CLINICAL RESEARCH

HYPOPHARYNGEAL CANCER: ANALYSIS OF THE EVOLUTION AND SURGICAL RESULTS

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ABSTRACT

Objective: Hypopharyngeal carcinoma is an aggressive malignancy that usually presents at a late stage, thereby resulting in an overall poor prognosis for these patients. The aim of this study is to determine the evolution and postoperative results of patients treated in our department for hypopharyngeal cancer. Methods: We retrospectively reviewed 60 patients who had undergone surgery followed by radiation therapy between 1980-1999. Most of them were advanced stage (III-IV) and 75% patients showed regional metastases at presentation. Results: The 5-year survival rate was 38.4%. The overall incidence of distant metastases and second neoplasms was 12.5% and 10.4%. Conclusions: Hypopharyngeal cancer remains one of the most lethal ones in head and neck cancer. The poor survival rate is related primarily to advanced stage disease and particularly to lymph node metastases.

KEY WORDS: Hypopharyngeal carcinoma. Surgical treatment. Survival.
INTRODUCTION

Hypopharyngeal carcinoma is a very aggressive cancer that is generally diagnosed in advanced stages and therefore with a bad prognosis and a low survival rate. The majority of cases present a late diagnosis as the initial stages are not symptomatic or the symptoms are not well evaluated, therefore when diagnosed they are already very large tumors.

Also hypopharyngeal carcinoma has the peculiarity of extending through sub-mucosa as well as to cause other distant lesions known as “skip lesions”. These lesions are not easy to identify and therefore the tumor is not well evaluated when seen and can take the surgeon to perform inadequate resections1.

There are not effective barriers to avoid the dissemination of hypopharyngeal carcinoma to other soft tissues in the neck. They have a high rate of local and distant metastases as well as in the neck nodes, and this is quite an indicative of its aggressiveness2.

It is considered that these patients need a wide surgical excision that generally include total laryngectomy with partial pharyngectomy or a total laryngo-pharyngectomy together with reconstruction techniques followed by radiotherapy in the majority of cases.

Despite treatment, survival rate in these patients is low, between 26% and 34.6% according to revised series3-7, being the recurrence the most frequent cause of failure.

The aim of this study is to present the evolution and therapeutical results of patient that underwent surgery in our center due to carcinoma of the hypopharynx and to correlate, when possible, clinical and pathological parameters with recurrence and mortality rates.

MATERIAL AND METHODS

Retrospective analysis from 1980 to 1998. Along this period, out of a total of 1025 laryngo-pharyngeal carcinomas, 60 were localized in the hypopharynx (5.8%). Of these hypopharyngeal ones 57 (95%) involved piriform sinus and 3 (5%) the posterior pharyngeal wall.

Mean age of the study group was 56.5 years, ranging between 38-81; 59 were male and only 1 was a female.

The relation between this type of carcinoma and smoking and alcohol is very marked; 94% of patients were smokers and 65% did take large amounts of alcohol; both habits were considered to be toxic in 63% of cases.

Patients were studied according to the 1997 UICC TNM classification. The majority were advanced stages, T3 58.3% and T4 15% (table 1)

75% of patients did present palpable nodes when first examined, being the majority of them N2 (45.7%). All patients were M0.

In regards to the surgery performed on the primary tumour, the majority of cases (95%) underwent partial pharyngectomy plus total laryngectomy (phonatory in 30% of cases), 3.3% of cases underwent circular total laryngo-pharyngectomy, and one case (1.66%) a partial pharyngectomy plus sub-total laryngectomy. In those cases of total circular surgery, reconstruction was carried out in one case with a mio-cutaneous muscle flap from pectoralis major and in the other case a free micro vascular flap from jejunum.

Nearly all cases underwent cervical node surgery (91.6%), being the most frequent techniques, the homolateral radical neck dissection (38.3%) and the homolateral radical neck plus contralateral functional neck dissection (26%). Only in three N0 patients, no neck dissection was performed considering previous surgery and age.

Postoperative radiotherapy was given in 71.6% of patients. It was not administered in the rest of cases due to: 7 patients had a recurrence even before radiotherapy could be started, 2 had previous radiotherapy for a different primary in the past, in one case metastases were found and palliative treatment was decided, 3 died in the early postoperative period, 1 because of the patients advanced age and 3 pN0 (no radiotherapy was decided).

We used the statistical program SPSS 6.13 to analyse results. We worked with the Pearson’s $\chi^2$, the Fisher test and the Kaplan-Meier curves to study survival.

RESULTS

Following the pathology study of surgical samples, we found the most frequent result to be...
epidermoid carcinoma (92.5%). Regarding the differentiation degree, 43% were well differentiated, 35% moderate, 17.6% poorly differentiated and 3.9% not-differentiated carcinomas.

