

## Review Article

# Management of the clinically negative cervical lymph nodes in patients with non-conventional squamous carcinoma of the larynx

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### Abstract

This paper discusses the indications for neck dissection in those patients with laryngeal tumours which prove to be, on pathologic examination, not conventional squamous carcinomas but rather fall into the category either of one of the uncommon histological subtypes of carcinoma, or another type of unusual histological variant of laryngeal malignancy, a mesenchymal tumour. It appears as though these unusual laryngeal malignancies may manifest both biological behaviours and propensities to metastasize to regional lymph nodes that differ from those of the more commonly encountered conventional squamous carcinomas of the larynx. This heterogeneous group of tumours accounts for about 10 per cent of all malignant tumours of the larynx.

**Key words:** Laryngeal neoplasms; Carcinoma, squamous cell; Neoplasm metastasis; Radical neck dissection

### Introduction

There is evidence that the optimal approach to the evaluation of 'clinically' negative nodes is yet to be defined. At present, we are unable to establish lymph node involvement accurately using non-invasive methods (computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, ultrasound-guided fine needle aspiration cytology (FNAC), ultrasound-guided fine needle aspiration biopsy (FNAB), single photon emission computed tomography, positron emission tomography (PET), radio-immunoscintigraphy) (Stern *et al.*, 1990; van den Brekel *et al.*, 1990; 1991; 1992; 1996; Snow *et al.*, 1992; Lenz *et al.*, 1993; Mendelsohn *et al.*, 1993; Steiner and Hommerich, 1993; de Bree *et al.*, 1994; Braams *et al.*, 1995; Ferlito and Silver, 1996; Takes *et al.*, 1996; Fielding, 1997; Schuller and Bier-Laning, 1997; Takes *et al.*, 1997; Yamamoto *et al.*, 1997; Myers *et al.*, 1998).

There is still no general agreement as to the best treatment of the stage N<sub>0</sub> neck in squamous cell carcinoma of the larynx. Treatment strategies range from watchful waiting to elective neck irradiation or even elective neck dissection. There are proponents

and opponents of all three types of management. The differences in outcome between these different strategies do not appear to be statistically significant. Of course, the neck would be prospectively treated in patients presenting cervical lymph node metastases.

In general, the primary histological diagnosis in a patient with a laryngeal mass clinically suggestive of a malignancy will be presumed initially to be a squamous cell carcinoma until biopsy results are available; however, it should be born in mind that approximately 10 per cent of malignant neoplasms of the larynx ultimately prove to be tumours of a different histology. If the tumour is not a squamous cell carcinoma, what kind of neck treatment should be applied when it is stage N<sub>0</sub>?

This matter has not been rigorously discussed in the surgical literature, because the designation N<sub>0</sub> neck is generally assumed to refer to the clinically negative neck in cases of primary squamous cell cancer. In its broadest sense, however, 'cancer' is a word which may be employed to describe many different histological tumour types with a different prognosis and distinct impact on patients survival

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(Ferlito *et al.*, 1998c). Discussions of cervical metastases often do not consider different types of laryngeal cancer, despite the fact that each histological type of laryngeal cancer possesses its own distinctive natural history. This article discusses the treatment of the N<sub>0</sub> neck in a variety of uncommon primary malignancies of the larynx (including both uncommon epithelial tumours as well as mesenchymal tumours), considering the biological behaviour and propensity to metastasize to regional lymph nodes of different epithelial and mesenchymal neoplasms.

### Treatment of N<sub>0</sub> neck in uncommon primary malignancies of the larynx

#### *Verrucous carcinoma*

This tumour is characterized by slow growth and a relatively indolent course. Regional lymph node and distant metastases from laryngeal verrucous carcinoma have not been reported to date (Ferlito and Recher, 1980). Any kind of neck dissection is therefore not indicated, even when enlarged and tender lymph nodes can be palpated. In fact, histological examination of these nodes has revealed only an inflammatory reaction (Ferlito, 1987; McCaffrey *et al.*, 1998). Radiotherapy is far less effective than surgery because this tumour, although not radio-resistant, is less radio-sensitive than conventional squamous carcinoma (Ferlito *et al.*, 1998a). The prognosis is excellent (Orvidas *et al.*, 1998).

#### *Papillary squamous cell carcinoma*

This tumour is an uncommon, distinct and little-recognized variant of squamous cell carcinoma. It generally has a better prognosis than that of conventional squamous cell carcinoma (Thompson *et al.*, in press). Ishiyama *et al.* (1994) believe that patients with lesions in stage T<sub>3</sub> or greater should undergo a prophylactic neck dissection, in consideration of the high rate of neck metastasis.

