Intraoperative biopsy of the major cranial nerves in the surgical strategy for adenoid cystic carcinoma close to the skull base

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Objective. Adenoid cystic carcinoma of the salivary glands has a propensity for perineural invasion, which could favor spread along the major cranial nerves, sometimes to the skull base and through the foramina to the brain parenchyma. This study evaluated the relationship between neural spread and relapse in the skull base.

Study Design. During surgery, we performed multiple biopsies with extemporaneous examination of the major nerves close to the tumor to guide the surgical resection.

Results. The percentage of actuarial local control at 5 years for patients with a positive named nerve and skull base infiltration was 12.5%, compared with 90.0% in patients who were named nerve–negative and without infiltration of the skull base (P = .001).

Conclusions. Our study shows that local control of disease for patients who are named nerve–positive with skull base infiltration is significantly more complex compared with patients who are named nerve–negative without infiltration of the skull base. (Oral Surg Oral Med Oral Pathol Oral Radiol 2012;113:214-221)

Adenoid cystic carcinoma (ACC) constitutes fewer than 10% of all salivary gland neoplasms, including benign and malignant lesions, but about 40% of all malignancies of the major and minor salivary glands.[1] ACC occurs most frequently in the fifth decade of life and no gender predilection exists. It is seen in both the minor and major salivary glands, but is more common in the minor salivary glands. It is the most common malignancy in the submandibular gland and the minor salivary glands, and it can also occur in other glandular tissue,[2] the lacrimal glands, and the ceruminous glands of the external auditory canal.[3] This tumor is characterized by a prolonged natural history with slow growth, multiple recurrences, a long clinical course, and late metastasis.[4] Tumor infiltration into adjacent tissues is frequently without well-defined borders, so when computed tomography (CT) and magnetic resonance imaging (MRI) are used, the true extent of these tumors is often underestimated.

Efforts to unearth reliable prognostic factors for this disease have dominated the ACC literature for the past decade, but no universal interstudy consensus has been established regarding the key prognostic factors. Negative clinical prognosticators identified in previous studies include tumor site within the minor salivary glands, infiltrative patterns of localized growth and spread, increasing size and stage of tumor, predominantly solid histologic features,[5] presence of cervical metastases, positive margins at surgery,[6] and perineural invasion.[1]

When compared with other cancers of the head and neck, ACC requires more complex surgical management because residual positive margins often remain after tumor removal owing to perineural invasion. This could favor spread along the major cranial nerves, sometimes to the skull base and through the foramens to the brain parenchyma. Perineural spread is a precursor of cranial nerve infiltration, skull base invasion, and cavernous sinus involvement.

These findings have a profound negative effect on survival and may drastically change the therapeutic plan, including the surgical approach and adjuvant therapy.[1] Patients with cancer of the nasal cavity, paranasal sinuses, nasopharynx, orbit, and parotid gland commonly have neural spread along branches of cranial nerves I to VII. This provides a route of invasion of the cranial base along the cribiform plate, optic canal, superior and inferior orbital fissures, foramina ovale and rotundum, pterygoid canal, and stylomastoid foramen. Tumors extending to the parapharyngeal space, carotid sheath, and infratemporal fossa may involve

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Received for publication Dec 30, 2010; returned for revision Feb 7, 2011; accepted for publication Feb 11, 2011.

2212-4403/$ - see front matter
doi:10.1016/j.tripleo.2011.02.014

neural spread along the lower cranial nerves (IX to XII). This enables a route of invasion to the skull base along the jugular foramen and hypoglossal canal. Cranial base invasion usually heralds intracranial extension of the tumor. Although the dura is an effective barrier that delays brain invasion to some extent, dural involvement has a major negative effect on the survival of patients with skull base cancer.[7] Failure to detect neural spread before surgical resection may result in poor planning of the surgical approach and an inability to obtain tumor-free margins. Although postoperative radiation, chemotherapy, or both have been advocated in the treatment of patients with positive margins, the outcome of such patients is still poor. Thus, detecting neural involvement is critical for the management of patients with ACC of the head and neck.

This study evaluated the relationship between neural spread and relapse in the base of the skull using intraoperative biopsy of the major nerves close to the tumor.

PATIENTS AND METHODS

This case series reports our multicenter experience in the treatment of 25 consecutive patients with a histologic diagnosis of head and neck ACC who underwent surgery at the Maxillofacial Surgery Unit at S. Orsola-Malpighi Hospital in Bologna or the Maxillofacial Surgery Unit at Bufalini Hospital in Cesena, with the collaboration of the Neurosurgery Unit at the Bellaria Hospital in Bologna. This study took place between February 1999 and December 2008.

The study group consisted of 13 men and 12 women aged between 39 and 76 years, with an average age of 55. The tumors were located in the minor salivary glands of the palate in 15 patients, submandibular gland in 5 patients, sublingual gland in 2 patients, lacrimal gland in 2 patients, and parotid gland in 1 patient. Eighteen of these patients were treated for the first time; the remaining 7 came to us after relapse.

The presurgical evaluation included a history and clinical examination, along with CT or MRI of the lesion, CT-positron emission tomography (CT-PET), and a chest radiograph to assess any distant metastases. No patient had radiographically evident distant metastases at the time of surgery.

All patients underwent surgery. The specimens were examined at the Institute of Pathological Anatomy of S. Orsola-Malpighi Polyclinic and at the Pathological Anatomy Department at the Bufalini Hospital of Cesena.

Adjuvant radiotherapy was performed on 10 patients. One patient received adjuvant polychemotherapy for systemic disease. Both primary tumor resection and neck dissection were performed on 3 patients in whom clinical and radiographic examinations revealed lymphatic spread.

Table I. Surgical approach

Surgical approach	*No.*
Transoral approach	7
Transfacial approach	7
Transfacial + transcranial approach	5
Submandibular approach	5
Preauricular approach	1
Total	25

Small and medium-sized tumors were removed using the intraoral approach, whereas the larger tumors were treated via transfacial surgical access; submandibular and preauricular access were performed for tumors located in the submandibular and parotid space, respectively. When the neoplasm was close to the skull base, we performed transfacial and transcranial combined access (Table I).

The patients underwent en bloc tumor resection, with wide excision margins when possible. During surgery, we performed multiple biopsies with extemporaneous examination of perineural tissue and major nerves (*named nerves*) close to the tumor to guide the surgical resection. The maxillary, mandibular, and vidian were the most frequently biopsied nerves.

When the neoplasm involved the skull base, we combined transcranial/transfacial surgery.

The skull base was resected in 3 patients; in 5 patients, we resected the tumor as far as the skull base foramina and resected the major cranial nerves that had been infiltrated by cancer.

When the extemporaneous histologic examination of the main nerve branches in close proximity to the tumor mass was positive, the surgical resection was wider than initially planned. In these cases, we followed the nerve backward.

In 3 cases, total sacrifice of the involved nerve was necessary: a temporal basal craniotomy was performed and the main branches of the fifth cranial nerve were exposed and cut extradurally using a microsurgical technique.

The use of optical magnification helped avoid damage to nearby neurovascular structures (e.g., the internal carotid artery and lateral wall of the cavernous sinus) and allowed accurate hemostasis and the sealing of dural defects caused by microsurgical maneuvers.

In 10 patients, the surgical defect was large enough to require reconstructive microvascular surgery: we used anterolateral thigh free flaps in 6 patients, fibula free flaps in 2 patients, and forearm flaps in 2 patients. Microvascular surgery was carried out in the Plastic Surgery Unit of S. Orsola-Malpighi Hospital in Bologna.