Principles and management of head and neck cancer

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Abstract

Head and neck cancer is predominantly squamous cell carcinoma and affects the whole of the upper aerodigestive tract. It is traditionally associated with tobacco and alcohol use in older males. Cancer of the oropharynx has the most rapid increase in incidence at the present time due to human papillomavirus-related malignancy, with a younger age presentation in both sexes. This subtype has been termed 'a viral epidemic of cancer'. This article outlines the relevant anatomy, aetiology, presentation, examination and investigatory pathway for this group of patients including relevant national guidelines. An overview of surgical and non-surgical managements available for early and late stage tumours is given. This is supported by information about the multidisciplinary approach to these cancers which is current best practice. Potential future developments in management are discussed.

Keywords Cancer; diagnostic; head; malignancy; neck; squamous; treatment

Introduction

Head and neck cancer (HNC) refers to malignancy presenting in the anatomical area below the skull base and above the clavicles. A wide variety of malignancies are found in the head and neck, including sarcoma, lymphoma and salivary gland carcinomas. This article will concentrate on primary squamous cell carcinoma (SCC) of the upper aerodigestive tract (UADT) as it represents over 90% of primary malignancy in the head and neck.

The head and neck region is divided into six overall sites: nasal cavity, pharynx, oral cavity, oropharynx, larynx and hypopharynx (Figure 1). This area of the body is responsible for airway protection, swallowing and speech production, and malignancies can affect all of these functions.

Management of HNC can be a challenging task. Being inaccessible to simple clinical examination, it is not uncommon to have late presentation of disease. Therefore patients may present with: life-threatening airway obstruction; starvation due to near total dysphagia; torrential bleeding due to carotid invasion. Treatment can cause further difficulties due to the delicate nature of the tissues of the UADT which are difficult to replace or reconstruct once damaged by the disease or the treatment.

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Background

HNC of all sites and types has a prevalence of 9.9 cases per 100,000 and incidence of 8.3 new cases per 100,000 annually. The incidence of laryngeal SCC steadily fell until 1990 at which point it levelled out. The incidence of oropharyngeal SCC has been on the rise during the past decade, with a 51% increase between 1989 and 2006 in the UK.[1] Human papillomavirus (HPV) associated with orogenital sex is widely believed to be responsible for part of this increase.[2]

The emergence of HPV-related oropharyngeal carcinoma resulted in changing demographics in the head and neck cancers. Previously a typical head and neck cancer patient would have been a male in his 50s with a significant history of tobacco and alcohol use. Whilst this remains true for laryngeal cancer, there has been a sharp rise in the incidence of oropharyngeal malignancies and over 25% of cases are now diagnosed in the under-55 age group.[3]

Management of head and neck cancer is a complex process with specialties such as otolaryngology, oromaxillofacial surgery (OMFS), plastic surgery and oncology working together. Along with radiology, pathology, specialist nurses, speech and language therapy, dietetics and restorative dentistry, clinical psychology these specialties form the multidisciplinary team (MDT) which is a key organization for optimum management of all HNC patients.

The ideal composition of a head and neck MDT was described in *Guidance on Cancer Services: Improving Outcomes in Head and Neck Cancer*. The Manual, which was published in 2006,[4] was updated in May 2012.[5] The key recommendations are that a head and neck MDT should work in a cancer centre serving a population of greater than a million, and manage at least 100 new SCC cases of the UADT per year. In 2011, a consensus guideline on the management of head and neck cancer was published by ENT UK and professional bodies for other clinical disciplines.

Aetiology

Multistep carcinogenesis

As with other malignancies, head and neck cancers follow a multistep model of carcinogenesis. In order for a normal cell to evolve into a malignant cell, it must go through genetic alteration of multiple independent genes. The genes that are altered are almost invariably either proto-oncogenes, tumour suppressor genes, or both.[6] The current evidence indicates that signal pathways involving p53 and Rb, both tumour suppressor proteins, are among the commonest molecular mechanisms through which head and neck SCC is manifested.[7] There may be premalignant changes such as various grades of dysplasia and carcinoma in-situ. External carcinogens which potentiate HNC include tobacco, ethanol alcohol and viruses (Epstein–Barr virus and HPV).