#### *Spindle-cell carcinoma*

There is no significant difference in clinical behaviour between laryngeal spindle-cell carcinoma and conventional squamous cell carcinoma (Hellquist and Olofsson, 1989; Olsen *et al.*, 1997). Considering that the same treatment policy is advocated for both lesions, there is consensus to treat surgically the N<sub>0</sub> neck in laryngeal spindle-cell carcinoma, if the primary lesion is surgically treated.

#### *Basaloid squamous cell carcinoma*

This tumour has aggressive biological behaviour and neck dissection is recommended because of the high likelihood of cervical lymph node metastases (Ferlito *et al.*, 1997a).

#### *Lympho-epithelial carcinoma*

The tumour is radioresponsive, and radiotherapy is appropriate initial locoregional therapy for patients with this disease (Ferlito *et al.*, 1997b).

TABLE I

INDICATIONS FOR NECK DISSECTION ACCORDING TO ONCOTYPE IN THE TREATMENT OF THE 'CLINICALLY NEGATIVE' NECK IN UNUSUAL LARYNGEAL TUMOURS

Laryngeal tumour	Is neck dissection indicated?
Verrucous squamous cell carcinoma	No
Papillary squamous cell carcinoma	Yes
Spindle-cell carcinoma	Yes
Basaloid squamous cell carcinoma	Yes
Lympho-epithelial carcinoma	No
Carcinoid tumour	No
Atypical carcinoid	Yes
Small cell neuroendocrine carcinoma	No
Paraganglioma	No
Melanoma	No
Mucoepidermoid carcinoma	Yes
Adenoid cystic carcinoma	No
Adenosquamous carcinoma	Yes
Fibrosarcoma	No
Malignant fibrous histiocytoma	No
Liposarcoma	No
Leiomyosarcoma	No
Rhabdomyosarcoma	No
Haemangiopericytoma	No
Synovial sarcoma	No
Chondrosarcoma	No
Lymphomas	No

Neck dissection is not indicated. Surgery should be reserved for patients who have persistent lymph node disease six weeks after completing radiotherapy (Dubey *et al.*, 1998).

#### *Carcinoid tumour*

Neck dissection is not indicated since the likelihood of metastases is very low (El-Naggar and Batsakis 1991; Ferlito *et al.*, 1998b).

#### *Atypical carcinoid*

Neck dissection is advisable in all cases of atypical carcinoid because of the high likelihood of cervical lymph node metastases, as well as the high incidence of regional node involvement during the course of this disease (Goldman *et al.*, 1985; Moisa and Silver, 1991; Ferlito *et al.*, 1998b).

#### *Small-cell neuroendocrine carcinoma*

Neck dissection does not appear necessary, in view of the fact that the treatment of choice is the combination of chemotherapy and radiotherapy (Ferlito, 1986).

#### *Paraganglioma*

Any kind of neck dissection is not indicated in laryngeal paraganglioma because this tumour is almost always benign (Ferlito *et al.*, 1998b). Essentially, all reported cases of aggressive and metastasizing malignant paraganglioma of the larynx were actually atypical carcinoids (Barnes, 1991; Ferlito *et al.*, 1994). The presence of a neck mass might be indicative of a metachronous carotid body paraganglioma. The possibility of multicentric paraganglioma should be considered before concluding that a given tumour has metastasized (Ferlito *et al.*, 1995).

### *Melanoma*

Neck dissection is not usually recommended for malignant melanoma (Duwel and Michielssen, 1996) because the incidence of cervical lymph node metastases is considered low (Panje and Moran, 1986). Therapeutic neck dissection is indicated for involved lymph nodes in patients with no evidence of distant metastatic disease. Lymph node metastases usually indicate an advanced and uncontrolled or uncontrollable neoplasm (Ferlito, 1987) and the presence of metastatic disease generally portends a rapidly fatal outcome (Wenig, 1995).

### *Mucoepidermoid carcinoma*

The tumour may metastasize to cervical lymph nodes and visceral metastases may also occur, particularly in the lung. Neck dissection is indicated in particular in high grade mucoepidermoid carcinomas.

### *Adenoid cystic carcinoma*

Any kind of neck dissection is not indicated in this tumour because regional metastases to the cervical lymph nodes are extremely rare. Ferlito *et al.* (1990) consider that the lymph nodes are reached by direct extension of the lesion and that true embolic lymph node metastases are exceptional. Conversely, distant metastases may be detected (in the lung, liver, bones, brain) in the terminal stage. A cervical mass is not always a lymph node secondary, as it may be a recurrence or persistence of the primary tumour (Ferlito and Caruso, 1983; Ferlito *et al.*, 1990). Occasionally, a metastasis from a basaloid squamous cell carcinoma may be mistaken for an adenoid cystic carcinoma (Ferlito *et al.*, 1997a).

