Perineural invasion of the facial nerve by a cutaneous squamous cell cancer: A case report

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Abstract

We report a case of perineural invasion of the facial nerve by a cutaneous squamous cell carcinoma in a 59-year-old man who presented with a slowly progressive facial paralysis. We performed a distal facial nerve dissection and a simple mastoidectomy with facial recess exposure for resection to negative margins. We also performed a simultaneous facial reconstruction and reanimation procedure with excellent results. External-beam radiation completed the treatment regimen. In addition to describing this case, we review current concepts in diagnosis and therapy, as well as the historical background of malignant perineural invasion of the cranial nerves.

Introduction

Perineural invasion of the cranial nerves was first described by Cruveilhier in 1835. In 1862, Neumann reported a carcinoma of the lower lip that invaded both mental nerves; this was the first recorded case of perineural invasion of the cranial nerves by a primary tumor of the head and neck. The propensity of adenoid cystic carcinoma of the parotid gland to invade peripheral nerves was first described by Quattlebaum in 1946.

In 1963, Ballantyne et al observed that many perineural invasions by malignancies of the head and neck were cutaneous in origin. In their study of 80 patients with perineural invasion of the cranial nerves by head and neck tumors, 26 (32.5%) had a cutaneous malignancy as the primary lesion. However, this was clearly a selected population, and other authors have estimated that perineural invasion occurs in fewer than 5% of patients with carcinoma of the skin.

Any unexplained facial neuropathy should raise a suspicion of malignant perineural invasion. In such cases, the basis for an accurate and timely diagnosis is a high index of suspicion and a careful history.

We report a case of perineural invasion of the facial nerve by a cutaneous squamous cell carcinoma in a patient who presented with a slowly progressive facial paralysis. We also review current concepts in the diagnosis and treatment of this disease process.

Case report

A 59-year-old man presented with a 4-year history of a progressive left facial paralysis in the buccal branch. The paralysis had begun after the patient had undergone excision of a dime-sized lesion of his left cheek. Pathology at that time revealed that the lesion was a squamous cell carcinoma. The lesion was excised with adequate margins, and there was no evidence of perineural invasion.

Our physical examination confirmed the left facial paralysis. We also noted the small, well-healed left midface scar from the previous surgery. Notably, the patient’s trigeminal nerve sensation was normal in all distributions, and there were no other cranial neuropathies. Laboratory investigations revealed that the complete blood count, the erythrocyte sedimentation rate (4 mm/hr), and the angiotensin-converting enzyme level (54 IU/L) were normal. The patient was also negative for Borrelia burgdorferi and varicella-zoster virus. Lumbar puncture was performed and cerebrospinal fluid analysis revealed that his glucose level (62 mg/dl), protein level (35 mg/dl), and cell count were normal and that his fluorescent treponemal antibody absorption (FTA-ABS) and Venereal Disease Research Laboratory (VDRL) assays were nonreactive. Finally, findings on computed tomography (CT) of the head and neck (with thin cuts through the temporal bones and internal auditory canal), magnetic resonance imaging (MRI) of the brain, and magnetic resonance angiography (MRA) of the brain were all normal.

Initially, the patient underwent scar excision at the site of his previous malignancy and a biopsy of a distal buccal branch. Pathologic examination revealed only scar tissue and normal nerve tissue; there was no evidence of malig-
nancy. However, given our strong clinical suspicion of perineural invasion, we decided to undertake a more aggressive search. We performed a peripheral facial nerve exploration, including a total parotidectomy. Intraoperatively, tumor was discovered in all distal divisions. Retrograde exposure via a canal-wall-up mastoidectomy was required to achieve negative margins. The nerve was traced to the level of the second genu (figure 1). Frozen-section analysis revealed perineural invasion with microscopic features suggestive of a squamous cell origin (figure 2). Reconstruction was undertaken with both facial suspension and reanimation. The upper and midface were suspended with a fascia lata graft, and a lower lid tarsorrhaphy was performed. The lower face was reanimated via a masseteric sling.

The patient’s postoperative course was unremarkable, and he underwent adjuvant radiation therapy. At the 6-month postoperative follow-up, he was doing well from both a functional and cosmetic standpoint, and he demonstrated no evidence of disease.

