1%) among approximately 2700 parotid surgeries performed over this 20-year time period. Among all salivary gland malignancies, perineural spread is most common in adenoid cystic carcinoma (50%) and adenocarcinoma NOS (not otherwise specified) (42%) and occurs in less than a fourth of cases involving squamous cell carcinoma.

Figure 3. Two cases demonstrating locoregional recurrence after a proximal temporal bone facial nerve margin was not cleared. (A) A 70-year-old man with high-grade adenocarcinoma experienced recurrence at the right skull base 4 years following primary treatment. (B) A 45-year-old man with adenoid cystic carcinoma developed locoregional recurrence at the right temporal bone and cerebellum 3 years following surgery and adjuvant radiation therapy.
often insidious, occurring over weeks to months. Bell's palsy, paralysis from parotid carcinoma is frequently subtle and is complicated by the finding that radiologic evidence of perineural invasion is not available. Several other large series have included patients with advanced parotid malignancies in a pooled analysis of subjects treated for temporal bone malignancies; however, detailed subgroup analyses are lacking. To the best of our knowledge, the remaining publications on this topic are limited to single-digit case series or individual case reports.

The current series raises several important points that are relevant to both the head and neck surgeon and the otologist. First, a parotid mass associated with facial paralysis and/or pain should be considered cancer until proven otherwise, even when the FNA result is "negative." Both symptoms are ominous findings and frequently indicate perineural spread. In contrast to acute idiopathic facial palsy (Bell's palsy), paralysis from parotid carcinoma is often insidious, occurring over weeks to months. Furthermore, paralysis from benign parotid tumors is exceptionally rare. Notably, 40% of FNAs in the current series yielded either benign or nondiagnostic results. This high rate of false-negative FNA has been corroborated by many earlier studies, although recent studies have demonstrated better yield with ultrasound-guided core needle biopsy.

Second, in the absence of gross temporal bone invasion, predicting the need to perform mastoidectomy for facial nerve exploration prior to surgery is often challenging. Defying the adage that a functioning nerve never requires sacrifice, approximately a fourth of the patients in the current series had normal preoperative function. Similar observations have been reported in previous series. Radiologic evidence of perineural invasion is frequently subtle and is complicated by the finding that normal physiologic enhancement of the intratemporal facial nerve may occur in a significant number of patients. In the current series, approximately a third of patients lacked radiologic findings to suggest the possibility of temporal bone perineural spread. As well, duration or severity of paralysis did not appear to reliably predict proximal extent of involvement, nor did topognostic testing through acoustic reflex testing. Thus, it behooves the surgeon to include the possibility of facial nerve sacrifice and temporal bone surgery in preoperative counseling and consent for all cases of suspected parotid malignancy. While it may not be practical to have an otologist available for all cases of parotidectomy, we generally co-list cases in patients with upper and lower division paresis, likely indicating involvement proximal to the pes anserinus, or in cases where the tumor is adjacent or abuts the stylomastoid foramen. In our experience, this strategy will capture the great majority of cases that require mastoid surgery for proximal intratemporal facial nerve involvement.

