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Original article

Epidemiology, prognosis and treatment of simultaneous squamous cell carcinomas of the oral cavity and hypopharynx

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ABSTRACT

Objective: The study was designed to assess the prevalence, management and survival of patients with simultaneous squamous cell carcinomas of the oral cavity and hypopharynx (OC/HP).
Material and methods: A multicenter, retrospective study (2 university hospitals) was conducted between 2003 and 2007 on a series of 96 patients with simultaneous squamous cell cancers of the OC/HP.
Results: A total of 88 men and 8 women were included in the study: 81 patients presented double sites, 14 presented triple sites and one presented quadruple sites. The tumour sites most frequently observed were: hypopharynx in 61% of cases (involving the pyriform sinus in 42% of cases) and the oropharynx in 59% of cases (involving the palatine tonsil in 30% of cases). Upper aerodigestive tract endoscopy under general anaesthesia revealed a simultaneous lesion not suspected on clinical examination in 45% of patients: the site discovered on endoscopy was hypopharyngeal in 2 out of 3 cases; the tumour was classified T1 or T2 in 95.5% of cases. Patients treated simultaneously for all sites had a better prognosis than patients in whom each tumour was treated separately. The 5-year specific survival was 34% and the 5-year overall survival was 28%.
Conclusion: The prevalence of simultaneous squamous cell carcinomas of the oral cavity and hypopharynx ranges between 1 to 7.4% in the literature and was 4.6% in the present series. A common treatment strategy for each of the patient's tumours appears to be superior to the current theoretical approach that consists of considering each tumour separately.

1. Introduction

Since the first description by Billroth in the 19th century, a large number of studies have described the phenomenon of multiple cancers. However, few studies on simultaneous cancers of the oral cavity and hypopharynx have been published in the literature, but the management of these tumours raises specific problems. This article is designed to contribute to the study of these cancers based on clinical observation of a series of 96 patients managed in head and neck surgery departments at Amiens and Lille university hospitals between January 2003 and December 2007.

2. Material and methods

The medical charts of 2096 patients with primary cancer of the oral cavity and hypopharynx (OC/HP) were retrospectively reviewed and 96 patients with simultaneous squamous cell carcinoma of the OC/HP were selected.

Inclusion criteria of these patients were:

- at least two simultaneous squamous cell carcinomas of the OC/HP;
- no previous history of cancer;
- no other simultaneous cancers other than in the OC/HP.

Paranasal sinus and nasopharyngeal tumours, due to their different epidemiology, and oesophageal and lung cancers were excluded. Data collection comprised epidemiological and histological parameters, anatomical distribution and tumour stage, and data concerning the treatment strategy and follow-up. Data collection was performed in two different centers, but by the same person. Survival was analysed according to the Kaplan–Meier method and statistical analysis was based on the log rank method and Chi^2 test. Multivariate analyses were performed according to the Cox model. A P value less than 0.05 was considered significant.

Initial staging comprised the same examinations in both centers:

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- endoscopy under general anaesthesia, including oropharyngolaryngoscopy;
- contrast-enhanced CT scan of the neck and mediastinum;
- upper GI fibroscopy and bronchoscopy.

The primary objective of the study was to determine the incidence of simultaneous OC/HP cancers. The secondary objectives were to evaluate the yield of endoscopic screening, identify patient groups at high risk of developing these simultaneous cancers, and finally analyse the management and survival of patients with multiple cancers.

The criteria used to define multiple cancers were established in 1932 by Warren and Gates [1] and were modified by Moertel [2].

These criteria are:

- each distinct tumour must be confirmed histologically;
- the possibility that one of the two tumours is a metastasis from the other tumour must be excluded;
- each tumour must be separated from the healthy mucosa by at least 1.5 cm (with no submucosal communication).

Finally, multiple cancers were classified into three groups according to their chronological order:

- simultaneous cancers are those diagnosed at the same time as the first tumour;
- synchronous cancers are those diagnosed during the six months following the diagnosis of the first tumour;
- metachronous cancers are those diagnosed more than six months after the diagnosis of the first tumour.

