INTRODUCTION

In spite of advancements in surgical intervention and chemoradiotherapy (CRT) for head and neck cancer, the prognosis for advanced-stage squamous cell carcinoma of the hypopharynx (HPSSC) remains poor. The relatively poor prognosis and frequently advanced stage at diagnosis can be attributed to the relative lack of symptoms from early-stage disease in this region. Apart from that, these tumours are locally aggressive, with a propensity for submucosal spread, invasion into adjacent structures, and metastasis due to abundant lymphatic drainage.

KEYWORDS: chemoradiotherapy (CRT), hypopharynx (HPSSC), submucosal spread.

ABSTRACT

In spite of advancements in surgical intervention and chemoradiotherapy (CRT) for head and neck cancer, the prognosis for advanced-stage squamous cell carcinoma of the hypopharynx (HPSSC) remains poor. While HPSSC represents only 3% to 7% of head and neck cancers,[1,2] approximately 75% to 80% are advanced (stage III or IV) at diagnosis,[3,4] leading to significant therapeutic challenges. Cervical metastases are present in 60% to 80% of patients and signify more advanced disease with a relatively poor prognosis.[5-9] Squamous cell carcinoma accounts for 95% of hypopharyngeal pathology. Reported 5-year survival rates for stage III and IV HPSSC are 36% and 24% respectively.[10] The relatively poor prognosis and frequently advanced stage at diagnosis can be attributed to the relative lack of symptoms from early-stage disease in this region. Apart from that, these tumours are locally aggressive, with a propensity for submucosal spread, invasion into adjacent structures, and metastasis due to abundant lymphatic drainage.[11,12]

Recent advances in reconstruction techniques and perioperative care have allowed resection of advanced disease with single-stage reconstruction of a functional alimentary tract. However, overall survival rates remain poor and largely unaffected because of a shift in the pattern of failure from local to distant disease and the development of second primary tumours.

CLINICAL BEHAVIOUR

The hypopharynx may be described as the region of pharynx, which begins at level of hyoid bone above and extends to the lower border of cricoid cartilage below. There are three anatomic subsites within the hypopharynx – the paired pyriform sinuses, the postcricoid area and the posterior hypopharyngeal wall. The pyriform sinus is the most commonly involved site, representing greater than 60% of all cases, while the postcricoid region is the least commonly involved, accounting for less than 5% of cases.[13] Isolated early-stage lesions of the pharyngeal wall or pyriform sinus have the best prognosis and long-term survival. However, they comprise less than 20% of hypopharyngeal carcinomas.[5,9,14-16]

The cancer of hypopharynx is unique in demonstrating a high propensity for extensive submucosal spread. The true extent of disease may be initially underestimated because of submucosal extension and the presence of skip lesions.[5] Ho et al conducted whole organ serial sectioning studies[17] and found that submucosal tumour extension was present in 60% of specimens. In one third of patients, submucosal spread was not detectable on gross examination, appearing histologically as tongues and islands of tumour infiltration beneath an intact mucosa. It is pertinent to mention that the limits of submucosal extension in this series were 10 mm superiorly to oropharynx, 25 mm medially, 20 mm laterally and 20 mm inferiorly towards the oesophagus. The incidence and extent of submucosal spread were higher in patients who had undergone previous radiation therapy, with macroscopically undetectable submucosal spread in 82% of patients.[17] These data provide useful guidelines for treatment planning.
The hypopharynx is drained by an extensive lymphatic network. The lymphatic drainage proceeds first to the jugular lymphatics and then to the tracheoesophageal nodes, lateral pharyngeal and retropharyngeal nodes, and the parapharyngeal space. Tumours that involve the posterior hypopharyngeal wall and the medial wall of the pyriform sinus have bilateral nodal drainage and have a high incidence of involvement of contralateral neck. Between 60% and 75% of patients will have clinically involved neck nodes (node positive – N+) at presentation, while more than one third of patients without clinical evidence of nodal disease harbour occult metastasis. In patients with N+ disease, levels II (72%-75%), III (55%-72%), and IV (21%-45%) are most often affected; levels I (1%-10%) and V (11%-15%) are less commonly affected. Contralateral occult metastases are present in 37% of patients with N+ disease. In patients with clinical N0 tumours, 36% harbour occult nodal metastasis in the ipsilateral neck and 27% have occult disease in the contralateral neck.

