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Review Article

Hypopharyngeal Carcinoma: A Review

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Abstract

Hypopharyngeal carcinoma is not a common tumour. Few risk factors increase the risk of this cancer including tobacco smoking, alcohol drinking, chewing of betal nuts. If it is diagnosed in advanced age, its outcome is fatal. So awareness of the risk factors among the persons at risk of this cancer and early diagnosis is recommended. [*Journal of Current and Advance Medical Research, 2016;3(1):26-30*]

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Introduction

Carcinomas of the posterior hypopharyngeal wall are often symmetrical and are exophytic in nature rather than infiltrative. These do not usually invade anteriorly into the larynx and their lower limit is usually just above the arytenoids cartilages[1].

Surgical Anatomy

The hypopharynx lies below and behind the base of the tongue, and behind and on each side of the larynx. It extends from the level of the hyoid bone superiorly to the lower border of the cricoid cartilage inferiorly. The three anatomical sub sites are the pyriform fossa, the postcricoid area and the posterior pharyngeal wall[1]. The pyriform fossae are situated on either side of the larynx. The lateral walls are continuous with the posterior pharyngeal wall, and the medial wall on each side contributes to the aryepiglottic fold and merges posteriorly with the postcricoid mucosa[1]. The upper part of the fossa is bounded laterally by the thyrohyoid membrane, and medially by the aryepiglottic fold. The deepest (most inferior) portion of the fossa is known as the apex. The Postcricoid area lies behind the larynx and extends from the level of arytenoid cartilages to the inferior border of the cricoid cartilage. It is continuous below with the upper end of the oesophagus. The posterior pharyngeal wall is less well defined. It begins superiorly at the level of the hyoid bone and ends inferiorly at the level of the arytenoids. It is separated from the prevertebral muscles by a fascial space[1].

The hypopharynx is lined by squamous epithelium. There is a rich network of lymphatics in the pyriform fossae but less in other subsites. The lymphatics generally drain to the deep cervical

chain. The inferior part of pyriform fossa and the postcricoid area also drain to the paratracheal nodes, the posterior pharyngeal wall is served by retropharyngeal nodes[1]. Malignant tumours of the hypopharynx are almost exclusively squamous cell carcinoma. Moderately and poorly differentiated tumours predominate, especially pyriform fossa tumours. Batsaki[2] stated that 'the great majority' of hypopharyngeal tumours are poorly differentiated[2]. In any event, the malignant tumours of the hypopharynx carry a poor prognosis, with most series reporting less than 30% 5-year survival.

Surgical Pathology

Tumours are classified according to the anatomical site of origin. It can be difficult to ascribe a site of origin when the tumour has spread to involve one or more anatomical sites. Tumours of the pyriform fossa which involve the lateral wall may invade through the thyrohyoid membrane and become palpable in the neck. This can be mistaken for a nodal metastasis rather than direct extension. However, a nodal metastasis generally will not move with swallowing. Tumours of the medial wall may invade the aryepiglottic fold and enter the paraglottic space. This will lead to vocal cord fixation. Vocal cord paralysis will also occur if either the recurrent laryngeal nerve or the cricoarytenoid joint is invaded. This is more likely with postcricoid carcinoma than with pyriform fossa tumours[1].

Course of Metastasis

Hypopharyngeal tumours may metastasize early to the cervical nodes. This is most likely in pyriform fossa lesions and least likely in postcricoid tumours[1]. The most common tumour is that of the pyriform fossa, which forms between half and two-thirds of the total. There is no doubt that tumours on the posterior wall of the hypopharynx are the least common tumour, forming approximately 10.0% of all these tumours. Postcricoid tumours make up the remaining 40.0% or so and almost all carcinomas of the hypopharynx are squamous cell type[3]. Approximately two-thirds to three quarters of these patients have palpable neck nodes metastasis at presentation which usually affects the upper and mid-deep cervical groups (levels II-IV) and 5.0% will have bilateral enlarged lymph glands at presentation[3]. Tumours arising laterally extend through the thyroid cartilage and through the thyrohyoid membrane to produce a palpable mass in the neck, should be differentiated from a separate lymph node metastasis by its movement on deglutition. When such tumour spread occurs, invasion in this direction will involve the carotid sheath and the thyroid gland in about 25.0% of cases[3]. Any large tumour in the pyriform fossa can extend superiorly across the pharyngo-epiglottic ligament, into the tongue base, often infiltrating beneath the mucosa[3]. Tumours of the postcricoid space are the next most common hypopharyngeal tumour. When first seen, they are seldom confined to the postcricoid space and extend down the cervical oesophagus to some degree.

