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Original research article

Temporal bone carcinoma: Classical prognostic variables revisited and modern clinico-pathological evidence

Elisabetta Zanoletti[a,*], *Gino Marioni*[a], *Sebastiano Franchella*[a], *Sara Munari*[a], *Roberto Pareschi*[b], *Antonio Mazzoni*[a,1], *Alessandro Martini*[a]

[a] *Department of Neurosciences, Otolaryngology Section, Padova University, Padova, Italy*
[b] *E.N.T. Department, Legnano Hospital, Italy*

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ABSTRACT

Aim: Prognostic factors, rational management, and the ongoing investigations regarding temporal bone squamous cell carcinoma (TBSCC) have been critically reviewed.
Background: TBSCC is an uncommon, aggressive malignancy. Although some progress has been made in treating this aggressive tumor, the prognosis in advanced cases remains poor.
Materials and methods: A systematic search of the literature for articles published between 2009 and October 2014 was performed using the PubMed (http://www.pubmed.gov) electronic database.
Results: Given the particular anatomical site of TBSCC, its prognosis is significantly influenced by any direct involvement of nearby structures. The extent of the primary tumor is generally considered one of the most important prognostic factors and it is frequently related to prognosis even more strongly than N stage. For TBSCC, biomarker investigations in surgical specimens are only just beginning to appear in the oncological literature.
Conclusion: Given the particular features of TBSCC, the sub-specialty of otologic oncology seems to be emerging as a defined area of practice involving multidisciplinary team comprising oto-neurosurgeons, head and neck surgeons, plastic surgeons, oncologists, radiotherapists, dedicated radiologists, and pathologists.

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* *Corresponding author at*: Department of Neurosciences, Otolaryngology Section, University of Padova, Via Giustiniani 2, 35128 Padova, Italy. Tel.: +39 0498218778; fax: +39 0498211994.
E-mail address: elisabetta.zanoletti@tiscali.it (E. Zanoletti).
[1] Formerly at ENT Unit, Ospedali Riuniti Bergamo, Bergamo, Italy.

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1. Background

Squamocellular carcinoma of external-middle ear is an uncommon (less than 0.2% of head and neck cancers) and aggressive malignancy. It accounts for the 60–80% of tumors arising in the external auditory canal.[1–3]

The reason for this malignancy aggressiveness may be found in the disease biological behavior but also in the various potential routes of diffusion to the surrounding structures. Temporal bone does not protect from tumoral invasion and microscopic invasion seems to be frequent through the intraosseous vessels and Haversian canals. In available literature, the association between the tumor and middle ear chronic inflammatory disease has been reported,[4,5] as well as genetic predisposition.[4] A role has been hypothesized for chlorinated disinfectants in the etiopathogenesis of middle ear carcinoma and for human papillomavirus in cases of temporal bone squamous cell carcinoma (TBSCC) associated with inverted papilloma.[6,7] TBSCC is usually diagnosed with delay[1,4] since clinical signs (otorrhea, polyps or granulation tissue, hearing loss, bleeding) and patients complaints (ear pain) are similar to other common inflammatory diseases of the ear. When present, facial nerve paralysis is a sign of advanced disease.

Perineural invasion and angio-lymphatic diffusion are local features of tumor aggressiveness.[4,8] The temporal bone may be eroded by obvious extension or microscopic undetectable intra-osseus infiltration. Adjoining sites (jugular foramen, dura mater, internal carotid artery, facial nerve, parotid, condyle) may be involved by local tumor growth. Diagnosis is mostly clinico-radiological and necessarily confirmed by local deep biopsies. Cervical lymphnodes metastases are relatively common (10–20%).[4,9,10] Temporal bone contrast-enhanced, high-resolution CT scan and MRI are mandatory. Neck ultrasonography and/or contrast-enhanced CT scan can effectively investigate regional metastases. PET scan can be important to rule out distant metastasis. Differential diagnosis involves[1,4] skull base osteomyelitis, infectious complications of the skull base and other local neoplasms.

Curative treatment is an extensive radical surgery followed by radiotherapy and chemotherapy in advanced stages or if required by postoperative pathological evidence (including involved margins). The anatomical complexity of this area involves technically difficult surgery and the need of extending the surgical field beyond macroscopically free margins in order to obtain oncologically safe margins.

Despite improvements in early diagnosis, surgical techniques and adjuvant therapies, prognosis remains poor, especially for advanced TBSCCs. It has been diffusely reported that several cases recurred even after radical surgical excision with pathologically free margins. Further investigations exploring the biological behavior of the tumor seem nowadays to be mandatory to predict prognosis and promote modern treatments for TBSCC.

2. Aim

Critical review of the current status of knowledge, prognostic factors, rational management and the ongoing investigations regarding primary temporal bone squamous cell carcinoma (TBSCC).

3. Materials and methods

A systematic search of the literature for articles published between 2009 and October 2014 was performed using the PubMed (http://www.pubmed.gov) electronic database; only articles in English were included. The searched terms used were: “temporal bone cancer”, “temporal bone malignancy”, “temporal bone carcinoma”, “ear malignancy”, “ear cancer”, “ear carcinoma”. The “Related articles” option on the PubMed homepage was also considered. Some papers were found in more than one search. The texts of the publications identified were screened for original data and reference lists were checked for other relevant studies.

Studies considered acceptable for inclusion were those addressing TBSCC prognostic factors. All investigations discussing malignancies other than squamous cell carcinoma, case reports, very limited series, and clinical reviews were excluded. Other recent series referring to carcinoma of the parotid skin, retroauricular, preauricular area involving the external-middle ear were also excluded.

4. Results

4.1. *Conventional clinico-pathological variables and prognosis*

Among the considered series, the significant prognostic factors in terms of disease-free survival (DFS) and disease-specific survival (DSS) were critically analyzed.

The pathological status of surgical margins was diffusely reported as the main factor influencing the outcome and the recurrence rate,[10–16] although how reliable “free margins” could be in the bone is still a matter of discussion.[10]

There is quite a general agreement on the significant role of T stage according to the Pittsburgh staging system[10,12,13,15,16] as a factor determining prognosis, since the latter was good in T1–T2 and poor in T3–T4. The different outcome of the group of patients with anterior vs. non-anterior extension of T4 tumors was recently investigated[17] showing a significantly better prognosis in the anterior T4. The proposal of a modified classification system for tumor local extension has been reported in a recent paper by Mazzoni et al.[17] (Table 1). Extensive erosion of the bone was also a negative prognostic factor.[11,13,16,17] The pathological grading of the tumor was reported as a factor related to worse prognosis only in a limited number of series.[10,18] In part, facial nerve involvement continues to be controversial with a significant negative prognostic role found by most[11,12,15,16,19–22] but not all groups.[23] Dura mater infiltration evidence (both radiological and/or pathological) was reported in most of the series[10,11,21,22] as the strongest negative prognostic factor affecting survival.

Different conclusions have been reported about the prognostic value of neck lymph-nodes clinical status (cN). Clinically positive neck has been significantly related with poor prognosis by some groups[10,11,18,21,22] but not by others.[23,8]

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