In 20% of patients with hypopharyngeal cancer, metastasis may involve the retropharyngeal lymph nodes. The true incidence of retropharyngeal lymph nodes is probably not known, as dissection of this level is not routinely performed. The incidence of clinically involved retropharyngeal nodes by imaging criteria in patients with hypopharyngeal cancer is 5%. Imaging studies may underestimate the incidence of retropharyngeal involvement, based on the small size (< 1.5 cm) of nodes in this location, thus possibly missing occult metastasis. Amatsu et al presented a histologic study which showed that routinely dissected retropharyngeal nodes exhibited metastasis in 20% of patients with hypopharyngeal carcinoma. The highest incidence of retropharyngeal metastasis was noted in patients with involvement of posterior wall of hypopharynx (57%) or the cervical esophagus (50%). Retropharyngeal nodes were positive for occult metastasis in 15% of patients with N0 disease.

Lymphogenic metastasis to the thyroid gland and parapharyngeal nodes occur in 30% of patients who have hypopharyngeal tumours. A 20% incidence of occult nodal metastasis to ipsilateral parapharyngeal nodes was reported in patients with postcricoid lesions and tumours that involve the apex of pyriform fossa, staged as N0. Occult metastasis may be present in lymph nodes in the parapharyngeal space, which has been described as a site of recurrent disease in 5% of patients when untreated. As an inference, all these data taken together suggest that both sides of the neck including retropharyngeal, tracheoesophageal and parapharyngeal nodes must be included in treatment planning.

In 6% of patients, distant metastasis are present at initial presentation. The most common sites of involvement are lungs, bone and liver. 12% to 32% of patients develop clinically apparent distant metastasis during the course of treatment. The incidence is higher in patients who have stage IV disease, advanced stage neck disease (N2 or N3), involvement of retropharyngeal nodes, extracapsular spread and lymphovascular invasion. Most mortality in the first 2 years following diagnosis is caused by locoregional recurrence, while after 2 years, distant metastatic disease is responsible for a greater proportion of treatment failures.

Most patients with cancer of hypopharynx present with advanced stage disease. Hoffman et al (1997) presented a review of 2939 cases of hypopharyngeal cancer, which showed that 9% of patients had stage I disease, 11% had stage II disease, 22% had stage III disease, while most (56%) had stage IV disease at presentation. The 5-year disease-specific survival rates were 63% for stage I, 58% for stage II, 42% for stage III and 22% for stage IV disease.

7% of patients present with second primary tumours at the time of initial diagnosis. Between 10% and 17% of patients will subsequently develop a second primary tumour, which is a significant cause of mortality in patients who survive for more than 2 years after the initial diagnosis of hypopharyngeal cancer. A history of previous head and neck cancer is present in 16% to 23% of patients, and prior treatment, such as radiation therapy, may significantly limit the treatment options available to the patient.

FACTORS AFFECTING PROGNOSIS
As stated previously, in spite of recent advancements, the prognosis for advanced-stage hypopharyngeal cancer remains poor. Milisavljevic et al (2009) presented a retrospective review of 89 patients of hypopharyngeal cancer, treated over a period between 1995 and 2004. The sites of origin were pyriform sinus in 75 patients, postcricoid in 8, posterior pharyngeal wall in 3 and superior hypopharynx in 3 patients. Laryngeal preservation surgery was achieved in 11.2% of patients, while 88.8% had laryngectomy with partial or total pharyngectomy.

The authors reported that TNM stage was a highly significant parameter of outcome. The 5-year survival was 100% for stage I, 66.6% for stage II, 53.9% for stage III and 33.3% for stage IV. The second most important parameter of outcome was localization of disease. Retrocricoid carcinoma resulted in very poor survival rate (12.5%), high residual disease, positive lymph node metastasis and formation of pharyngocutaneous fistula.

POSTOPERATIVE QUALITY OF LIFE
Dysphagia can be a consequence of total laryngectomy (TL) or pharyngolaryngectomy (PL). Even in the absence of symptoms, it could directly or indirectly compromise the quality of life. Queija et al (2009) conducted a study to evaluate the characteristics of swallowing after total laryngectomy and pharyngolaryngectomy with pharyngeal T closure,
correlating them with the Quality of Life in Swallowing Disorders questionnaire. A prospective evaluation was performed in 28 patients, 15 undergoing total laryngectomy and thirteen undergoing pharyngolaryngectomy.

Swallowing was evaluated through videofluoroscopy, regarding the preparatory, oral and pharyngeal phases of swallowing. Quality of life related to swallowing questionnaire was employed to measure quality of life. The dysphagia score was 46.7% in patients of TL and 61.5% in patients of PL. The questionnaire indicated an overall good quality of life in almost all scales.

CONFLICT OF INTERESTS
The author declares that there was no conflict of interests that could influence this work.

FUNDING ACKNOWLEDGEMENTS
The author declares that there was no financial aid obtained from any source for the preparation of this manuscript.

REFERENCES
23. Morrissey DD, Talbot M, Cohen JI, Wax MK, Andersen PE. Accuracy of computed tomography in determining the presence or absence of metastatic

www.wjpmr.com