Table 1: Incidence of Lymph Node Metastases at Presentation[4,5]

Sites	N_o (%)	$N_{1/2/3}$(%)
Pyriform fossa	35	65
Postcricoid area	70	30
Posterior pharyngeal wall	60	40
Overall	55	45

About 20.0% of patients will develop an involved lymph node in the mediastinum involving the paratracheal nodal chain. Extension can also readily occur in an anterior direction to involve the partition wall between the oesophagus and the trachea, and laterally to involve the thyroid gland[3]. About 10.0% of patients with a postcricoid carcinoma have an immobile vocal cord. The cause of this include invasion of the tumour outside the pharynx into the tracheo-oesophageal groove to involve the recurrent laryngeal nerve, invasion of the cricoarytenoid joint and, very rarely, extension of the tumour into the larynx itself[3]. As a general rule, 75.0% of patients with primary hypopharyngeal tumours will have regional nodal metastases at some time during the course of their disease[3]. Bilateral nodal metastases may occur, especially in tumours which cross the midline; the rich lymphatic network also crosses the midline, so late contralateral nodal metastatic recurrences are to be expected[1]. Many patients with clinically negative nodes will be found to have occult metastases. Distant metastases commonly lung, liver and bone usually occur late; generally only those patients who attain loco regional control live long enough for them to become symptomatic[1].

Epidemiology[1]

Post-cricoid carcinoma is the only cancer in bucco-pharyngeal region more common in women than men, and with wide geographical variation in its frequency relative to other hypopharyngeal sites. Post-cricoid cancer forms up to 50.0% of hypopharyngeal cancers in the UK and Canada; however, it is uncommon in North America and

Australia[6]. Age specific incidence rates for pharyngeal cancer reveal an increased risk of developing the disease with increasing age, for both men and women. Even though the incidence rate is greater in people aged over 70 years, the number of people in this age group in the general population is low[4].

Risk Factors

Blot et al[7] found that tobacco smoking and alcohol drinking separately increase the risk of oral and pharyngeal cancer. They found that approximately three-fourth of all oral and pharyngeal cancer s in the study areas, and probably in the United States, are caused by smoking and drinking, with most of the cancers due to heavy consumption. Smoking and drinking combined seem to have a multiplicative effect[8-9]. Wolfensberger et al[10] described on the data of 636 patients with squamous cell carcinoma of the oral cavity (174 patients), oropharynx (177), hypopharynx (97) and larynx (188). Among the patients male were 87.0%, and 90.0% were aged between 40 to 80 years. Of them 85.0% were smokers and consumed alcohol regularly[10]. Laforest et al[11] found a possible association between exposure to formaldehyde and hypopharyngeal cancer with a dose response pattern for probability of exposure. An increased risk of hypopharyngeal cancer, although not significant, was found for exposure to formaldehyde. There was a clear dose response pattern with the probability of exposure (trend test $p>0.005$). Exposure to coal dust was associated with a significantly increased risk of hypopharyngeal cancer, and the risk increased with cumulative level and probability of exposure[11]. Several studies suggest that some dietary constituents could influence laryngeal and pharyngeal tumours[12]. A major dietary risk factor, iron deficiency, has been reported to be associated with postcricoid carcinoma, especially in patients with Plummer-Vinson Syndrome[13]. Ahlbom[14] and Jacobson[15] subsequently analyzed a large number of hypopharyngeal and tongue cancers there and reported a 90.0% incidence of sideropenia in the woman involved. Kean et al[16] observed that the incidence of both Plummer-Vinson syndrome and hypopharyngeal cancer in Sweden has decreased with improvement in nutrition and a better health service. Rahman[17] found smoking tobacco and chewing of betel nuts and tobacco leaves have got relation in the causation of pharyngeal malignancy. Lower standard of living, low income, overcrowding and poor orodental hygiene are risk factors in the development of pharyngeal malignancy, possibly by lowering the level of body immunity or due to chronic irritation. Spicy and hot foods contribute to the development of pharyngeal malignancy.

