Laryngeal Carcinoma

14

Typically presenting in 50–60 year old males with persistent hoarseness, tobacco and alcohol use are the usual risk factors. Investigation is by indirect laryngoscopy with biopsy. Chest x-ray and endoscopy of the upper aerodigestive tract are done to exclude a concurrent cancer elsewhere. CT and MRI scans are used to stage the tumour and cervical lymph node enlargement necessitates ultrasound guided fine needle aspiration cytology (FNAC) to establish if there are metastases. Tumour stage and fitness of the patient determine the appropriate choice of treatment i.e. radiotherapy, laser resection, local excision, laryngectomy, or neck dissection. Laryngectomy may also accompany a pharyngectomy for cancer of the hypopharynx.

14.1 Gross Description

Specimen

- Biopsy/transoral laser resection/hemi-/partial or total laryngectomy/neck dissection.
- Size (cm) and weight (g).

Tumour

Site

Supraglottic	20 %
Glottic	70 %
Infraglottic	5 %
Transglottic	5 %

Supraglottis: from the tip of the epiglottis to the true cords including the aryepiglottic folds, false vocal cords and ventricles.

Glottis: true cords and anterior commissure.

Subglottis: from the lower border of the true cords to the first tracheal cartilage.

Anterior/posterior/lateral(right, left)/commissural/ventricles/false cords.

Anterior glottis is the commonest site (Fig. 14.1).

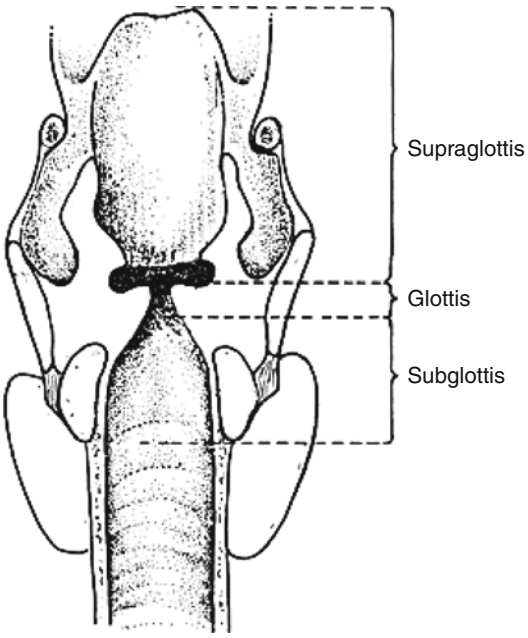

Fig. 14.1 Larynx (Reproduced, with permission, from Wittekind et al. (2005), © 2005)

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Size

- Length × width × depth (cm) or maximum dimension (cm).
- Tumour size is the main contributor to pathological stage as it is an indicator of disease extent. The maximum depth of invasion is subordinate to the nature of the tissue planes involved. Invasion of thyroid or cricoid cartilage are important staging criteria.

Appearance

- Polypoid/verrucous/plaque/ulcerated/multifocal.
- Ulcerated endophytic cancers do less well than exophytic polypoid cancers.

Edge

- Circumscribed/irregular.

14.2 Histological Type

Squamous Cell Carcinoma

- *90 % of cases*.
- Keratinising/non-keratinising.
- Prognosis is *better* (verrucous/papillary), *usual* (spindle cell/adenoid squamous) or *worse* (basaloid/adenosquamous)
- variants:
- *Verrucous*: broad based exophytic and "church-spire" hyperkeratosis with a pushing deep margin of cytologically bland bulbous processes arising in the glottis. Locally invasive, rarely metastatic, radiation may result in anaplastic change although this association is anecdotal. Seventy percent 5 year survival.
- *Papillary*: >70 % papillary or exophytic fronds, covered by malignant type epithelium with focal invasion at the base. Better prognosis (70 % 5 year survival).
- *Spindle cell*: polypoid, glottic, elderly, ± history of irradiation for previous carcinoma. A minor squamous cell element is present (in situ or invasive) with a major variably monomorphic to pleomorphic fibrosarcoma like component. Diffuse or focal cytokeratin (AE1/AE3, CK5/6) and p63 positivity suggests that it is a metaplastic form of squamous cell carcinoma. Prognosis is better if polypoid and superficial than infiltrative when the outlook is poor. Distinguish from sarcoma and bizarre post-irradiation granulation tissue.
- *Basaloid*: poor prognosis, nests of basaloid cells with peripheral palisading and central comedonecrosis. Presents with more extensive disease but is more radiosensitive than other squamous cell carcinoma subtypes.
- *Adenoid squamous*: usual prognosis, acantholytic (pseudoglandular) pattern.
- *Adenosquamous*: poor prognosis, mixed differentiation squamous cell carcinoma and adenocarcinoma (either obvious glands or solid with mucin positive cells).

