Laryngeal cancer: an overview

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The authors outline the clinical features of laryngeal cancer, explain how a diagnosis is reached and describe the implications of the various treatment modalities.

Laryngeal cancer is uncommon, with 2300 new cases diagnosed in the UK in 2009.[1] It is far more common in males, with an incidence of 5.3 per 100 000 population, compared to 1.0 per 100 000 in females; it caused 685 male and 164 female deaths in the UK in 2008.[1] Almost all cases of laryngeal cancer arise in the squamous epithelium. Tumours may arise above, below or at the level of the vocal folds and are described as supraglottic, subglottic or glottic tumours, respectively (Figure 1).

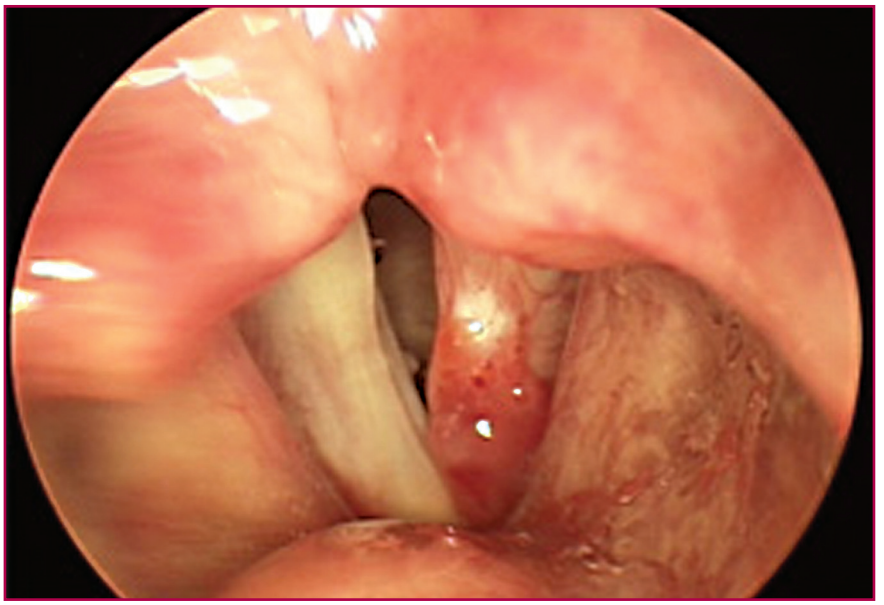

Figure 1. Right-sided glottis tumour as seen via flexible laryngoscopy. (Image courtesy of Lucian Sulica, MD, voicemedicine.com)

RISK FACTORS

Lifestyle choices are among the most important risk factors for developing laryngeal cancer. Smoking tobacco is the overwhelming risk factor, with an odds ratio of over 17 for the development of laryngeal cancer between smokers and non-smokers; the risk increases with the number of years as a smoker.[2]

Excess alcohol consumption is also significant, and the combined influence of tobacco and alcohol may account for up to 90 per cent of all laryngeal cancers.[3] Chewed tobacco or betel nut is also associated with an increased risk.

Investigators have recently reported that smokers with polymorphisms of a gene encoding the cytochrome P450 enzyme have a significantly increased risk of developing laryngeal cancer compared with smokers without the polymorphism, suggesting there may be a genetic basis to a predisposition to the effect of tobacco smoke.[4]

Quitting smoking has been demonstrated to reduce risk, although the number of smoke-free years required to have a significant effect has been suggested to range from between 6 and 20.[1]

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BOX 1. Risk factors for laryngeal cancer

- Smoking or chewing tobacco
- Drinking excess alcohol
- Chewing betel nut
- Genetic predisposition
- Age
- Previous history or family history of head and neck cancer
- Diet poor in fruit and vegetables and high in red or processed meat
- Gastro-oesophageal reflux disease
- *Helicobacter pylori* infection
- Human papillomavirus type 16 infection
- HIV infection

Risk factors for laryngeal cancer are summarised in Box 1.

CLINICAL FEATURES

The symptoms of laryngeal cancer depend on the site of the originating lesion. Glottic tumours often present with hoarseness, although most patients presenting with this in general practice are unlikely to have laryngeal cancer. Even small glottic tumours will have a marked effect on voice as a result of interruption of the normal vibratory characteristics of the vocal cords.[5] Supra- or subglottic tumours affect the voice when they have spread to the vocal cords and normally present with hoarseness later; they are therefore commonly associated with poor prognosis if presenting with hoarseness alone.

The symptoms of laryngeal cancer include dysphagia, odynophagia, otalgia, stridor, dyspnoea and haemoptysis. Therefore anyone presenting with ongoing otalgia and no symptoms of ear disease should have their larynx visualised for potential malignancy. Tumours can also present with metastatic cervical lymphadenopathy without laryngeal symptoms; this is especially common for supraglottic lesions because of the rich lymphatic supply of the larynx. In contrast, however, glottic lesions metastasise late as the vocal cords themselves are poorly supplied by lymphatics. Therefore patients presenting with ongoing lymphadenopathy in the presence of head and neck oncological risk factors should be referred early, even in the absence of overt laryngeal symptoms.