Tobacco and alcohol

Over 90% of patients have a history of smoking. The relative risk (RR) of developing laryngeal cancer for a smoker of up to 10 cigarettes per day is 4.4, this goes up to 34.4 if smoking 40 or more per day. Stopping smoking leads to a reduction in the relative risk, however heavy smokers retain a threefold lifelong

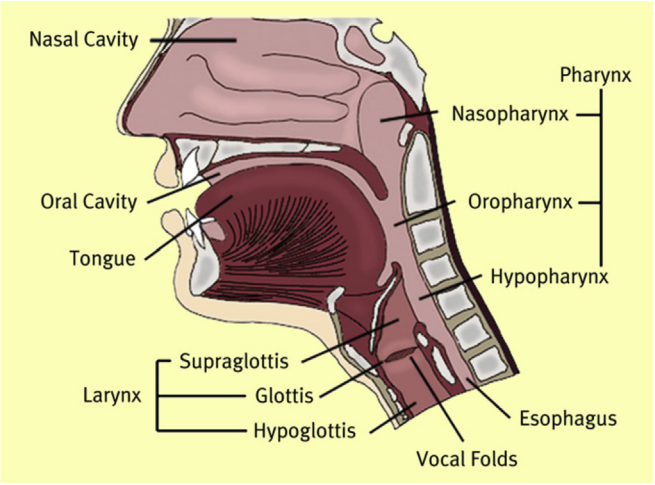

Figure 1 Anatomical subsites of the head and neck. (From http://www.headandneckoncology.org).

risk compared to non-smokers even after 10 years of smoking cessation.[8]

Alcohol potentiates the carcinogenesis of tobacco and may be an independent risk factor in some subsites. The RR from their combined use is 50% more than expected from a purely additive effect.[4] Grain alcohol (spirits and beer) has a more significant effect than wine. A moderate amount of wine intake (7–21 units per week) appears in one study to have a mildly protective effect (RR 0.5). The RR of excess alcohol intake (>21 units per week) was notably higher for grain alcohol (5.2) than for wine drinkers (1.7).

Social deprivation

Social deprivation has a complex relationship with HNC. National audit data have demonstrated a higher number of laryngeal and hypopharyngeal cancers in areas with relative social deprivation. For laryngeal cancer, the most deprived have the greatest incidence, being 20% above the national average for some networks (especially North of England). However these risks are multifactorial and also represent higher uses of tobacco, alcohol and drugs, poor diet, little or no exercise,[5] poorer education and poor use of the health services.[9] This is an area for further research.

Inhaled carcinogens

Nickel and chromate refinery workers have an increased incidence of laryngeal SCC, whereas woodworkers are at a higher risk of developing adenocarcinoma of the sinonasal tract due to wood dust.[7]

Human papillomavirus (HPV)

HPV serotypes 16 and 18 are most commonly linked to head and neck carcinogenesis via oncoproteins E6 and E7. HPV infection is commonly found in tonsil cancer (74%), as well as larynx, tongue and nasopharynx (20–30%). HPV-positive tonsil cancers may to be found in younger, non-smoking, and non-drinking patients.[7] Possibly due to the different molecular pathogenesis, HPV-positive tonsil cancers show a better prognosis with a hazard ratio of death from cancer of 0.77 compared with HPV-negative tumours.

Epstein–Barr virus (EBV)

EBV is associated with endemic type nasopharyngeal malignancy. The antibody titre to EBV antigen may have positive correlation with the stage of nasopharyngeal carcinoma. The use of specific antibodies to parts of the EBV DNA may be useful in the future for monitoring disease activity.[7,8]

Presentation and pathways

The Government White Paper entitled *The New NHS – Modern, Dependable* enshrined the idea of the 2-weeks rule whereby GPs could refer patients on a fast track for suspected cancer when certain criteria were met (Box 1). The guidelines, updated in 2011, provide a framework for identifying suspicious signs and symptoms that could indicate HNC. As oral and oropharyngeal malignancies can be discovered by dental examinations, much work has been done to involve dentists in the recognition of suspicious signs requiring onward referral. As for all cancers the 'clock starts' at the day of referral, with a 31-day target for completion of investigations and a 62-day target for starting treatment.

There has been much discussion about whether the 2-weeks rule improves patient care and this has been investigated by several studies looking at whether patients were more accurately diagnosed when these criteria were applied. One study[10] of 1079 HNC patients found most patients were diagnosed by the 'routine' referral route and that 2-weeks' wait referral did not lead to earlier stage referral. It noted that only 78% of the referrals actually conformed to the guidelines and that the referrals following the guidelines were better at identifying cancers than those not following guidelines. It is therefore essential that as long as this pathway continues, there is feedback to primary care when the guidelines are not followed.

Primary care 2-weeks' wait criteria for head and neck cancer urgent referral

Refer urgently patients with:

- an unexplained lump in the neck, of recent onset, or a previously undiagnosed lump that has changed over a period of 3–6 weeks C
- an unexplained persistent swelling in the parotid or submandibular gland D
- an unexplained persistent sore or painful throat D
- unilateral unexplained pain in the head and neck area for more than 4 weeks, associated with otalgia (earache) but a normal otoscopy D
- unexplained ulceration of the oral mucosa or mass persisting for more than 3 weeks C
- unexplained red and white patches (including suspected lichen planus) of the oral mucosa that are painful or swollen or bleeding.

For patients with persistent symptoms or signs related to the oral cavity in whom a definitive diagnosis of a benign lesion cannot be made, refer or follow up until the symptoms and signs disappear. If the symptoms and signs have not disappeared after 6 weeks, make an urgent referral. D

Box 1