Undifferentiated Carcinoma

- There is an absence of squamous cell or glandular differentiation.
- Includes lymphoepithelioma type which is aggressive with propensity for cervical lymph node and distant metastases.

Neuroendocrine Tumours/ Carcinomas

- Chromogranin/synaptophysin positive ± CD56/CAM 5.2. Variable Ki-67 index and mitotic counts.
- Well differentiated/low-grade: *carcinoid tumour*. Low Ki-67 index (≤2 %) and mitotic count (<2/10hpfs).
- Moderately differentiated: *atypical carcinoid tumour* with characteristic spread to locoregional lymph nodes.
- Poorly differentiated/high-grade: *small cell/large cell carcinoma* 60–90 % of which present with distant metastases. High Ki–67 index and mitotic count.

Atypical carcinoid and large cell neuroendocrine carcinoma are commoner in the larynx than

well differentiated neuroendocrine (carcinoid) tumour and they are *aggressive lesions with 50% mortality*.

Adenocarcinoma

- *Salivary type* e.g. adenoid cystic, mucoepidermoid carcinomas of mucosal gland origin.
- *Adenocarcinoma of no special type*.

Metastatic Carcinoma

- *Direct spread*: thyroid, oesophagus.
- *Distant spread*: malignant melanoma, kidney, breast, lung, pancreas, colon, ovary, and prostate carcinomas. Usually associated with disseminated disease.

14.3 Differentiation

Well/moderate/poor/undifferentiated, or, Grade 1/2/3/4.

- For squamous carcinoma based on cellular atypia, keratinisation and intercellular bridges.
- Undifferentiated carcinoma shows no squamous or glandular differentiation (grade 4). When differentiation varies prognosis relates to the worst area.

14.4 Extent of Local Tumour Spread

Border: pushing/infiltrative. An infiltrative pattern of invasion at the deep aspect of the tumour is of adverse prognostic value.

Lymphocytic reaction: prominent/sparse and desmoplastic stroma.

A glottic tumour is best sliced horizontally to demonstrate its anatomical relationships, a supraglottic tumour sagitally.

Anterior

- Mucous membrane, cricothyroid membrane, thyroid cartilage, thyroid gland, strap muscles, jugular vein.

Superior

- Base of epiglottis, vestibular folds, pyriform fossa and limits.

Inferior

- Trachea and limit.

The TNM7 classification applies only to carcinomas.

pTis	Carcinoma in situ

Supraglottis

pT1	One subsite, normal mobility
pT2	Mucosa of more than one adjacent subsite of supraglottis or glottis or adjacent region outside the supraglottis; without fixation
pT3	Cord fixation or invades post cricoid area, pre-epiglottic tissues, paraglottic space, thyroid cartilage erosion
pT4a	Through thyroid cartilage and/or into trachea, soft tissues of neck: deep/extrinsic muscle of tongue, strap muscles, thyroid, oesophagus
pT4b	Prevertebral space, mediastinal structures, carotid artery

Glottis

pT1	Limited to vocal cord (s), normal mobility (a) One cord (b) Both cords
pT2	Into supraglottis and/or subglottis and/or impaired cord mobility
pT3	Cord fixation and/or into paraglottic space and/or thyroid cartilage erosion

(continued)

pT4a	Through thyroid cartilage or into trachea, soft tissues of neck: deep/extrinsic muscle of tongue, strap muscles, thyroid, oesophagus
pT4b	Prevertebral space, mediastinal structures, carotid artery (Fig. 14.2)

Subglottis

pT1	Limited to subglottis
pT2	Extends to vocal cord(s) with normal/impaired mobility.
pT3	Cord fixation
pT4a	Through cricoid or thyroid cartilage and/or into trachea, deep/extrinsic muscle of tongue, strap muscles, thyroid, oesophagus
pT4b	Prevertebral space, mediastinal structures, carotid artery

14.5 Lymphovascular Invasion

Present/absent.