### *Adenosquamous carcinoma*

This tumour is considered as a highly malignant neoplasm and neck dissection is indicated because of the high frequency of regional metastases.

### *Fibrosarcoma*

The bloodstream is the usual route for the spread for fibrosarcomas, which are much less commonly encountered tumour types than were once thought (Ferlito *et al.*, 1983a). Examples of pure laryngeal fibrosarcoma are exceedingly rare (Ferlito, 1990) and regional lymph node metastasis are rarer still, making any kind of neck dissection unnecessary (Ferlito *et al.*, 1983a).

### *Malignant fibrous histiocytoma*

Neck dissection is not justified, considering that lymph node metastases are rare in this condition (Ferlito *et al.*, 1983b).

### *Liposarcoma*

To date, none of the reported liposarcomas of the larynx have metastasized to the lymph nodes (Wenig and Nakayama, 1996), so any kind of neck dissection is not indicated.

### *Leiomyosarcoma*

Neck dissection is not indicated because metastases from this tumour are almost always hematogenous and usually go to the lungs, followed in order of frequency by the liver and skeleton (Barnes and Ferlito, 1993), while the incidence of metastases to cervical lymph nodes is low (Lippert *et al.*, 1997).

### *Rhabdomyosarcoma*

All histological variants of rhabdomyosarcoma (embryonal, botryoid, alveolar and pleomorphic) have been described in the larynx (Barnes and Ferlito, 1993), but about 65–75 per cent are of embryonal and/or botryoid type. Multimodality regimens with a combination of non-radical surgery, radiation and multi-agent chemotherapy have markedly improved the survival of patients with embryonal, botryoid and alveolar rhabdomyosarcomas. In these cases, elective neck dissection is not indicated because of the low incidence of cervical metastases, and because of the fact that regional control is excellent with adjuvant chemotherapy and radiation (Wharam *et al.*, 1987). Neck dissection is not indicated for pleomorphic rhabdomyosarcoma either, since this would represent an overtreatment (Da Mosto *et al.*, 1996). In fact, metastatic lymph node involvement has only been reported in one case (Wilhelm *et al.*, 1980).

### *Haemangiopericytoma*

Any kind of neck dissection does not appear indicated because metastasis in laryngeal haemangiopericytoma has only been reported in one case and the secondary site was not specified (Stout, 1956).

### *Synovial sarcoma*

No lymph node metastases have been described in any of the reported cases of laryngeal synovial sarcoma and is quite exceptional in hypopharyngeal lesions so any kind of neck dissection is unnecessary (Amble *et al.*, 1992; Dei Tos *et al.*, 1998).

### *Chondrosarcoma*

Approximately 340 cases of chondrosarcomas of the larynx have been documented to date and only 12 of the patients had neck metastases, a figure that corresponds to less than four per cent of cases (Nicolai *et al.*, 1998). Cervical metastases are rare, and neck dissection is not consequently mandatory, except when clinically suspicious lymph nodes are present (Nicolai *et al.*, 1990; Gripp *et al.*, 1998).

### *Lymphomas*

Radiotherapy is considered to be the treatment of choice when the lesion has not involved extranodal sites (solitary laryngeal lymphomas). Neck dissection is not indicated (Kato *et al.*, 1997).

Other malignant tumours have been reported in the larynx, i.e. salivary duct carcinoma, epithelial-myoepithelial carcinoma, clear cell carcinoma, acinic cell carcinoma, carcinoma in pleomorphic adenoma, adenoid squamous cell carcinoma, sebaceous carcinoma, giant cell carcinoma, malignant myoepithelioma, osteosarcoma, angiosarcoma, Kaposi's sarcoma, Ewing's sarcoma, primitive neuroectodermal tumour, malignant granular cell tumour, malignant mesenchymoma, malignant nerve sheath tumour, etc. The behaviour of these neoplasms in this particular location is difficult to assess accurately in view of their rarity.

Before performing a neck dissection, it is important to understand the natural history of a specific phenotype, so that any kind of neck dissection is not performed in cancers which never metastasize to cervical lymph nodes (i.e. verrucous squamous cell carcinoma, adenoid cystic carcinoma, etc.), but rather will be held in reserve for use in those cancers with a well-established propensity for regional spread (i.e. basaloid squamous cell carcinoma, atypical carcinoid, etc.).

Table I summarizes the indications for neck dissection in the treatment of the clinically negative neck in unusual tumours of the larynx.

Cervical lymphadenopathy may be aetiologically unrelated to metastatic disease in laryngeal cancer patients (Ferlito and Silver, 1996) and the clinician should always consider this possibility. Dual lymph node pathologies sometimes exist (Ferlito *et al.*, 1986; Pacheco-Ojeda *et al.*, 1991).

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