3. Results

The frequency of simultaneous cancers involving the OC/HP was therefore 4.6% (96/2096). This series comprised 88 men (92%) and 8 women (8%) with a mean age of 55 years (range: 40–75 years). The sex ratio was 1 female for 11 males. A history of smoking and drinking was reported by 89 patients (93%). The distribution by stage according to the UICC TNM classification was based on the stage of the most advanced tumour. This series comprised 12% of stage I, 15% of stage II, 21% of stage III, and 52% of stage IV tumours.

3.1. Anatomical distribution of simultaneous cancers

Eighty-one of these 96 patients had double tumour sites, 14 had triple tumour sites and one patient had quadruple tumour sites. The relative frequency of each anatomical site in this series of simultaneous cancers was determined on the basis of all tumours observed (Table 1).

This analysis demonstrated a very marked variability of the frequency of multiple cancers according to the tumour site (14% for the larynx and 32% and 35% for the oropharynx and hypopharynx, respectively). The larynx appeared to be underrepresented as a site of simultaneous cancers. In contrast, the oropharynx and especially the hypopharynx presented a higher risk of multifocal tumours. The pyriform sinus accounted for almost two-thirds of all hypopharyngeal tumours, while the tonsil accounted for almost one half of all oropharyngeal tumours.

3.2. Endoscopic findings

Endoscopy demonstrated a simultaneous tumour site not suspected on the initial clinical examination in 45% of patients ($n = 43$). The tumour sites discovered on endoscopy predominantly concerned the hypopharynx (64%), especially the pyriform sinus (42%).

Table 1
Distribution of tumour sites in patients with multiple cancers.

	Number of tumours for each site (208)	
Oral cavity		$n = 39$ (19%)
Floor of the mouth	23 (11%)	
Mobile tongue	9	
Oral commissure	7	
Oropharynx		$n = 67$ (32%)
Palatine tonsil	30 (14%)	
Vallecula	11	
Soft palate	13	
Base of tongue	5	
Posterior wall	5	
Glosso-epiglottic fold	1	
Junctional zone	2	
Larynx		$n = 29$ (14%)
Epiglottis	9	
Vocal cord	10	
Ventricular band	2	
Aryepiglottic fold	5	
Arytenoid	2	
Hemilarynx	1	
Hypopharynx		$n = 73$ (35%)
Pyriform sinus	49 (24%)	
Pharyngeal wall	13	
Proximal oesophagus	2	
"Three-fold" region	7	
Retrocricoid	2	

The tumours discovered at endoscopy logically corresponded to less advanced tumours (95% of Tis, T1, and T2 tumours).

3.3. Treatment

Various treatment strategies were applied to each of these 208 tumours considered separately, as summarized in Fig. 1. Patients managed by symptomatic treatment ($n = 6$) or palliative chemotherapy ($n = 3$) were classified separately (9 patients, 19 sites).

Patients were classified into three groups according to the treatment strategy:

- common treatment group: all of the patient's tumours were treated according to the same treatment strategy;
- dissociated T treatment group: each of the patient's tumours were treated in a different way;
- dissociated T/N treatment group: different treatment modalities were proposed for the patient's tumours and lymph nodes.

3.4. Follow-up

Three patients were lost to follow-up. The mean follow-up was 32 months (range: 1–89 months). Progressive disease was observed in 27 patients (29%). No synchronous cancers were observed in this series. Nine patients developed a metachronous cancer (9.7%)., 16 patients (17%) developed local recurrence, 21 patients (23%) developed metastases during follow-up and 5 patients (5.4%) developed lymph node recurrence.

3.5. Survival

Sixty-seven (72%) of the 93 patients of the series have died. Mean survival was 24 months. The five-year specific survival, i.e. the survival related to head and neck cancer was 34%, while the five-year overall survival was 28%. Survival curves were plotted according to the Kaplan–Meier method (Fig. 2). Univariate analysis of several parameters likely to influence survival was then performed using the log rank method. As expected TNM tumour stage and lymph node status had a statistically significant impact on