CLINICAL EXAMINATION

All patients presenting with laryngeal symptoms or those associated with laryngeal cancer should undergo a detailed head and neck examination. Within a primary care setting this will involve oral examination, looking specifically for tumours within the oral cavity, poor dental hygiene, which can be associated with head and neck malignancy, and any signs of active infection within the mouth or pharynx (*ie* tonsillitis) that could account for the presenting symptoms.

Following this, palpation of the neck should be undertaken, noting previous scars (*eg* thyroid surgery, which could account for hoarseness), lymphadenopathy (which could result from infection or metastasis), tenderness or any other symptoms or signs confirming or excluding the possibility of laryngeal cancer. Flexible laryngoscopy is unlikely to be available in primary care; however, indirect mirror laryngoscopy, if available, may give clues as to the likely diagnosis. It should be noted that indirect laryngoscopy does not adequately visualise the hypopharynx and results can depend on the tolerance of the patient to suppress a gag reflex. Therefore, if this examination is normal and the patient still exhibits symptoms, referral should be undertaken according to the two-week rule (Box 2).[6]

INVESTIGATION

Detailed investigations in those presenting with a history of a hoarse voice persisting for more than three weeks are not advised to be undertaken within primary care as this may delay treatment.[6] However, an urgent chest X-ray is indicated in higher-risk patients (smokers over the age of 50) as this will guide the route of referral, with chest malignancy referred to chest physicians and all other causes of hoarseness seen by ear, nose and throat (ENT) surgeons.

Upon review by specialist ENT services, flexible laryngoscopy will be undertaken in clinic to fully examine the larynx (see Figure 1). If suspicious lesions or areas are found, radiological imaging is critical in the full evaluation of any suspected laryngeal lesion.[7] This is normally via computed tomography (CT) or magnetic resonance imaging (MRI), with CT usually being the first investigation of choice. MRI is superior to CT in assessing cartilage invasion and discriminating soft tissue structures; however, it cannot be carried out in the presence of metal foreign structures (*eg* pacemakers), is more costly and time consuming and is prone to motion artefact.

Imaging is usually followed by an examination under anaesthetic with biopsies to aid in the diagnosis and guide management. This is usually performed as a day-case procedure. If a neck mass is present, fine-needle aspiration cytology will further aid diagnosis and staging, although definitive histology via biopsy is superior.

BOX 2. NICE guidelines for urgent referral of patients with suspected laryngeal cancer[6]

- Unexplained lump in the neck, of recent onset, or a previously undiagnosed lump that has changed over a period of three to six weeks
- Unexplained persistent swelling in the parotid or submandibular gland
- Unexplained persistent sore or painful throat
- Unilateral unexplained pain in the head and neck area for more than four weeks, associated with otalgia but a normal otoscopy

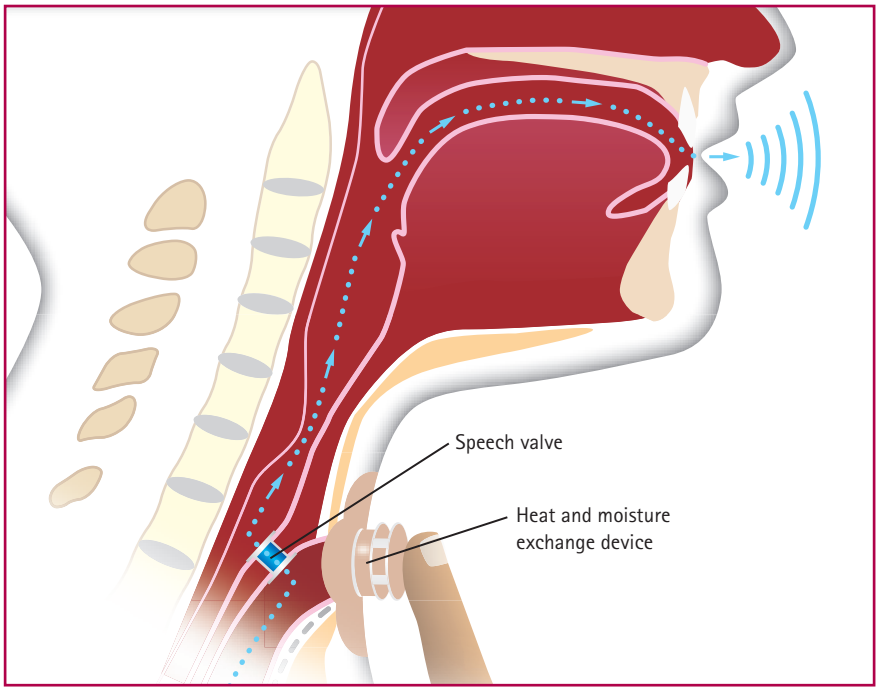

Figure 2. Voice restoration via trachea–oesophageal puncture. The blue arrow indicates the direction of air flow when the valve is occluded with the patient's finger

Occasionally, in some patients presenting with cervical lymphadenopathy alone, a primary tumour cannot be found initially and may present later in the course of the disease.