Intra-/extratumoural.

Vascular invasion is a relatively weak indicator for cervical lymph node metastasis. *Perineural invasion* indicates *more aggressive disease* with likelihood of local recurrence, cervical nodal metastasis and the need for adjuvant therapy.

14.6 Lymph Nodes

The *incidence of lymph node metastases at presentation* varies according to the site of the primary tumour from glottic (<10 %) to supra-/infraglottic (30–50 %). Well differentiated carcinomas are less likely to metastasise than poorly differentiated cancers.

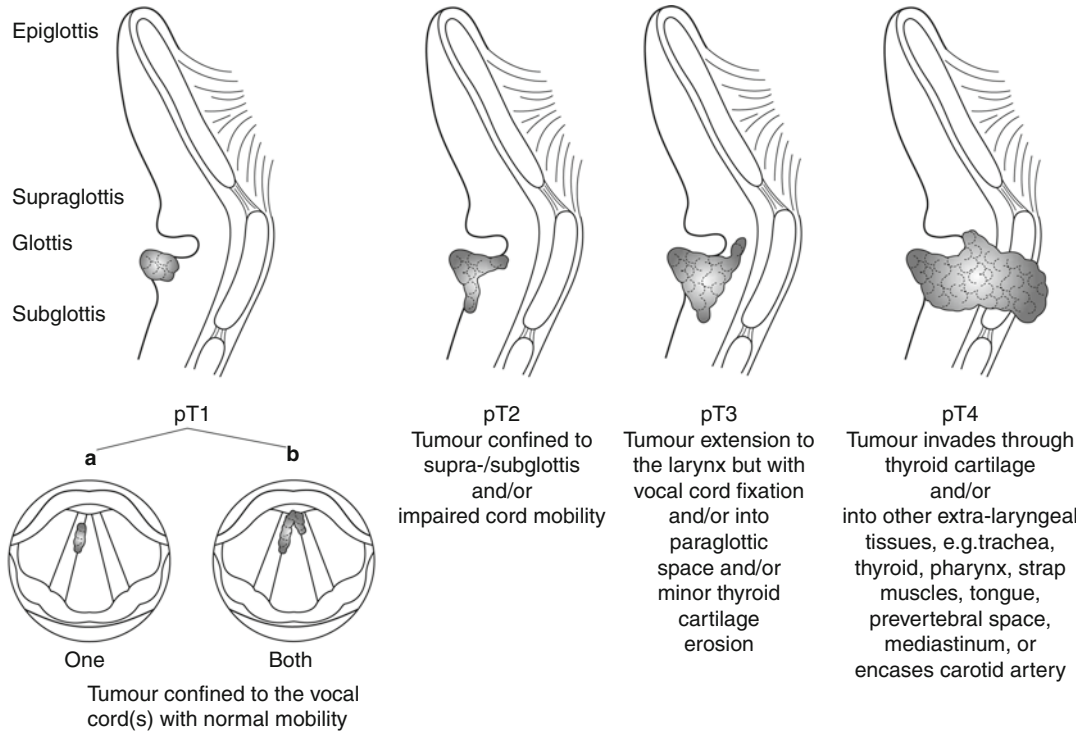

Fig. 14.2 Laryngeal carcinoma: glottis (Reproduced, with permission, from Allen (2006), © 2006)

Site/number/size/number involved/limit node/extracapsular spread.

Regional nodes: cervical.

Level I	Submental, submandibular
Level II	Upper jugular
Level III	Middle jugular
Level IV	Lower jugular
Level V	Posterior triangle

A selective neck dissection will ordinarily include a minimum of six lymph nodes, a (modified) radical dissection ten lymph nodes.

pN0	No regional lymph node metastasis
pN1	Metastasis in single ipsilateral node ≤3 cm
pN2	Metastasis in: (a) Single ipsilateral node >3 cm but ≤6 cm (b) Ipsilateral multiple nodes ≤6 cm (c) Bilateral, contralateral nodes ≤6 cm
pN3	Metastasis in lymph node >6 cm

Extracapsular lymph node spread is an adverse prognostic indicator with an increased risk of local recurrence and distant metastasis.