According to the pTN (table 2) staging the majority of them were advanced stages pT3-4 (38%-47% respectively). N0 were 20.75% of patients and N+ 79.25%, being the majority pN2 (60.4%). We found occult metastatic nodes in 33% of cases. Table 3 shows the T-pT distribution.

The pathologist reported affected margins in 18.3% of cases. We found extra-pharyngeal disease in 67.3%, being the larynx the most frequent site (44.2%), followed by the oropharynx and by both sites together. 10% had a multicentric localization.

Of the 78 neck dissections performed, 65.38% were found to be positive; of these 84.3% were homolateral and 15.6% contralateral (in these cases the homolateral was also positive). Few cases were reported to have a capsular disruption (17 cases) and peripheral invasion (12 cases). The mean number of nodes found when doing a dissection was 20.61, being the mean of colonized nodes in the positive dissections of 3.6.

We did study the 5-year evolution in our group of patients. The 5-year recurrence index was 42%, with an equal distribution in regards to T and N of 21%. The mean lapse of time between surgery and the time of recurrence was 14 months (ranging between 2 and 48). In 5 cases recurrence was obvious even before starting radiotherapy (3 in N and 2 in T).

Distant metastases were reported in 12.5% (2 in lungs, 2 in bone, 1 in brain and 1 in liver) and the incidence of a second tumour 10.4% (1 in tongue, 2 in lungs, 1 in stomach and 1 in pancreas). The mean lapse of time between surgery and the time of a second tumour to appear was 3.5 years (ranging between 1.5 and 4.5 years).

5-year survival was 38.4%. Of the patients that died, 33% did it due to a cause not related to the tumour (we consider metastases as a cause due to the tumour and a second tumour as a non related one), 1 died in the very early postoperative period, 2 due to CVA and 3 due to second tumours (stomach, pancreas and lung). The mean lapse of time between surgery and death due to a specific cause was 2.5 years (ranging between 2 months and 5 years).

We have not found statistical significant differences when relating the invasion of the margins, the recurrence and the survival. Neither has been found a relation between the extra-pharyngeal invasion and the recurrence.

We have not found statistical significant relation between different variables such as the pN and RT with the N recurrence and the survival or between pT with the T recurrence and survival, probably due to the fact that our sample is a small one.

Last of all we have also studied the mean of colonized nodes from which there is a higher incidence of N recurrence, being this of 4.3 colonized nodes (1.69 nodes more than in those patients that did not have a recurrence). We cannot talk of a significant difference probably as well due to the size of the sample.

DISCUSSION

It is very characteristic of these tumours the fact that when they are diagnosed they are already big and have extended. In our series 73.3% were stage T3 or T4 at the time of diagnosis. If we look at the T-pT distribution (table 3), we can see that approximately 39.6% of cases were probably under-staged due to the sub-mucosa extension and the skip lesions that they frequently present.

The size of the tumour and the clinical stage are considered as bad prognostic factors in relation to survival, the bigger the tumour is the
fewer are the chances of survival at 5 years. In our study, even though we have not been able to find statistically significant differences between variables such as pT with T recurrence and survival, there is probably one but we have not seen it due to the fact that our sample is a small one.

The other basic characteristic of these tumours is the high incidence of clinical adenopathies they present at the time of diagnosis. As in other studied series, in ours 75% of patients presented palpable adenopathies at diagnosis. Regarding node invasion 79.25% were pN+, being the majority pN2 (60.4%).

According to the revised bibliography⁹,¹⁰, capsular disruption seems not to have an incidence in neither survival nor recurrence and therefore it is not a prognostic factor in these tumours. Nevertheless, per-neural invasion is considered a survival prognostic factor conditioning the T and N recurrence.

There seems to be a correlation between the number of colonized nodes seen at dissection and the incidence of node recurrence¹¹, in a study carried out by Leemans and cols¹², they saw that patients with 1 or 2 positive nodes had the same incidence of recurrence that others with a higher node invasion. In our study we decided to find out the mean number of affected nodes from which the incidence of N recurrence was bigger, being this number 4.3 (1.69 nodes more that in those that did not present recurrence).

One aspect that has been widely discussed is the role that the invasion of the surgical margins has in survival. For some authors¹³ this factor was the main one when predicting survival of these patients. However, for others this has not been proved at all¹⁵,¹⁴. In our series this factor was not found to be relevant at all, maybe due to the postoperative radiotherapy or probably due to a wrong interpretation of the margins. Neither we could find a statistical significant relation between the extension of the disease outside the pharynx and the recurrence rate.