Third, temporal bone surgery to achieve a negative proximal facial nerve margin is a safe and worthwhile endeavor when performed by an experienced team. The ability to make intraoperative decisions regarding extent of resection based on microscopic margin status is largely dependent on the reliability of intraoperative frozen section pathology, which is institution specific. At centers with limited experience or those without a frozen section laboratory, the decision to proceed with mastoidectomy for a negative facial nerve margin may be more challenging and in many cases may require a staged surgery, only pursuing temporal bone disease after permanent section results are complete. We recently reviewed our experience over 10 years managing 1339 parotid surgeries and found that intraoperative frozen section analysis demonstrated a 98.5% sensitivity and 99% specificity for malignancy, and overall there were only 3 cases in which a change in diagnosis on permanent section pathology was not reported as negative, proved instead to be positive on permanent section pathology. Specific to the study cohort, intraoperative frozen section and permanent section pathology results were in agreement in all cases. We found that a negative margin could be achieved in 87% of cases, almost always distal to the second genu of the facial nerve in the mastoid segment or stylomastoid foramen. As a general rule, we do not pursue margins proximal to the geniculate ganglion. In the majority of cases, clearance of the facial nerve margin granted negative overall margin status on the surgery. We found that a negative proximal facial nerve margin improved locoregional disease control, a finding that has been corroborated by others. Adjuvant therapy is not a substitute for a negative facial nerve margin, since all cases with local recurrence occurred in patients who received adjuvant radiation or radiation and chemotherapy. Ultimately, adjuvant radiation therapy will be used in most cases given the advanced nature of disease in this population. Long-term follow-up with a low threshold for MRI or PET-CT is critical to detect early recurrence in this challenging subgroup of patients.
The decision for facial nerve sacrifice with parotid malignancy is relatively straightforward in patients with preoperative paralysis. However, treatment should always be individualized to the patient. For example, we generally do not perform facial nerve sacrifice in patients with good preoperative function and known distant metastatic disease since the benefit in this setting is limited and does not justify the associated morbidity. Similarly, an elderly or infirm patient with good preoperative function and perineural invasion from advanced adenoid cystic carcinoma may enjoy many years of good facial nerve function despite tumor involvement, and overall survival may not be significantly improved with aggressive resection.

Without involvement of the ear canal or temporomandibular joint, an intact canal wall mastoidectomy with facial nerve decompression is generally sufficient to obtain a negative margin and expose a proximal stump for an interposition nerve graft when desired. On a technical note, if postauricular access is required for mastoidectomy after a modified Blair incision has been made, we generally limit the length of the postauricular incision limb to avoid vascular compromise of the pinna. This is particularly relevant to patients with advanced parotid malignancies since the external carotid, superficial temporal artery, and occipital arteries are usually already compromised from total parotidectomy and upper selective neck dissection, and adjuvant radiotherapy will often be pursued following surgery.

In closing, several strengths and limitations of this study deserve mention. We identified a relatively large group of patients specifically presenting with occult temporal bone invasion from perineural spread along the facial nerve from a 20-year experience at a high-volume tertiary head and neck referral center. This group presents a unique set of diagnostic and therapeutic challenges that have received little attention to date. Previous publications generally have been limited to case reports or have included this group together in a pooled dataset, without robust subgroup analysis. The primary limitation is the retrospective nature of study; the authors were dependent on the accuracy and completeness of the medical record. Heterogeneous pathology and patient numbers precluded multivariable analysis. In particular, the limited size of certain subgroup populations, such as those with positive margin status, limited statistical induction. Finally, the average duration of follow-up was 49 months. Longer clinical follow-up is particularly important to primary parotid malignancies such as adenoid cystic carcinoma, where recurrence may surface even decades after therapy.

Conclusions
Occult perineural invasion of the intratemporal facial nerve by parotid malignancy is uncommon. Normal preoperative facial nerve function does not preclude facial nerve involvement. Radiologic findings of intratemporal perineural invasion are often subtle. Even in the presence of a negative FNA result, parotidectomy for definitive diagnosis should be performed in the setting of progressive facial palsy. Temporal bone facial nerve exploration should be considered when a positive margin is encountered at the stylomastoid foramen since a proximal margin can be safely cleared in the majority of patients, improving locoregional control.

Author Contributions
Matthew L. Carlson, concept, data collection, review of data, manuscript writing, manuscript revision; Neil S. Patel, concept, data collection, review of data, manuscript revision; Mara C. Modest, concept, data collection, review of data, manuscript revision; Eric J. Moore, concept, review of data, manuscript revision; Jeffrey R. Janus, concept, review of data, manuscript revision; Kerry D. Olsen, concept, review of data, manuscript drafting, manuscript revision.

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