14.7 Excision Margins

Distances (mm) to the tracheal limit, aryepiglottic fold and pre-laryngeal anterior fascia of infiltrating carcinoma and any mucosal dysplasia or carcinoma in situ. Tumour or mucosal dysplasia at or near (<5 mm) a margin indicates a *greater likelihood of local recurrence* and requires consideration of adjuvant therapy. Intraoperative frozen section assessment of surgical margins may be required.

14.8 Other Pathology

Laryngeal carcinoma: predominantly (>95 %) in males who smoke and are 50–60 years of age. Smokers and heavy voice users can develop keratosis with hoarseness and thickened white cords on laryngoscopy. A proportion may be associated with dysplasia and progression to carcinoma in situ, and eventually over a period of years infiltrative squamous cell carcinoma. These premalignant changes can be treated by *local excision*, *laser* or *irradiation*. Carcinoma in situ may be leukoplakic, erythroplakic or inapparent and biopsy is necessary.

Radionecrosis: post-radiotherapy laryngeal dysfunction due to confluent necrosis which may lead to local airway obstruction ("crippled larynx") and necessitate laryngectomy.

Concurrent carcinoma bronchus/oropharynx: 10–15 % of cases. Can become apparent on CT staging scan of the primary laryngeal cancer and may require upper aerodigestive tract endoscopy and biopsy.

Verrucous squamous cell carcinoma: has to be distinguished from benign squamous epithelial papilloma (viral or non-viral) and hyperplasia by its pushing deep margin. It can also co-exist with squamous cell carcinoma of usual type. Beware granular cell tumour with overlying pseudoepitheliomatous hyperplasia – the granular cells (Schwann cell origin) are S100 protein positive.

Juvenile laryngeal papillomatosis: multiple HPV related squamous cell papillomas of the upper respiratory tract and a rare cause of squamous cell carcinoma, usually after erroneous application of radiotherapy. These papillomata often require *repeated endoscopic laser or microdebrider debulking* to avoid airway obstruction. A minority persist and can spread to trachea and bronchi.

Prognosis

Prognosis relates to tumour site, *stage and histological grade*. Early (pT1, pT2) glottic and supraglottic carcinomas may be treated by voice sparing *local excision*, *laser* or *radiotherapy*. *Partial laryngectomy* (supraglottic or vertical hemilaryngectomy) may be carried out for small

volume T2 or T3 cancers. Advanced (T3/T4) carcinoma, infraglottic and transglottic tumours and cancers refractory to radiotherapy usually necessitate *laryngectomy supplemented by radiotherapy*.

Site-related 5 year survival:

Glottic	80 %
Supraglottic	65 %
Transglottic	50 %
Subglottic	40 %

Stage-related 5 year survival:

Glottic	I	90 %
	II	85 %
	III	60 %
	IV	<5 %

Most glottic carcinomas are well to moderately differentiated while non-glottic carcinomas are more frequently moderately to poorly differentiated.

14.9 Other Malignancy

Malignant lymphoma/leukaemia

- Primary MALToma or more commonly secondary to lymph node/systemic disease.
- Sinonasal (angiocentric) T/NK cell lymphoma.

Plasmacytoma/Myeloma

- Initially localised but generally becomes part of disseminated myeloma. Look for κ, λ light chain restriction and evidence of systemic disease (elevated ESR, serum immune paresis and monoclonal gammopathy, Bence-Jones proteinuria, radiological lytic bone lesions).

Sarcoma, Particularly low-Grade Chondrosarcoma and Rhabdomyosarcoma (Embryonal – Childhood), Occasionally Synovial Sarcoma, Angiosarcoma, Liposarcoma, Fibrosarcoma

Malignant Melanoma

- Primary or secondary (commoner). S100, HMB-45, melan-A positive.
- *Aggressive* (*20% 5 year survival*) and recognised as such in TNM7 by designation as moderately advanced (pT3: mucosal) or very advanced (pT4: beyond mucosa) disease.

Kaposi's Sarcoma

- HIV.

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