Clinical Features

Patients with hypopharyngeal carcinoma usually present with dysphagia, pain or discomfort on swallowing, or a neck mass.

Symptoms which may reflect the presence of a Tumour of the Hypopharynx[1,6]

- Pain usually lateralized, often radiating to, or most noticeable in the ipsilateral ear.
- Dysphagia usually constant, and progressive. If food 'sticks' on swallowing this must be viewed with extreme suspicion.
- Haemoptysis this is an unusual, but important symptom which may appear particularly with pyriform fossa tumours.
- Hoarseness in association with dysphagia and/or referred otalgia, this suggests extension to the larynx.
- Neck mass always should be regarded as a possible nodal metastasis in adults.
- Weight loss should be asked about, as it suggests serious disease in the absence of an attempt to lose weight.

Staging

The staging classification is shown in below.

Treatment Policy[3]

Approximately 25% of patients with hypopharyngeal carcinoma are not treatable at presentation. The most important causes of untreatability include advanced age, poor general condition, local tumour inoperability and extensive neck disease. Advanced age and poor general condition are difficult to define. Those patients over the age of 75 years or those with some generalized disease that has rendered them incapable of working or running a household (low performance status) should not be offered surgery, both because of the poor chances of long term survival. Tumours of the pyriform fossa which extend in to the tongue base are rarely cured by surgery. A post-cricoid tumour which is fixed to the pre vertebral fascia is usually inoperable.

Table 2: Overall staging of hypopharyngeal tumours (UICC 1997/AJC)

T	Primary tumour.
Tx	Primary tumour cannot be assessed.
To	No evidence of primary tumour.
Tis	Carcinoma in situ.
T 1*	Tumour limited to one subsite of hypopharynx and 2cm or less in greatest diameter.
T 2*	Tumour invades more than one subsite of hypopharynx, or an adjacent site, or measures more than 2cm but not more than 4 cm in greatest dimension**,** without fixation of hemilarynx.
T 3*	Tumour measures more than 4 cm in greatest dimension, or with fixation of hemilarynx.
T 4*	Tumour invades adjacent structures, e.g. thyroid/cricoid cartilage, carotid artery, soft tissues of neck, prevertebral fascia/muscles, thyroid and/or oesophagus.
N X	Regional nodes cannot be assessed.
N 0	No regional lymph node metastasis.
N 1	Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension.
N2	Metastases in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension.
N 2a	Metastases in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension.
N 2b	Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension.
N 2c	Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension.
N 3	Metastasis in a lymph node more than 6 cm in greatest dimension.

UICC (1997) *New inclusion

A more common event indicating inoperability is a vocal cord paralysis due to extension of the tumour outside the oesophagus to invade the recurrent laryngeal nerve in the tracheo-oesophageal groove. Patients with extensive nodal disease are rarely cured. This is because not only is nodal disease significant because of the size and number of the nodes involved, but also prognosis is affected by their position. Extension of disease into the tracheo-oesophageal groove and the upper mediastinum represents an ominous sign.

Table 3: Prognostic Factors in Hypopharyngeal Carcinoma[3]

1.	Tumour size (less or more than 5cm)
2.	Tumour site (Pyriform fossa and Posterior pharyngeal wall tumours do best)
3.	Vocal cord paresis
4.	Presence or absence of lymph node metastases
5.	Size and number of lymph nodes involved
6.	Presence or absence of distant metastases
7.	Presence of perineural spread

It used to be thought that bilateral neck nodes indicated incurability but more recent studies have shown that this not true if the nodes are small (i.e. less than 3 cm) in diameter on both sides. Bilateral nodes which are larger than this, and in particular when they are fixed on one side, usually indicate incurability[3]. Patients who are deemed surgically untreatable on the basis that the disease is unresectable may be considered for radiotherapy with palliative intent. Chemotherapy has no established role. Patients who are deemed unsuitable for surgery on the grounds of extreme old age or poor general condition may also be considered for radiotherapy.

Conclusion

Long term results for treatment are by surgery or by radiotherapy and are not good. Results from famed institutions quoted overall 5 year survival figures of approximately 35% for hypopharyngeal tumours with majority of tumours being treated with surgery with or without post operative radiotherapy.

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