MANAGEMENT AND STAGING

Management is dependent upon the staging and location of the laryngeal tumour. Staging is based on the TNM classification, which relates to tumour size and extent, involvement of locoregional lymph nodes and the presence of distant metastasis.

Management normally consists of radiotherapy, surgery, chemotherapy or a combination of all three. All patients with overt or suspected cancer are discussed within a multidisciplinary team (MDT) consisting of surgeons, oncologists, radiologists, speech therapists and specialist nurses; a combined decision is made on the best treatment to offer patients based on their individual circumstances. Surgical treatment options depend on the location and staging of tumours.

Transoral laser microsurgery

This minimally invasive approach offers excellent results in early to intermediate glottic and supraglottic tumours with minimal postoperative morbidity compared with open surgery.

Partial laryngectomy

This operation involves resection of the vocal fold, thyroid cartilage and paraglottic space. It may be offered for carefully selected less advanced glottic cancers (T1–3) and may spare patients the morbidity of a total laryngectomy.

Total laryngectomy

This involves surgical removal of the entire larynx with diversion of the trachea to form an end stoma at the skin of the anterior neck. This is indicated with advanced tumours or if the patient has failed more conservative resections.

SPEECH RESTORATION

In patients undergoing total laryngectomy, the vocal cords are removed and therefore patients will be unable to speak normally; however, with the help of a speech and language therapist and the MDT, patients are usually able to regain the ability to communicate with speech.

Several approaches are available. Oesophageal speech involves the patient swallowing air, which can then be used to create vibrations of the residual upper aerodigestive tract. Patients are able to form words by moving their mouth and tongue while taking in or expelling this air. Devices such as the electrolarynx mechanically stimulate air in the residual upper aerodigestive tract and speech is formed in a similar way.

For patients able to manage more complex devices, a voice prosthesis may be suitable. This involves creating a fistula between the oesophagus and trachea (trachea-oesophageal puncture) and inserting a valve, which allows air from the lungs to be directed into the upper aerodigestive tract for speech when the tracheal stoma is occluded, while preventing aspiration of swallowed food into the trachea (Figure 2).

PROGNOSIS

Overall, 60 per cent of patients survive longer than five years and more than 50 per cent survive ten years following a diagnosis of laryngeal cancer.[1] Glottic cancers have the best prognosis as they present early (*ie* hoarseness) and metastasise late because of poor lymphatic supply.

Increase in the T (tumour) stage is associated with a poorer prognosis; however, the nodal stage is more predictive of survival than the T stage.[8] Following treatment of laryngeal cancers there is a risk of presentation with a second primary cancer. Rates of second primaries vary, with one large study suggesting it could be in the region of 26 per cent of patients at 10 years and 47 per cent at 20 years.[9]

More recently, there has been an increase in the detection of human papillomavirus (HPV)-related head and neck tumours and in the case of oropharyngeal tumours, they

KEY POINTS

- **Laryngeal cancer is uncommon: a GP with a list of 2000 patients is likely to see one new case every 10 years**
- **Red-flag symptoms outlined should raise suspicions of laryngeal cancer, especially in male patients who smoke or are heavy drinkers**
- **Initial investigation in primary care should be limited to clinical examination and urgent chest X-ray to exclude a lung lesion, followed by prompt referral to ENT**
- **Early diagnosis improves outcomes and survival is good, particularly for early tumours**
- **Patients treated for laryngeal cancer benefit from excellent multidisciplinary support in the community and hospital setting**

exhibit significantly improved survival rates. Recently, investigators have found that men were significantly more likely than women to have HPV-associated laryngeal tumours in a study of 79 patients; however, they were unable to demonstrate an associated survival benefit in this group, although the numbers were small.[10]

Because of its location, laryngeal cancer affects some of life's most basic functions, including breathing, chewing, swallowing and communicating, and therefore has a significant effect on quality of life. Patients' self-reported quality of life after treatment for laryngeal cancer is often good, although those undergoing more extensive surgery with combined chemoradiotherapy and those with more advanced tumours or nodal metastases are more likely to report worse quality of life.[11]

The patient group affected by laryngeal cancer is more than twice as likely to be from lower social class V than from classes I and II; they are often heavy users of tobacco and alcohol and are more likely to reflect some pre-existing difficulties with social integration. For this reason, patients often benefit significantly from co-ordinated community support teams, including specialist nurses and other health professions, which liaise closely with all levels of the patients' care providers.[12] These teams may also be a useful source of advice for colleagues and patients regarding specific aspects of patient care, for example stoma and speech valve care.

Declaration of interests: *none declared.*

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