Discussion
Although the subject of much investigation, the biologic mechanism of perineural invasion is still poorly understood. Jentzer and Askanazy first coined the term neurotropism to describe this process. In 1905, Ernst was one of the first to suggest that carcinoma may spread via the “perineural lymphatics”; however, the existence of perineural lymphatics is still a matter of some debate. More recently, investigators have proposed that malignant cells invade and spread via potential spaces in the connective tissue planes of the perineurium and endoneurium without inciting an inflammatory response in the surrounding stroma or invading the nerve fibers themselves. In either case, the tumor advances in a contiguous fashion distally or proximally along the tract of the nerve and may extend to the skull base and central nervous system. This can occasionally be the only form of tumor progression, and it is generally believed to represent an aggressive phenotype and portend a poorer prognosis.

It is reasonable to suspect that malignant cells with this ability express cell-surface molecules that enable them to initially traverse the perineurium. Studies of the neurotropic desmoplastic variant of melanoma have correlated the overexpression of the 75-kD neurotrophin receptor (p75NTR), a cell-surface molecule, and its ligand, nerve growth factor, with the propensity for perineural invasion. This receptor could potentially be used as a molecular marker for the neurotropic phenotype or to detect perineural invasion on histologic examination of melanoma. Furthermore, in studies of squamous cell tumors of the head and neck, inhibition of intracellular signal-related kinases (ERK1/ERK2) has been shown to significantly inhibit invasiveness, including neurotropism, of oral cancers in vivo. These and other studies indicate that we are now beginning to understand the process of perineural invasion at the molecular level.

In 1980, Jackson et al addressed the issue of facial paralysis of neoplastic origin. They cited several clinical features that are highly suggestive of a malignant etiology: (1) single-branch palsy, (2) slow progression beyond 3 weeks, (3) no return of function at 6 months, (4) facial hyperkinesia, especially hemifacial spasm, (5) associated cranial neuropathies, (6) recurrent ipsilateral paralysis, and (7) pain; some of these features were seen in our case. Patients with these findings should undergo a complete neurologic diagnostic work-up, including audiometric evaluation as well as a radiographic survey with CT of the temporal bone, MRI and MRA, and possibly positron-
emission tomography. However, as was the circumstance in our case, there is no consistently reliable diagnostic tool to replace clinical judgment. Patients whose signs and symptoms raise sufficient clinical suspicion of malignant perineural invasion should be advised to undergo surgical exploration of the facial nerve from the peripheral branches to the internal auditory canal for diagnostic and therapeutic purposes.

The standard approach to perineural invasion remains undefined. Patients have been divided into asymptomatic and symptomatic groups:

**Asymptomatic patients.** In the asymptomatic group, the diagnosis of perineural invasion is made incidentally by microscopic pathologic examination of the resected skin lesion on frozen or permanent section. In this group, resection of the primary tumor and the involved nerve to negative intraoperative margins is recommended. Oncologic principles must guide the surgical approach, and functional and cosmetic consequences should be considered, as well. Therapy also includes adjuvant postoperative radiotherapy. The local control rate for patients treated with both modalities approaches 80% at 5 years.

**Symptomatic patients.** Symptomatic patients, of course, have more advanced disease, and a more aggressive surgical approach is necessary for tumors that are grossly resectable. Again, surgery is followed by radiation therapy. If the tumor is deemed unresectable or if resection imposes unacceptable morbidity, primary radiation therapy may be considered as a palliative measure. Yet despite more aggressive therapy, local control can be expected in only 45 to 50% of symptomatic patients.

The case we describe here highlights the insidious nature and elusive clinical presentation of this disease process. The otolaryngologist is reminded to maintain a high index of suspicion for perineural invasion in cases of facial nerve paralysis, especially in those that arise in an isolated distal division. However, it must be acknowledged that even in highly suggestive cases, a thorough clinical and radiographic work-up may fail to demonstrate the etiology. Under these circumstances, surgical exploration of the entire course of the facial nerve may be necessary to achieve a definitive diagnosis and to deliver timely surgical and adjuvant therapy.

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References