Another cause of failure in the treatment of hypopharyngeal carcinoma, even in those cases in which a good regional control has been managed, is the existence of distant metastases or second primary tumours. In our study we have seen distant metastases in 12.5% of cases (2 in lungs, 2 in bone, 1 in brain and 1 in liver) and second primary tumours in 10.4% of patients (1 in tongue, 2 in lungs, 1 in stomach and 1 in pancreas), these data are coincident with other revised studies that have proved an incidence of 5% to 17% for distant metastases and 8.9% to 16% for second primaries¹⁶-¹⁷. Incidence rate in hypopharyngeal tumours is three times bigger than that for laryngeal carcinoma and is very related to the T and N staging.

The hazards for performing a good resection of the tumour and of the nodes in order to avoid recurrence and have a high survival rate, has given way to many different treatments or combinations of them. In our department the most frequently used has been the surgical resection with a total laryngectomy plus partial pharyngectomy together with neck dissection, radical or functional according to the neck stage, and complementing this with postoperative radiotherapy. With this protocol we have managed a survival rate at 5 years of 38.4% with a recurrence rate of 42%. This combination of surgery plus radiotherapy is the most widely used and the one that manages a higher survival rate according to the literature revised which goes from 25% to 40% at 5 years⁴,⁵,¹⁸-²⁰.

Hypopharyngeal neoplasias do often require very wide resections being necessary to perform a posterior reconstruction. There are many different procedures now a days to reconstruct the digestive tract: gastric elevation²¹, jejunum micro vascular anastomoses²²-²⁴, miocutaneous flap of pectoralis major²⁵, micro vascular radial flap²⁶,²⁷; and in general the different studies show good results with any of these techniques, even though the one that has more supporters is the micro vascular anastomoses.

The use of radiotherapy as a sole treatment has been left only for tumours in the very early stages, in which it has proved to have similar results as surgery²⁸.

Recently, for advanced stages of the disease there are many essays trying to combine radiotherapy plus chemotherapy²⁹-³³. In hypopharyngeal carcinoma the results of these techniques are very good for local control of the disease, despite its toxicity, but the survival rate has not improved.

**CONCLUSIONS**

Hypopharyngeal carcinoma still is the Head and Neck malignancy with a worst prognosis. The majority of them when seen are already too large for surgical procedures with voice preservation or for primary radiotherapy, requiring generally a wide tumour and neck resections.
These patients frequently have an associated high rate of recurrences and of second primary tumours. It is important to do an extensive study in all patients diagnosed of a hypopharyngeal carcinoma including thoracic X-rays, CT of head and neck, upper tract endoscopies, and even CT of the brain and liver ECO.

Survival rate seems to be related primarily with the stage of the tumour at diagnosis and in particular with the status of cervical nodes.

REFERENCES

11.- Sasaki T, Baker H, Yeager R, McConnell D, Vetto M. Aggressive surgical management of pyriform sinus carcino-
14.- Soo K, Shah J, Gopinath K, Gerold F, Jaques D, Strong E. Analysis of prognostic variables and results after supraglottic partial laryngec-
17.- Spector JG, Sessions DG,Haughery BH, Clifford Chao KS,Simpon J, El Mofy S, Perez CA. Delayed regional metastases, distant metastases, and second primary malign-
nancies in squamous cell carcinomas of the larynx and hypopharynx. Laryngoscope 2001; 111: 1079-1087.
20.- Marks SC, Lolachi CM, Shamshas F, Robinson K, Aref A, Jacobs JR. Outcome of pyriform sinus cancer: A retrospective institutional review. Laryngo-
21.- Sasaki CT, Salzer SJ, Cahow E, Son Y, Ward B. La-
ryngopharyngeal and esophageal squamous cell carcinoma: The Yale expe-
22.- Ayyshford CA, Walsh RM, Watkinson JC. Reconstructive techniques currently used following resection of hypopha-
yngeal carcinoma. J of Laryngol Otol 1999; 113: 145-
148.
24.- Benazzo M, Ochini A, Rossi V, Aresi G, Alessiani M. Jejunum free flap in hypo-
25.- Spriano G, Pellini R, Roselli R. Pectoralis major myocuta-
26.- Díaa JJ, Pusic AL, Hidalgo DA, Cordeiro PG. Microvascular reconstruction of the hypo-
pharynx: defect classification, treatment algorithm, and functional outcome based on 165 consecutive cases. Plast Re-
constr Surg 2003; 111: 652-663.
27.- Schwager K, Hoppé F, Hagen R, Brunner FX. Free flap reconstruction for laryngeal pres-
servation after partial laryngectomy in patients extended tumors of the oro-
29.- Bensadoun RJ, Etienne MC, Dassonville O, Chauvel P, Pivot X, Marcy PY, et al. Concomitant BID. Radiothe-
31.- Magne N, Marcy PY, Chamorey E, Guardiola E, Pivot X, Schneider M, et al. Comcomitant twice-a-day radio-